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## ORGANIC FERTILIZER AS THE BASIS FOR ORGANIC AGRICULTURE IN UKRAINE

Adamenko A. (Kharkiv)

Language supervisor: Cherkashina N.I.

**Summary:** The article considers the relevance and prospects of organic fertilizers usage in the system of organic farming.

**Key words:** organic farming, biofertilizer, soil, vermicomposting, composting, anaerobic method.

**Анотація:** У статті розкрито актуальність та перспективи застосування органічних добрив у системі органічного землеробства.

**Ключові слова:** органічне землеробство, біодобрива, ґрунт, вермикомпостування, анаеробний метод, компостування.

**Аннотация:** В статье раскрыта актуальность и перспективы использования органических удобрений в системе органического земледелия.

**Ключевые слова:** органическое земледелия, биоудобрения, почва, вермикомпостирование, анаэробный метод, компостирование.

The greatest wealth of Ukraine is soils. Today, it is important not only to obtain profit from them, but also to maintain or restore their fertility. One way to restore the natural properties of soil is organic farming (OF).

Due to the following factors organic farming relevance is:

- the safest methods of production;
- spread of vegetarianism;
- maintaining and restoring soil fertility (due to the balance of chemical elements);
- use of only natural fertilizers when growing crops.
- relative accessibility of organic fertilizers (such as by-products from livestock facilities and waste disposal method).

Unfortunately, today OF is used only by individual farms and gardens, because organic products are 2-2.5 times more expensive, their demand is low. The development of biological production requires certain social and administrative conditions.

One of the well-known organic farms in Ukraine are an agricultural joint stock company of the „Horizon” and a private enterprise „Agroecology” (Poltava region). These farms specialize on grain growing and industrial crops as well as production of milk and meat. Since 1976 SAT „Horizon” has been the basic economy that industrially tested soil-protective technology cultures of cultivation, expanded reproduction activities of soil fertility and production of ecologically safe food products. Since 1979 conservation technologies of biological agriculture have been introduced in the economy and since 1990- the technology of organic agriculture.

Thus, the introduction of organic fertilizers is one of the most important levers to improve soil health. In the system of measures to increase the productivity of soil fertility and crops the most important place is given to organic fertilizers. This is because they not only enrich the soil with all the elements of power, but also improve its properties.

Growing agricultural cultures without fertilizers leads to a reduction in the content of humus in the soil and reduction of soil fertility, which is caused by salinity of

humus. In particular, the reduction of humus content in soil by 1% leads to lower yields by 5 C/ha of grain units.

The rate of humus mineralization in soils rises in the conditions of intensive cultivation, of tilled crops cultivation, monoculture and lack of perennial grasses in crop rotation and lack of fertilizers. In case of humus content reduction water-physical, chemical and biological properties of soil deteriorate.

When adequate standards of organic fertilizers are used the humus content of the soil is maintained at the same level, and after introduction of high standards, even increases. Improvement of the humus content in the soil at a rapid pace is noticed in the first years of the systematic application of organic fertilizers, then the rates are reduced and then balanced.

The level of humus content depends on the type of soil, climate-and environment, crop rotation, farming methods. Under favorable conditions 20-30% of carbon in organic matter can be transformed into humus. The magnitude of the coefficient of humification affects granulometric composition of soil [2].

When adding fertilizers, the soil is supplied with nutrients (macro - and microelements), soil acidity reduces, the content of absorbed foundations increases, as well as absorption capacity and buffering. Organic fertilizers contain biologically active substances – vitamins and toxins necessary for the growth and development of plants and microorganisms, which carry out constant biosynthesis and mineralization of organic matter. Soil enriched by microflora intensifies its biological activity and releases carbon dioxide, which is an additional source of carbon dioxide to the air power plants. Organic fertilizers reduce the resistance of the soil in the mechanical process and improve its heat regime because dark-coloring of humus helps to absorb heat [3].

Currently the problem is the violation of organic fertilizers application rules, which escalates with the development of farming in the region. The danger lies in the accumulation of nitrates in the soil and groundwater. Nitrate (salts of nitric acid) is one of the elements of power plants. In the human body under the influence of the intestinal microflora it transforms nitrates to nitrites to form methemoglobin, blocks hemoglobin in the blood and this will inhibit the transport of oxygen to the tissues. The danger of nitrates and nitrites to the body is in high quantities associated with their expressed carcinogenic effect [3]. It is obvious that the accumulation of nitrates in the products depends on the type of fertilizer, its dose, culture, soil type, and other factors. In maintaining health there are two key principles: the use of only organic fertilizers and the absence of any artificial substances. And if the use of chemicals is easy to limit, the absence of high-quality organic fertilizers is a more significant problem.

Organic fertilizers can be obtained by aerobic, anaerobic methods and by the use of animals (vermicomposting) [1].



Table 1 – Comparative characteristics of biofertilizing methods

Aerobic method (composting)	Anaerobic method	Vermicomposting
Cost (capital and operating costs)		
Capital: 1200-1600 USD per 1 ton / year Performance:200 UAH. / T	Capital:.. 3300USD per 1 ton/year Performance:70 UAH./ T	Capital:250-300USD per 1 ton/year Performance:150 UAH. / T
Time of preparing		
Less than 3 weeks (with active mixing); 3-6 months (with constant stirring).	3-4 weeks	4-6 weeks
Content of chemical elements		
Low C:N=20-30:1	High C:N=11:1	Middle C:N =15:1
Method of the transformation of organic substances		
Anaerobic decomposition	Methane fermentation	Transformation of animals
Process automation		
The average automation	Almost fully Autonomous process	Low automation
Efficiency of use (biomass)		
20-30%	20%	30-40%

The use of aerobic method is advantageous because it disposes of almost all groups of organic waste, suppresses pathogenic organisms, accelerates processing, a large part of weed seeds is lost, up to 70% of the chemical elements are supplied,

greenhouse gas emissions reduce. The economic component is in quick cheap compost at average capital costs and high operating costs (with the active composting).

The anaerobic method is disposal of almost all groups of organic waste, suppression of the pathogenic organisms, the rotting of weed seeds, conservation of valuable chemical elements of power plants and reduction of environment pollution (aerobic method of greenhouse gases source), slowing down the recycling process. The economic component: considerable initial investments, derivatives of saturated organic fertilizers and biogas).

The application of vermiculture is obtaining a valuable fertilizer from relatively clean organic waste, limited in application (some types of organic waste without additives), loss of nutrients, slow process. This processing method with small investments brings valuable fertilizers. And there is an opportunity to sell additional vermiculture as protein mass. The economic component is low capital costs of average operating costs, production of rich biohumus.

Ukraine has a great potential for the cultivation of organic agricultural products, but its main part is currently exported through the weak domestic market. Improvement of economic efficiency of OZ is possible with the use of organic fertilizers. The most economically expedient for small farms is vermicomposting, for medium and large – aerobic and anaerobic methods of organic fertilizers preparation depending on the characteristics of raw materials and the requirements to the final product. From the ecological point of view, the most appropriate is the anaerobic decomposition of organic waste.

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УДК 577

## **EFFECT OF GLUCOSE ON THE DETERGENT AND OSMOTIC HEMOLYSIS, CHOLESTEROL CONTENT IN ERYTHROCYTE WITH ACTION OF HEMIN AND FERRIC CHLORIDE (III) IN VITRO**

**Akopian A.S. (Kharkiv)**

**Language supervisor: Nikitina L.D.**

**Summary:** The study showed that 2-hour preincubation without glucose and by the action of hemin resulted cholesterol content in increase control erythrocytes. Cholesterol increased by the action of ferric chloride observed in all periods of incubation. Glucose adding to the incubation medium prevented the increase of cholesterol content in the studied effects. 2-hour preincubation without glucose caused a decrease in the detergent lysis by saponin under the action of hemin on erythrocytest, which was prevenec by the addition of glucose to the incubation medium.

**Key words:** ferric chloride, hemolysis, hemin, erythrocytes, detergent.

**Анотація:** Дослідження показало, що 2х-годинна попередня інкубація без глюкози та під дією геміну приводила до підвищення вмісту холестерину у контрольних еритроцитів. При дії

хлориду заліза підвищення холестерину відзначено в усі терміни інкубації. Додавання глюкози в середу інкубації запобігало підвищенню вмісту холестерину при вивчених впливах. 2-х годинна попередня інкубація без глюкози викликала зниження детергентного лізису сапоніном при дії на еритроцити геміну, що попереджалося додаванням глюкози в середу інкубації.

**Ключові слова:** хлорид заліза, гемоліз, гемін, еритроцити, детергенти.

**Аннотация:** Исследование показало, что 2-х часовая предварительная инкубация без глюкозы под воздействием приводила к повышению содержания холестерина у контрольных эритроцитов. При действии хлорида железа повышение холестерина отмечено во все сроки инкубации. Добавление глюкозы в среду инкубации предотвращало повышение содержания холестерина при изученных воздействиях. 2-х часовая предварительная инкубация без глюкозы вызывала снижение детергентного лизиса сапонином при действии на эритроциты гемина, которое предотвращалось добавлением глюкозы в среду инкубации.

**Ключевые слова:** хлорид железа, гемолиз, гемин, эритроциты, детергенты.

## Introduction

Currently, intravascular lysis of erythrocytes is considered as a separate etiologic factor in the development of vascular disorders [1] and thrombosis [2].

Accumulation of iron and hemin as main products of hemolysis may provoke further lysis of erythrocytes, which promoted by practical study of action mechanisms of ferric and hemin on membranes of blood cells.

The resistance of erythrocytes is an important parameter that characterizes their structural state to hemolysis induced by various factors. The hemolysis by amphiphilic substances, in particular by detergents occupies a special place among all types of hemolytic effects [3]. The detergents are divided into two groups – ionic and nonionic. The anionic detergent SDS lyses cell and nuclei, denatures proteins and, forming with them a negatively charged complexes, destroys nucleoproteins. Hemolysis of human erythrocytes with saponin affects the membrane structure. The incubation of cells and tissues with saponin makes lipid bilayer permeable to macromolecules. Hemolysis with saponin also affected the interaction between transmembrane proteins and cytoskeleton.

It is established that the increase the osmotic fragility of erythrocytes is one of the reasons for the increase of intravascular hemolysis in various pathological conditions and effect of stress factors [4]. Osmotic resistance is an effective indicator of the membrane and therefore is widely used in model experiments to study membrane properties in medical diagnostics, in the study of hemolytic and anti-hemolytic activity of various compounds.

Hemin relates to oxidative agents, which is a hydrophobic compound and is able to integrated into the cell membrane. It has a direct effect on the membrane, so erythrocytes immediately react to the appearance of hemin in the medium. Treatment with ferric chloride results in a more expressed lysis under the action of SDS than saponin.

Cholesterol is a main stability regulator of the erythrocyte membrane. It is known that cholesterol normally performs the function of an antioxidant, and its accumulation promotes the protection of cell membranes from free radicals. The increase of cholesterol concentration in erythrocytes can be result from lipid peroxidation [5].

## Methods

Human erythrocytes were taken to study from the donor erythrocyte mass (HOTSPK, blood (male) the group A (II), Rh +). Erythrocytes were prepared in a triple laundering of isotonic buffer ( $\text{NaH}_2\text{PO}_4$ ,  $\text{Na}_2\text{HPO}_4$ , 8,5%  $\text{NaCl}$ , pH 7.45). Isotonic

buffer was added to the precipitate of erythrocytes in a ratio of 1:10 and stirred gently by glass rod. The tubes centrifuged for 10 min at 3 thousand turnover/min. Washing and centrifugation was repeated 2 more times [6].

Erythrocytes (hematocrit 20%) were incubated for 2 hours with the access of oxygen at 37°C in isotonic buffer (IB) without glucose (Glc) and with 5 mM Glc, then the erythrocytes were precipitated and transferred into IB to incubate for 30 minutes at +37°C without additives (control) or in the presence of 3 mM FeCl<sub>3</sub>, 35μM hemin.

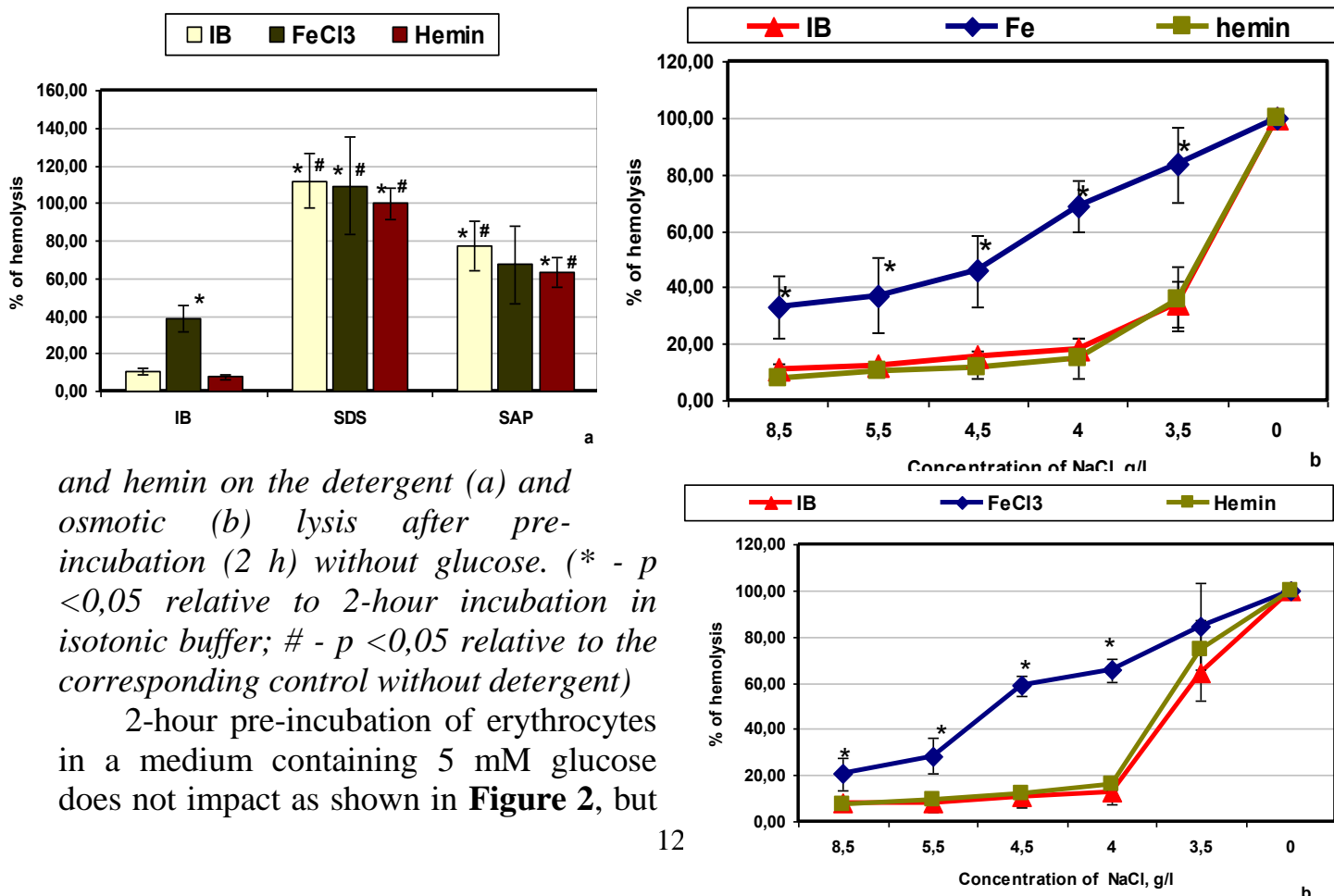
Osmotic resistance was evaluated by the degree of lysis in hypotonic solutions NaCl. Hemolysis of erythrocytes was evaluated by absorbance of hemoglobin (Hb) at a wavelength of 540 nm. The cholesterol content was determined in hemolysate using standard sets.

The normality of the distribution of the data (for each group) was evaluated by the Shapiro-Wilk test. Due to the fact that certain groups differed from a normal distribution, median and percentiles were calculated. Kruskal-Wallis test was used to assess the differences between the samples [7]. The work program was used for statistical data processing.

## Results

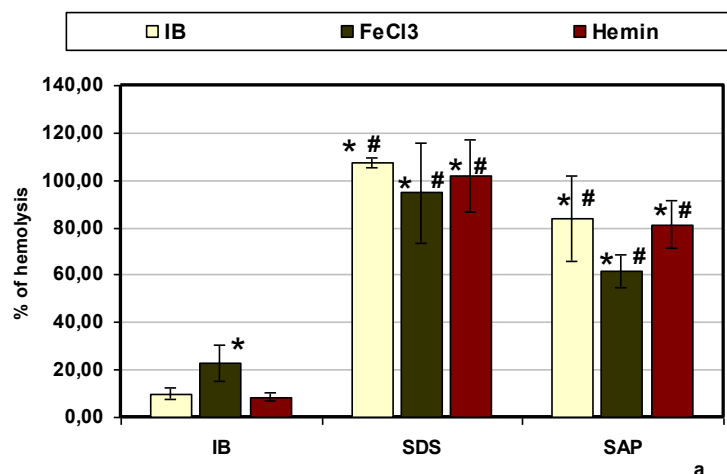
Ferric chloride treatment increased the lysis with SDS, but reduced by the action of saponin. As seen from **Figure 1**, the processing of detergents with a 2-hour pre-incubation increased the hemolysis in all kinds of influences. The anionic (SDS) and nonionic (Sap) detergents increased the degree of detergent lysis in 4-5 times. The lysis by ferric chloride of intact erythrocytes increased in two times.

**Fig.1.** Effect of ferric chloride (III)



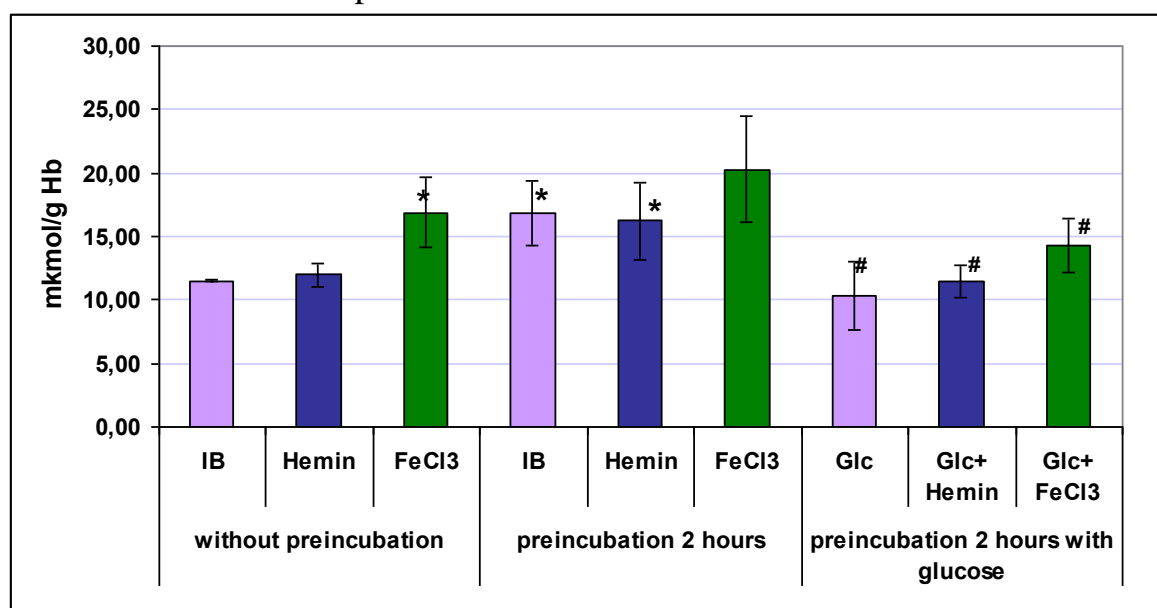
2-hour pre-incubation of erythrocytes in a medium containing 5 mM glucose does not impact as shown in **Figure 2**, but

the pre-treatment by ferric chloride, it increased the hemolysis of erythrocytes. Processing of hemin caused significant lysis in a detergent hemolysis. Ferric chloride after 2 hours of incubation with glucose induced increase in osmotic hemolysis of erythrocytes at concentrations of 4-5.5 g / l NaCl, in contrast to hemin.



**Fig.2.** Effect of ferric chloride (III) and hemin on the detergent (a) and osmotic (b) after pre-lysis incubation (2 h) with glucose (5 mM). ( \* -  $p < 0,05$  relative to 2-hour incubation in isotonic buffer with glucose; # -  $p < 0,05$  relative to the corresponding control without detergent)

Figure 3 shows that the pre-incubation without glucose resulted in an increase of cholesterol in the control erythrocytes and under the influence of hemin. Under the action of ferric chloride the increase of cholesterol was observed during all periods of incubation. Adding glucose to the incubation medium prevented the increase of cholesterol in the studied effects.



**Fig. 3.** Effect of preincubation with glucose on cholesterol content of the erythrocytes by the action of ferric chloride and hemin in vitro. ( \* -  $p < 0,05$  relative to the experiment without preincubation; # -  $p < 0,05$  relative to incubation without glucose for 2 hours).

## Discussion

Hemolysis of human erythrocyte by saponin is believed to influence the membrane structure. Incubation of cells and tissues with saponin makes lipid bilayer permeable to macromolecules. Hemolysis with saponin also impacted on interaction between transmembrane proteins and the cytoskeleton [8]. The anionic detergent SDS lyses cells and nuclei, denatures proteins and forms with them negatively charged complexes [9].

The inhibition of glycolysis by the action of hemin as the only source of ATP in erythrocytes led to the decrease of erythrocyte resistance to SDS and did not change the

resistance to saponin. The inhibition of glycolysis by the action of ferric chloride (III) caused a decrease in the stability of erythrocytes to saponin and did not alter resistance to SDS [10]. It is known that the parameters of fast hemolysis by SDS sensitive to structural rearrangements in erythrocyte membranes.

The structure of band 3 protein is changed by osmotic hemolysis, which forms anionic transport channel and it is the main integral protein, as in the erythrocyte membrane, it is approximately half of the total integral protein content [11]. Possibly, pre-incubation of glucose influences the mechanism action of proteins that form the channel for passage of water. Consequently, these processes are of great interest for further study.

The mechanisms of action of ferric chloride are related to oxidative damage of cells. Hemin led to the increase of lysis as an anionic detergent, which can integrate into the membrane.

The ferric chloride in osmotic lysis modifies transport proteins, this causes water entrance, so in the future hemolysis. It should be noted that, a much higher sensitivity of erythrocytes treated with iron to hypotonic lysis. Hemin does not have the same impact. The only source of increasing cholesterol is a more dense packing of erythrocytes in the precipitate, as the hemoglobin content did not change the pre-incubation, so cholesterol levels did not increase.

Finally, our study has illustrated that 2-hour preincubation without glucose and by the action of hemin resulted in cholesterol content the increase in control erythrocytes. Cholesterol increased by the action of ferric chloride was observed in all periods of incubation. Glucose adding to the incubation medium prevented the increase of cholesterol content in the studied effects. 2-hour preincubation without glucose caused a decrease in the detergent lysis by saponin under the action of hemin an erythrocytes, which was prevented by the addition of glucose to the incubation medium.

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## THE PROBLEM OF MEDICAL CARE IN UKRAINE

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**Summary:** The article considers the problem of medical care in Ukraine and the drawbacks existing in this field. The current legislation of Ukraine and legislation of the European countries were analyzed. The drawbacks in relations “a patient – a doctor” were found out. The problems of legal responsibility for making a malpractice, giving insufficient information concerning the individual about the standards of medical care, providing free medical aid were considered. Statistical data from Worldwide Organization of health protection experts for malpractices were analyzed.

**Key words:** free medical assistance, legal status of patients, malpractice, medical care, rights of doctors.

**Анотація:** Стаття присвячена розгляду суті надання медичної допомоги в Україні та виявленню недоліків в цій сфері. У результаті дослідження було проаналізоване чинне законодавство та законодавство європейських країн. Виявлені недоліки у відносинах «пацієнт – лікар». Розглянуто питання щодо юридичної відповідальності за скоєння «лікарської помилки»; щодо недостатньої проінформованості осіб з приводу стандартів надання медичної допомоги; щодо безоплатності надання медичної допомоги. Проаналізовано статистичні данні експертів Всесвітньої організації охорони здоров'я щодо лікарських помилок.

**Ключові слова:** безоплатність медичної допомоги, лікарська помилка, медична допомога, права лікарів, правовий статус пацієнтів.

**Аннотация:** Статья посвящена рассмотрению сущности оказания медицинской помощи в Украине и выявлению недостатков в этой сфере. В результате исследования было проанализировано действующее законодательство и законодательство европейских стран. Выявлены недостатки в отношениях «пациент – врач». Рассмотрены вопросы юридической ответственности за совершение «врачебной ошибки»; недостаточной проинформированности лиц по поводу стандартов оказания медицинской помощи; бесплатности оказания медицинской помощи. Проанализированы статистические данные экспертов Всемирной организации здравоохранения по поводу врачебных ошибок.

**Ключевые слова:** бесплатность медицинской помощи, медицинская помощь, медицинская ошибка, права врачей, правовой статус пациентов.

The protection of life and human health acquire particular importance nowadays, because the health of population is getting worse considerably every year. In accordance with article 3 of the Constitutions of Ukraine the individual, his life, health, honour, dignity, inviolability and security, are the main values, and in article 27 and 49 the human rights are envisaged on the protection of life and medical care [2, p. 15].

The drawbacks were found in legal relationships: “a patient – a doctor”.

In obedience to the legislation of Ukraine, namely articles 37 of Bases of legislation of Ukraine “on protection of the health care” the patient has the right to

refuse rendering medical aid of a doctor and to require the replacement of a doctor without strong reasons [3].

In his turn the doctor has the right to give up the further management of the patient, only in case if the patient does not execute medical doctor's prescriptions, internal regulations of medical establishment (article 34) or, if the establishment chosen by a patient cannot provide the appropriate treatment (part 2 of article 38). Thus, in case if a doctor feels not competent enough, he does not have the right to refuse medical treatment to the patient [3].

This gap causes not adequate treatment and increases malpractices.

There is no country in the world, where doctors avoid errors. Nevertheless, in the legislation there is no universally accepted legal definition of "Malpractice (medical error)". If we consider "medical crime" separately from "malpractice", then the latter is not legally envisaged, but responsibility for the damage caused as a consequence of "malpractice", envisaged by under section 2 of Criminal Codes of Ukraine and takes place at a certain form of the crime that is necessary to be determined in every special case.

The lack of definition of "Malpractice (medical error)" results in medical professionals' considering of "malpractice" only as a ghost. As practice shows, the overwhelming majority of medical workers and even leaders of establishments of health protection have a superficial understanding of legal responsibility which is set by a current legislation about offences in the field of health protection.

In addition, the knowledge about reasons, kinds and consequences of legal responsibility, on the one hand, discipline medical workers, and on the other hand reduces the probability of the causeless bringing in them to responsibility.

According to the experts of worldwide organization of health protection in Ukraine every day 6-7 persons die from malpractices, and it's in 3 times more become disabled. Also, as V.V. Veressaev specified: "Errors of doctors are the most important reasons for the decline of public confidence in medicine" [1, p. 302]. Therefore people lose confidence and become the side of non-conventional medicine, which in the future can bring both positive and negative consequences. People who have been victims of medical negligence often learn about it later, because medical professionals quite often hide the consequences of their incompetence, therefore it is difficult to prove medical negligence in court. Taking into account the increase of points of citizens' claims for improper rendering of medical care, the problems of legal responsibility of doctors for professional offences are necessary to spare considerably anymore attention and fasten a concept "Malpractice (medical error)" and devise it with the term "medical crime".

In our country problems arise up not only in the case of imperfection of the legislation, but also in the case where an ordinary person does not have the opportunity without obstacles to acquaint with one or another documents that have direct attitude toward their life and health. The problem is about the documents that determine the standards of medical care. In obedience to article 11 of Law of Ukraine "on state medical standards and state social guarantees" in Ukraine there are norms in the field of health protection, but is very difficult to acquaint with standards, because for an acquaintance it is necessary to pass the whole link of stages.

It grounds to assert that a patient has insufficient information about the rules of rendering to his medical care. And this is contrary to article 39 of principles of



legislation of Ukraine “about a health protection” – a “duty to provide medical information”. The president of Ukrainian national Council for protection and safety of the patients Victor Serdyuk adheres the same view: “The evolution of psychology of patient is needed – from excessive credulity to realization of their rights and ability to defend them”. And for this purpose it is necessary to have free access to all standards of treatment.

It is necessary to mark that most medical professionals carry out the professional activities, being in employment with health institutions. In obedience to the first part of article 1172 of the Civil Code of Ukraine a legal or physical person shall compensate for the damage inflicted by their employee during execution of the labour (official) duties [4, p. 344]. Overwhelming majority of lawsuits that are produced by patients to establishments of health protection, (including physical persons – performers of entrepreneurial activities, that are engaged in medical practice), are lawsuits about a material and moral damage to person inflicted to the health because of rendering of medical care of improper quality.

However, it is necessary to mark that the obligatory condition of responsibility for a causing damage is a causal link between unlawful conduct and the damage inflicted. For example, if a damage is not the consequence of unlawful conduct of a person inflicting a damage and happened on other reasons (because of failure to observe by the patient of medical recommendations or because of individual features of organism of patient), an inflicting damage will not be under an obligation to compensate a damage.

Professional rights of doctors who remain regardless became another problem, in fact they are defined only in two articles of the principles of legislation of Ukraine “about a health protection”, namely, in articles 34 and 77. In fact every day the doctors fight for patients’ lives, solve important problems, issues literally of life and death. Thus, they are responsible for the life of a patient; therefore doctors should have a wider spectrum of rights for their own defense. The legislative decision of this problem will help to raise the level of medical care.

Also, in our opinion, it is useful to define legal status of the patient by means of a special law on patient rights, according to such a sample which exists in the countries of European community and taking into account all the European standards in this area.

As it is marked in article 49 of the Constitution of Ukraine, the right on medical care is free of charge, nevertheless illegal sponsorship funds are created in state medical establishments in which patients are almost forced to invest money, otherwise without this condition doctors refuse to carry out the duties properly and give out free medicaments. It leads not only to worsening of patients’ health, but also to the concealment of public funds and use of them in the personal purposes of doctors.

Thus, having considered the problems of medical care, we came to the conclusion about the necessity of further improvement of the legal base of medical industry, which will contribute to the improvement of medical care in Ukraine.

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УДК 615.477.2

## **LIVES PROSTHESIS**

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**Language supervisor: Zhytnytska A.A.**

**Summary:** The article deals with the problem of post-traumatic cases and injuries where dentures are required, partly the article touches the whole process of prosthetics. Also it tells about all sorts and kinds of dentures

**Key words:** prosthesis, prosthetics, rehabilitation.

**Анотація :** Стаття присвячена розгляду питання протезування кінцівок людини, а саме розглядає різноманіття існуючих протезів, частково розглядає методи їх застосування та протезування в цілому.

**Ключові слова:** Протез, протезування, реабілітація.

**Аннотация:** Статья посвящена проблеме протезирования конечностей, рассматривает все возможные существующие протезы а так же частично затрагивает собственно процесс протезирования конечностей.

**Ключевые слова:** Протез, протезирование, реабилитация.

People can be also disabled from their birth, or can get seriously injured during their life's. People loose parts of their body in accidents, wars, can they be genetically injured. But how to live with such traumas? Can people return to their normal life and live like the others who had more luck in their? Fortunately this is possible due to prosthesis. For some people prosthesis is the only hope for normal life. And this is the thing no one must ever lose.

In medicine, prosthesis is an artificial device that replaces a missing body part lost through trauma, disease, or congenital conditions. The main types of prosthesis, craniofacial and somato (body), can be divided further by the anatomical region. Craniofacial prostheses include intra-oral and extra-oral prostheses. Extra-oral prostheses are further divided into hemifacial, auricular (ear), nasal, orbital and ocular. Intra-oral prostheses include dental prostheses such as dentures, obturators, and dental implants. Somato prostheses include breast and limb prostheses. Breast prostheses include full breast devices and nipple prostheses. Limb Prostheses include upper extremity and lower extremity prostheses. Upper extremity prostheses are used at varying levels of amputation: shoulder disarticulation, transhumeral, elbow disarticulation, transradial, wrist disarticulation, full hand, partial hand, finger, partial finger. Lower extremity prostheses are also used at varying levels of amputation. These include hip disarticulation, transfemoral, knee disarticulation, transtibial, symes, foot, partial foot, and toe. The type of prostheses needed will be designed and assembled according to the patient's appearance and functional needs. For instance, a patient may need a transradial prosthesis, but need to choose between an aesthetic functional device, a myoelectric device, a body-powered device, or an activity specific device. Depending on the patient's funding situation, she may have the option to choose more than one device [1].

A transhumeral prosthesis is a fake limb that replaces an arm missing above the elbow. Transhumeral amputees experience some of the same problems as transfemoral amputees, due to the similar complexities associated with the movement of the elbow.

This makes mimicking the correct motion with an artificial limb very difficult. In the prosthetic industry a trans-humeral prosthesis is often referred to as a "AE" or above the elbow prosthesis. A transradial prosthesis is an artificial limb that replaces an arm missing below the elbow. Two main types of prosthetics are available. Cable operated limbs work by attaching a harness and cable around the opposite shoulder of the damaged arm. The other form of prosthetics available are myoelectric arms. These work by sensing, via electrodes, when the muscles in the upper arm move, causing an artificial hand to open or close. In the prosthetic industry a trans-radial prosthetic arm is often referred to as a "BE" or below elbow prosthesis.

A transfemoral prosthesis is an artificial limb that replaces a leg missing above the knee. Transfemoral amputees can have a very difficult time regaining normal movement. In general, a transfemoral amputee must use approximately 80% more energy to walk than a person with two whole legs. This is due to the complexities in movement associated with the knee. In newer and more improved designs, hydraulics, carbon fiber, mechanical linkages, motors, computer microprocessors, and innovative combinations of these technologies are employed to give more control to the user. In the prosthetic industry a trans-femoral prosthetic leg is often referred to as an "AK" or above the knee prosthesis [3].

A transtibial prosthesis is an artificial limb that replaces a leg missing below the knee. Transtibial amputees are usually able to regain normal movement more readily than someone with a transfemoral amputation, due in large part to retaining the knee, which allows for easier movement. Lower extremity prosthetics are described artificially replaced limbs located at the hip level or lower. The two main subcategories of lower extremity prosthetic devices are 1.trans-tibial (any amputation transecting the tibia bone or a congenital anomaly resulting in a tibial deficiency) and 2.trans-femoral (any amputation transecting the femur bone or a congenital anomaly resulting in a femoral deficiency). In the prosthetic industry a trans-tibial prosthetic leg is often referred to as a "BK" or below the knee prosthesis while the trans-femoral prosthetic leg is often referred to as an "AK" or above the knee prosthesis [2].

Over the years there have been significant advancements in artificial limbs. New plastics and other materials, such as carbon fiber, have allowed artificial limbs to be stronger and lighter, limiting the amount of extra energy necessary to operate the limb. This is especially important for transfemoral amputees. Additional materials have allowed artificial limbs to look much more realistic, which is important to transradial and transhumeral amputees because they are more likely to have the artificial limb exposed [3].

In addition to new materials, the use of electronics has become very common in artificial limbs. Myoelectric limbs, which control the limbs by converting muscle movements to electrical signals, have become much more common than cable operated limbs. Myoelectric signals are picked up by electrodes, the signal gets integrated and once it exceeds a certain threshold, the prosthetic limb control signal is triggered which is why inherently, all myoelectric controls lag. Conversely, cable control is immediate and physical, and through that offers a certain degree of direct force feedback that myoelectric control does not. Computers are also used extensively in the manufacturing of limbs. Computer Aided Design and Computer Aided Manufacturing are often used to assist in the design and manufacture of artificial limbs [4].

Most modern artificial limbs are attached to the stump of the amputee by belts and cuffs or by suction. The stump either directly fits into a socket on the prosthetic, or—more commonly today—a liner is used that then is fixed to the socket either by vacuum (suction sockets) or a pin lock. Liners are soft and by that, they can create a far better suction fit than hard sockets. Silicone liners can be obtained in standard sizes, mostly with a circular (round) cross section, but for any other stump shape, custom liners can be made. The socket is custom made to fit the residual limb and to distribute the forces of the artificial limb across the area of the stump (rather than just one small spot), which helps reduce wear on the stump. The custom socket is created by taking a plaster cast of the stump or, more commonly today, of the liner worn over the stump, and then making a mold from the plaster cast. Newer methods include laser guided measuring which can be input directly to a computer allowing for a more sophisticated design.

One problem with the stump and socket attachment is that a bad fit will reduce the area of contact between the stump and socket or liner, and increase pockets between stump skin and socket or liner. Pressure then is higher, which can be painful. Air pockets can allow sweat to accumulate that can soften the skin. Ultimately, this is a frequent cause for itchy skin rashes. Further down the road, it can cause breakdown of the skin.

#### Body-powered arms

Current high tech allows body powered arms to weigh around half to only a third of the weight that a myoelectric arm has.

#### Sockets

Current body powered arms contain sockets that are built from hard epoxy or carbon fiber. These sockets or "interfaces" can be made more comfortable by lining them with a softer, compressible foam material that provides padding for the bone prominences. A self suspending or supra-condylar socket design is useful for those with short to mid range below elbow absence. Longer limbs may require the use of a locking roll-on type inner liner or more complex harnessing to help augment suspension.

#### Wrists

Wrist units are either screw-on connectors featuring the UNF 1/2-20 thread (USA) or quick release connector, of which there are different models.

#### Voluntary opening and voluntary closing

Two types of body powered systems exist, voluntary opening "pull to open" and voluntary closing "pull to close". Virtually all "split hook" prostheses operate with a voluntary opening type system.

More modern "prehensors" called GRIPS utilize voluntary closing systems. The differences are significant. Users of voluntary opening systems rely on elastic bands or springs for gripping force, while users of voluntary closing systems rely on their own body power and energy to create gripping force.

Voluntary closing users can generate prehensive forces equivalent to the normal hand, upwards to or exceeding one hundred pounds. Voluntary closing GRIPS require constant tension to grip, like a human hand, and in that property they do come closer to matching human hand performance. Voluntary opening split hook users are limited to forces their rubber or springs can generate which usually is below twenty pounds.

#### Feedback

An additional difference exists in the biofeedback created that allows the user to "feel" what is being held. Voluntary opening systems once engaged provide the holding force so that they operate like a passive vice at the end of the arm. No gripping feedback is provided once the hook has closed around the object being held. Voluntary closing systems provide directly proportional control and biofeedback so that the user can feel how much force that they are applying.

### Terminal devices

Terminal devices contain a range of hooks, prehensors, hands or other devices.

### Hooks

Voluntary opening split hook systems are simple, convenient, light, robust, versatile and relatively affordable. Hooks obviously do not match human hand in both appearance and overall versatility.

However, a hook's material tolerances can also exceed and surpass the human hand for mechanical stress (one can use a hook to slice open boxes or as a hammer whereas same is not possible with a hand), for thermal stability (one can use a hook to grip items from boiling water, to turn meat on a grill, to hold a match until it has burned down completely) and for chemical hazards (as a metal hook withstands acids or lye, and does not react to solvents as a prosthetic glove or human skin does).

### Hands

Prosthetic hands are available in both voluntary opening and voluntary closing versions and because of their more complex mechanics and cosmetic glove covering require a relatively large activation force, which, depending on the type of harness used, may be uncomfortable.

Commercial providers, materials

Hosmer and Otto Bock are major commercial hook providers. Mechanical hands are sold by Hosmer and Otto Bock as well; the Becker Hand is still manufactured by the Becker family. Prosthetic hands may be fitted with standard stock or custom made cosmetic looking silicone gloves. But regular work gloves may be worn as well. Other terminal devices include the V2P Prehensor, a versatile robust gripper that allows customers to modify aspects of it, Texas Assist Devices (with a whole assortment of tools) and TRS that offers a range of terminal devices for sports. Cable harnesses can be built using aircraft steel cables, ball hinges and self lubricating cable sheaths.

### Myoelectric

A myoelectric prosthesis uses electromyography signals or potentials from voluntarily contracted muscles within a person's residual limb on the surface of the skin to control the movements of the prosthesis, such as elbow flexion/extension, wrist supination/pronation (rotation) or hand opening/closing of the fingers. A prosthesis of this type utilizes the residual neuro-muscular system of the human body to control the functions of an electric powered prosthetic hand, wrist or elbow. This is as opposed to an electric switch prosthesis, which requires straps and/or cables actuated by body movements to actuate or operate switches that control the movements of a prosthesis or one that is totally mechanical. It is not clear whether those few prostheses that provide feedback signals to those muscles are also myoelectric in nature. It has a self suspending socket with pick up electrodes placed over flexors and extensors for the movement of flexion and extension respectively.

The first commercial myoelectric arm was developed in 1964 by the Central Prosthetic Research Institute of the USSR, and distributed by the Hangar Limb Factory of the UK.

### Robotic prostheses

In order for a robotic prosthetic limb to work, it must have several components to integrate it into the body's function: Biosensors detect signals from the user's nervous or muscular systems. It then relays this information to a controller located inside the device, and processes feedback from the limb and actuator (e.g., position, force) and sends it to the controller. Examples include wires that detect electrical activity on the skin, needle electrodes implanted in muscle, or solid-state electrode arrays with nerves growing through them. One type of these biosensors are employed in myoelectric prosthesis.

Mechanical sensors process aspects affecting the device (e.g., limb position, applied force, load) and relay this information to the biosensor or controller. Examples include force meters and accelerometers.

The controller is connected to the user's nerve and muscular systems and the device itself. It sends intention commands from the user to the actuators of the device, and interprets feedback from the mechanical and biosensors to the user. The controller is also responsible for the monitoring and control of the movements of the device. An actuator mimics the actions of a muscle in producing force and movement. Examples include a motor that aids or replaces original muscle tissue.

Targeted muscle reinnervation (TMR) is a technique in which motor nerves which previously controlled muscles on an amputated limb are surgically rerouted such that they reinnervate a small region of a large, intact muscle, such as the pectoralis major. As a result, when a patient thinks about moving the thumb of his missing hand, a small area of muscle on his chest will contract instead. By placing sensors over the reinnervated muscle, these contractions can be made to control movement of an appropriate part of the robotic prosthesis.

An emerging variant of this technique is called targeted sensory reinnervation (TSR). This procedure is similar to TMR, except that sensory nerves are surgically rerouted to skin on the chest, rather than motor nerves rerouted to muscle. The patient then feels any sensory stimulus on that area of the chest, such as pressure or temperature, as if it were occurring on the area of the amputated limb which the nerve originally innervated. In the future, artificial limbs could be built with sensors on fingertips or other important areas. When a stimulus, such as pressure or temperature, activated these sensors, an electrical signal would be sent to an actuator, which would produce a similar stimulus on the "rewired" area of chest skin. The user would then feel that stimulus as if it were occurring on an appropriate part of the artificial limb.

Recently, robotic limbs have improved in their ability to take signals from the human brain and translate those signals into motion in the artificial limb. DARPA, the Pentagon's research division, is working to make even more advancements in this area. Their desire is to create an artificial limb that ties directly into the nervous system.

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## ENERGY CONSERVATION IN CIVIL ENGINEERING

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**Анотація:** У статті розглядається проблема пошуку нових альтернативних джерел палива, головні особливості і риси потреб будівельної промисловості. Способи вирішення цієї проблеми та питання про можливість способів знаходження виробництва енергії із вторинних джерел сировини, як альтернативних джерел енергії, також розглядаються тут.

**Ключові слова:** навколишнє середовище, поновлюване паливо, пальне, водень, сировина, дамба

**Аннотация:** Данная статья затрагивает проблемы поиска новых альтернативных источников топлива, рассматривая главные особенности и черты потребностей строительной промышленности. Способы решения этой проблемы обсуждаются в этой статье. Вопросы о возможности способов нахождения производства энергии из вторичных источников сырья, как альтернативных источников энергии также рассматривается здесь.

**Ключевые слова:** окружающая среда, возобновляемое топливо, горючее, водород, сырье, дамба

**Summary:** This article deals with the problems of searching for the new alternative fuels considering the main peculiarities & features of civil engineering.

The ways of solving this problem are discussed in this paper. The possible ways of finding the new methods of energy production from secondary sources of raw materials are also considered here.

**Keywords:** environment, renewable fuel, combustible, hydrogen, raw, dam.

One of the major problems facing mankind is the energy problem. Think how many people will be able to use conventional oil, gas and coal? It's no secret that their reserves on earth are not unlimited. Therefore, their gradual depletion forces people to look for new, rational energy sources. Many scientists are trying to devise a perfect mechanism that will satisfy all the needs of modern society. But how to get the maximum performance and be environmentally friendly, how to decrease power consumption? It's possible! And this is some fantastic story about the future that is happening now, at present.

Energy conservation may be viewed as one increasing the productivity of primary energy inputs. For the individual firm this may be important as a way to reduce costs as the real price of energy rises [1, p.98].

At the national level there may be a number of reasons for analyzing and/or implementing conservation strategies. One important reason for examining conservation possibilities is determining potential energy savings and hence estimating possible future energy demands.

For many projects the energy associated with operating or using the finished structure greatly exceeds initial building energy requirements. Thus, in the case of the water resource programmes it is the volume of water required and the amount of pumping which determines overall lifetime energy requirements to a much greater extent than energy inputs to building a tidal barrage that are not particularly significant in comparison with the cumulative energy output over its expected lifetime (which is just as well for a system which is to be a net energy producer).

In recent years, many countries have expanded the use of wind turbines (windmills). Most of them are in Western Europe, the USA, India and China. The largest wind turbine in the world is now in Germany Enercon E-126. Its size is staggering. Its nominal capacity is 6 mega watts. It is enough to provide electricity to about 5,000 European homes. In South American countries, particularly in Brazil ethyl alcohol is increasingly used. This is a pretty profitable replacement of gasoline, since alcohol is less polluting [1, p.113].

#### ENERGY PRICES AND TECHNICAL CHANGE

Industries adapt, in the longer term, to changes in the real price of fuels by adopting the technology which keeps costs as low as possible.

Since the method of energy analysis used here traces the total(direct and indirect)primary energy resources sequestered it could be extended to provide clues as to the likely technical trends in the civil engineering industry in the face of considering indirect inputs is illustrated in the case of the pavements. It was expected in the industry that since most bitumen is derived from oil the bitumen pavement will be more sensitive to oil price changes than a concrete one. The analysis suggests, however, that this should not be the case, both types having similar primary energy requirements per m<sup>2</sup>. This conclusion is confirmed by the fact that despite the fuel price rise of recent years the relative proportion of the two types of construction have not markedly altered [2].

#### METHODS

Wind power, for example, specializes in the conversion of energy in the atmosphere of air masses in the electrical, mechanical, thermal, or in any other form of energy suitable for use in the economy. Such a transformation can be performed by such units as the wind turbine, windmill, etc. The damage caused by sources of energy - is minimized.

Solar energy is the direction of alternative energy, based on the direct use of solar radiation to produce energy in any form. Solar energy uses the inexhaustible source of energy and is environmentally friendly. But this seemingly simple form of energy generation has its drawbacks, depending on weather conditions, high cost of construction, heating of the atmosphere above the power station, etc. However, in the world this type of power generation is widely used by large helium thermal stations to small Christmas trees in large metropolitan areas. Stadiums, station cleaning and processing, transportation - all this and more is being increasingly used the energy of the sun [2].

Energy analyses aim to through all the energy inputs involved in the production of some item by the industrial system. This is called the Gross Energy Requirement (GER) of the good or service.

Any process of manufacture or construction will not only require energy in the form of direct fuel inputs (diesel, electricity, etc.) but will also consume energy direct indirectly in the form of materials and capital equipment. Consider, for example, the construction of a dam. This will involve the use of fuel directly in onsite applications. There will also be energy inputs involved in manufacturing the materials used on site in their transport to site. Allowance must also be made for the energy used in the manufacture and maintenance of plant (suitably apportioned to the construction of the dam) [3].



In fact, an exhaustive analysis of the energy required to provide the dam should, in theory at least, consider the entire industrial system. This is because any capital or consumer good can be considered as the end result of a long chain of productive processes, occurring both in the industry concerned directly with the final manufacture of the good (in the case of a dam, the civil engineering industry) and in the industries supplying raw materials and capital equipment to this industry manufacture.

Results from these sources are presented in the form of 'energy intensities' of industries, measured in MJ per pound. Since the energy intensities are based on published statistics they are only available for aggregate industries, or 'average products' of the industries, rather than individual products. This is satisfactory when an industry has a relatively homogeneous output (as in the case of steel or cement) but may lead to errors when a diversity of products and activities are classified to one industry group. Thus in the case of 'construction' which is a very large group, only two energy intensities are available - one for the private sector and another for the republic sector. Another problem with energy intensities is that, since they are based on money measures, one is confronted with the familiar problems of adjustment from year to year.

#### COMBUSTIBLE MATERIALS NOT NORMALLY USED AS FUELS

Unlike solar and space power it does not need the atmosphere, so its main advantage is that power generation does not depend on the weather and season. The transfer is carried out by means of radio waves through the huge 20 kilometer-long antennas and receivers on the ground. The second mode of transmission that can be used is the transmission of the light beam with lasers and receiving light catcher on the ground [3, p. 56].

As already mentioned, the GER includes all energy inputs to the provision of a good or service. It is essentially the calorific value of all fuel used in the provision of the good or in industry may be combustible, but not be in widespread use as fuels. Wood is an example of materials which causes problems in this respect. On Slesser's interpretation of the IFIAS conventions the GER of any good must include the calorific value of any inputs which could in principle be used as a fuel. We would argue that it is more useful in the context of energy policy if the contributions to the GER of a product or service are limited to those derived from energy sources conventionally classed as fuel sources (Oil, coal, hydroelectricity, natural gas, and nuclear power). The production of bitumen and plastics involve the depletion of fuel resources and the GER of these materials does include an allowance for the calorific value of these resources (namely the calorific value of the feed stocks from which bitumen and plastics are manufactured). The provision of one unit of energy to the final consumer requires the sequestration of greater than one unit of primary fuel resources (in, for example, mining, transformation and conversion). This ratio is measure of the "resource efficiency" of the fuel industries and varies from around four for electricity to close to one for coal. Since the energy analysis is concerned with the sequestration of primary fuels these ratios must be taken into account. A problem of convention arises in dealing with electricity generated in nuclear and hydro- electric stations. The problem is in deciding how to quantify the calorific value of the input into these stations [3, p.87].

Over the past ten years mankind has made a huge step towards the development of alternative energy, but even though the primary sources are still oil and coal, people will soon want to change to something new.

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## **LASERS IN CANCER TREATMENT**

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**Summary:** Lasers as one of the means in cancer treatment are examined in the presented article. The advantages and disadvantages of lasers compared with standard surgical tools, the mechanism of their work in treating or preventing side effects of common cancer treatments are described.

**Key words:** adenoma, angiogenesis, benign tumors, basal cell skin cancer, carcinoma, leukemia, lymphoma, malignant tumors, metastasis, sarcoma, photodynamic therapy, polyp.

**Анотація:** У поданій статті досліджуються лазери, як один із засобів, який застосовується при лікуванні рака. Описуються переваги і недоліки лазерів у порівнянні з стандартними хірургічними інструментами, механізм їх дії при лікуванні і при запобіганні небажаної побічної дії в ході традиційного лікування.

**Ключові слова:** аденома, ангиогенез, базально-клітинна ракова пухлина шкіри, доброякісні пухлини, злоякісні пухлини, карцинома, лімфома, лейкемія, метастазування, саркома, фотодинамічна терапія, поліп.

**Аннотация:** В представленной статье рассматриваются лазеры, как один из способов лечения рака. Описываются преимущества и недостатки лазеров в сравнении со стандартными хирургическими инструментами, механизм их работы в ходе лечения и при предотвращении побочных эффектов в ходе традиционного лечения.

**Ключевые слова:** аденома, ангиогенез, базально-клеточный рак кожи, доброкачественные опухоли, злокачественные опухоли, карцинома, лимфома, лейкемия, метастазирование, саркома, полип, фотодинамическая терапия.

Cancer is a class of diseases characterized by out-of-control cell growth. There are over 100 different types of cancer, and each is classified by the type of the cell that is initially affected.

Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors (except in the case of leukemia where cancer prohibits normal blood function by abnormal cell division in the blood stream). Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. Tumors that stay in one spot and demonstrate limited growth are generally considered to be benign.

More dangerous, or malignant, tumors form when two things occur:

1. A cancerous cell manages to move throughout the body using the blood or lymph systems, destroying healthy tissue in a process called invasion.
2. That cell manages to divide and grow, making new blood vessels to feed itself in a process called angiogenesis [5].

When a tumor successfully spreads to other parts of the body and grows, invading and destroying other healthy tissues, it is said to have metastasized. This process itself is called metastasis, and the result is a serious condition that is very difficult to treat.

Cancer is ultimately the result of cells that uncontrollably grow and do not die. Normal cells in the body follow an orderly path of growth, division, and death. Programmed cell death is called apoptosis, and when this process breaks down, cancer begins to form. Unlike regular cells, cancer cells do not experience programmatic death and instead continue to grow and divide. This leads to a mass of abnormal cells that grows out of control.

There are five broad groups that are used to classify cancer.

1. Carcinomas are characterized by cells that cover internal and external parts of the body such as lung, breast, and colon cancer.

2. Sarcomas are characterized by cells that are located in bone, cartilage, fat, connective tissue, muscle, and other supportive tissues.

3. Lymphomas are cancers that begin in the lymph nodes and immune system tissues.

4. Leukemias are cancers that begin in the bone marrow and often accumulate in the bloodstream.

5. Adenomas are cancers that arise in the thyroid, the pituitary gland, the adrenal gland, and other glandular tissues.

Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast.

Laser therapy involves the use of high-intensity light to destroy cancer cells. This technique is often used to relieve symptoms of cancer such as bleeding or obstruction, especially when the cancer cannot be cured by other treatments. It may also be used to treat cancer by shrinking or destroying tumors.

The word LASER actually stands for Light Amplification by Stimulated Emission of Radiation. Laser light is different from regular light. The light from the sun or from a light bulb has many wavelengths and spreads out in all directions. Laser light, on the other hand, has a single wavelength and can be focused in a very narrow beam. This makes it both powerful and precise. Lasers can be used instead of blades (scalpels) for very careful surgical work, such as repairing a damaged retina in the eye or cutting through body tissue.

Lasers are named for the liquid, gas, solid, or electronic substance that is used to create the light. Many types of lasers are used to treat medical problems, and new ones are being tested all the time. Today, 3 kinds of lasers are commonly used in cancer treatment: carbon dioxide (CO<sub>2</sub>), argon, and the neodymium.

The CO<sub>2</sub> laser is mainly a surgical tool. It can cut tissue with fairly little bleeding as the light energy changes to heat. This type of laser is used to remove thin layers from the surface of the skin without going into the deeper layers.

The argon laser only goes a short distance into tissue. It is useful in treating skin problems and in eye surgery. It is sometimes used during colonoscopies (tests to look for colon cancer) to remove growths called polyps before they become cancer. It can be used with light-sensitive drugs to kill cancer cells in a treatment known as photodynamic therapy (PDT) [3].

Light from neodymium laser can go deeper into tissue than light from other types of lasers, and it can make blood clot quickly. Neodymium lasers can be used through thin flexible tubes called endoscopes to get to hard-to-reach parts inside the body, such as the swallowing tube (esophagus) or large intestine (colon). This light can also travel

through optical fibers, which can be bent and put into a tumor to heat it up and destroy it.

Laser therapy uses high-intensity light to treat cancer and other illnesses. Lasers can be used to shrink or destroy tumors or precancerous growths. Lasers are most commonly used to treat superficial cancers (cancers on the surface of the body or the lining of internal organs) such as basal cell skin cancer and the very early stages of some cancers, such as cervical, penile, vaginal, vulvar, and non-small cell lung cancer.

Lasers also may be used to relieve certain symptoms of cancer, such as bleeding or obstruction. For example, lasers can be used to shrink or destroy a tumor that is blocking a patient's trachea (windpipe) or esophagus. Lasers also can be used to remove colon polyps or tumors that are blocking the colon or stomach.

Laser therapy can be used alone, but most often it is combined with other treatments, such as surgery, chemotherapy, or radiation therapy. In addition, lasers can seal nerve endings to reduce pain after surgery and seal lymph vessels to reduce swelling and limit the spread of tumor cells.

Lasers have some advantages and disadvantages compared with standard surgical tools.

Lasers are more precise than scalpels. Tissue near an incision is protected, since there is little contact with surrounding skin or other tissue. The heat produced by lasers sterilizes the surgery site, thus reducing the risk of infection.

Less operating time may be needed because the precision of the laser allows for a smaller incision.

Healing time is often shortened; since laser heat seals blood vessels, there is less bleeding, swelling, or scarring. Laser surgery may be less complicated. For example, with fiber optics, laser light can be directed to parts of the body without making a large incision.

More procedures may be done on an outpatient basis.

Few doctors and nurses are trained to use lasers. Laser equipment costs a lot of money. Strict safety precautions must be followed in the operating room when lasers are used. For example, the entire surgical team and the patient must wear eye protection. The effects of some laser treatments may not last long, so they may need to be repeated. And sometimes the laser cannot remove the entire tumor in one treatment, so more treatments may be needed.

Today one of the most common medical uses of lasers is in cancer treatment. They can be used in 2 ways to treat cancer:

1. *To shrink or destroy a tumor with heat;*

The CO<sub>2</sub> and neodymium lasers are used to shrink or destroy tumors. They can be used with thin, flexible tubes called endoscopes that let doctors see inside certain parts of the body, such as the bladder or stomach. The light from some lasers can be sent through an endoscope fitted with fiber optics. This lets doctors see and work in parts of the body that could not otherwise be reached except by major surgery. Using an endoscope also allows very precise aim of the laser beam.

Lasers can be used with low-power microscopes, too. This gives the doctor a larger view of the area being treated. When used with an instrument that allows very fine movement (called a micromanipulator), laser systems can produce a cutting area as small as 200 microns in diameter – that is less than the width of a very fine thread [4].

Lasers are used to treat many kinds of cancer. In the intestines or large bowel, lasers are used to remove polyps, small growths that may become cancer. The CO2 laser can be used to treat pre-cancerous tissue and very early cancers of the cervix, vagina, and vulva.

The neodymium laser has also been used to remove cancer that has spread to the lungs from other areas. This helps avoid surgery that would require removing large sections of lung. This type of laser cannot cure cancer, but it can improve breathing and other symptoms in many patients.

Cancers of the head, neck, airways, and lungs can be treated (but usually not cured) with lasers. Small tumors on the vocal cords may be treated with lasers instead of radiation in some patients. Tumors blocking the upper airway can be partly removed to make breathing easier. Blockages deeper in the airway, such as in the branches of the breathing tubes (bronchi), can be treated with a flexible, lighted tube called a bronchoscope and a neodymium laser.

Laser-induced interstitial thermotherapy (LITT), or interstitial laser photocoagulation, also uses lasers to treat some cancers. LITT is similar to a cancer treatment called hyperthermia, which uses heat to shrink tumors by damaging or killing cancer cells. During LITT, an optical fiber is inserted into a tumor. Laser light at the tip of the fiber raises the temperature of the tumor cells and damages or destroys them. LITT is sometimes used to shrink tumors in the liver [2].

2. Lasers are used to activate a chemical that kills only the cancer cells. (This is called photodynamic therapy or PDT.)

In photodynamic therapy (PDT), a special drug called a photosensitizing agent is put into the bloodstream. Over time it is absorbed by body tissues. The drug stays in or around cancer cells for a longer time than it does in normal tissue. Shining a certain kind of light on the drug that is in the cancer cells causes a chemical reaction that then kills the cancer cells. Photosensitizing agents are 'turned on' or activated by a certain wavelength of light. For example, an argon laser can be used in PDT. When cancer cells that contain the photosensitizing agent are exposed to red light from this laser, it causes the chemical reaction that kills the cancer cells. Light exposure must be carefully timed so that it is used when most of the agent has left healthy cells, but is still in the cancer cells.

PDT has some advantages over other treatments. Cancer cells can be singled out and destroyed but most normal cells are spared. The damaging effect of the photosensitizing agent happens only when the drug is exposed to light. The side effects are fairly mild.

Still, PDT as it is currently used is not without its problems. Argon laser light cannot pass through more than about 1 centimeter of tissue (a little more than one-third of an inch), which means it is not useful against deeper tumors. And the photosensitizing agents used today can leave people very sensitive to light, causing sunburn-like reactions after only very brief sun exposure. This can greatly limit the patient's activities until the body gets rid of the drug, which often takes weeks.

PDT is sometimes used to treat cancers and pre-cancers of the swallowing tube (esophagus), and certain kinds of lung cancer that can be reached with endoscopes. PDT is being studied for use in other cancers, such as those of the brain and prostate.

Researchers also are looking at different kinds of lasers and new photosensitized drugs that might work even better [1; 3].

Though lasers can be used alone, they are most often used along with other cancer treatments, such as chemotherapy or radiation.

Lasers are also being studied for treating or preventing side effects of common cancer treatments. For instance, some studies are looking at how lasers might be used to prevent or treat severe mouth sores caused by chemotherapy, and how they may be used to treat the swelling that can result after breast surgery. More research is needed to learn about these possible uses for lasers [5].

Because of their power and precision, lasers are well-suited for certain cancer surgeries, and doctors are trying to find new and better ways to use them. In clinical trials (research studies), doctors are using lasers to treat cancers of the brain and prostate, among others. As more cancer surgeons learn to use lasers, as the lasers themselves become smaller and cheaper, and as technology improves to allow tumors deep within the body to be treated, lasers will probably be used more often as part of cancer treatment.

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## **MODERN APPLICATIONS OF FLUORESCENCE SPECTROSCOPY**

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**Summary:** The article deals with some modern applications of such powerful and highly sensitive method of research as fluorescence spectroscopy. Fluorescent sensing and imaging as well as technique of single molecule spectroscopy are considered. Prospects of application of fluorescence spectroscopy are very large and promising, especially in the field of biological studies.

**Key words:** biological studies, energy transfer, fluorescence, imaging, proteins, spectroscopy.

**Анотація:** Стаття присвячена деяким сучасним використанням такого потужного і високочутливого методу дослідження як флуоресцентна спектроскопія. Розглянуто флуоресцентний кількісний аналіз та візуалізацію, техніку одномолекулярної спектроскопії. Перспективи використання флуоресцентної спектроскопії дуже великі та багатонадійні, особливо в області біологічних досліджень.

**Ключові слова:** білки, біологічні дослідження, візуалізація, перенос енергії, спектроскопія, флуоресценція.

**Аннотация:** Статья посвящена некоторым современным применениям такого мощного и высокочувствительного метода исследования как флуоресцентная спектроскопия. Рассмотрены

флуоресцентный количественный анализ и визуализация, техника одномолекулярной спектроскопии. Перспективы применения флуоресцентной спектроскопии очень велики и многообещающи, особенно в области биологических исследований.

**Ключевые слова:** белки, биологические исследования, визуализация, перенос энергии, спектроскопия, флуоресценция.

*Introduction.* The luminescence phenomenon, which involves the emission of electromagnetic radiation by chemical substances, is one of the most active current research fields [5]. The first observation of fluorescence from a quinine solution in sunlight was reported by Sir John Frederick William Herschel in 1845, and from that time the fast development of the fluorescence spectroscopy began [7].

Fluorescence spectroscopy and imaging have become powerful and widely used methods in almost any laboratory around the globe for the non-invasive study of polymers, inorganic materials and biological objects. With the development of elaborate single-molecule fluorescence techniques, energy and electron transfer methods have experienced a renaissance and today they are used successfully to study structure of macromolecules, molecular motion and interactions. New methods that have been introduced to increase the optical resolution of microscopy beyond the diffraction barrier enable researchers to study cellular structures with amazingly high resolution, which seemed impossible to achieve only a few years ago [6].

*Fluorescence sensing.* Fluorescence sensing of various analytes is an active area of modern research. The efforts of scientists to develop new effective fluorescent sensors are driven by the desire to eliminate the use of radioactive tracers which are costly to use and dispose of. There is also a need for rapid and low-cost testing methods for a wide range of clinical and environmental applications [7].

First of all, concentration of different analytes such as  $O_2$ ,  $CO_2$ ,  $NO$ ,  $H_3O^+$  (pH), metal cations, various anions, carbohydrates etc. can be determined with the methods of fluorescence spectroscopy. Any phenomenon that results in a change of fluorescence wavelength, intensity, lifetime, or anisotropy can be used for sensing.

There are several mechanisms of sensing including 1) quenching, 2) resonance energy transfer (RET), 3) photoinduced electron transfer (PET) and other mechanisms that are based on different spectral properties of fluorophore in the presence of analyte and without it [7]. Let us consider some of these mechanisms in details.

1) A fluorescence quencher is a compound, the presence of which in the vicinity of a fluorophore leads to the decrease of the fluorescence quantum yield and lifetime of the latter. For example, those molecules or ions can function as a quencher that are added to the solution and introduce new or promote already existing non-radiative deactivation pathways (solute quenching) by molecular contact with the chromophore. Further possibilities are self-quenching by simply another fluorophore molecule of the same type, and quenching by solvent molecules [3]. Molecular oxygen, iodide, bromide and chloride ions, acrylamide are common quenchers [3, 8, 10]. So these species and many other quenchers can be detected and quantitatively characterized with different fluorophores.

For instance, for use as an oxygen sensor the metal-ligand complexes (TMCs), such as  $[Ru(Ph_2phen)_3]^{2+}$ , are usually dissolved in silicone in which oxygen is rather soluble and freely diffusing. Due to their long life-times, large shifts between excitation

and emission and efficient luminescences, TMCs have become important O<sub>2</sub> sensors [7].

2) Resonance energy transfer plays important role in fluorescence sensing. Energy transfer occurs whenever the donor and acceptor are within the Förster distance. In RET-based sensing the donor can be selected for use with the desired light source, and need not be intrinsically sensitive to the analyte. The acceptor can be chosen to display a change in absorption in response to the analyte. The representative life-time based sensor for pCO<sub>2</sub> consists of donor [Ru(dpp)<sub>3</sub>]<sup>2+</sup> (“dpp” – 4,7-diphenyl-1,10-phenanthroline) and acceptor Sudan III which displayed a CO<sub>2</sub>-dependent absorption spectrum [7].

3) Photoinduced electron transfer is an electron transfer resulting from an electronic state produced by the resonant interaction of electromagnetic radiation with matter [2]. PET can be used for sensing of pH, concentrations of metal and nonmetal ions. For example, phosphate ions can bind to anthracene derivative with an aminoalkyl side chain. Anthracene fluorescence increases due to hydrogen bonding of phosphate to the amino groups [7].

Probes for analyte recognition can bind to analyte in specific way (e.g. form a chelate complex) and at the same time change their spectral properties. Extensive efforts have been directed toward the design and synthesis of fluorescent probes for cations: Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and many others. The examples of probes for analyte recognition also include fluorophores that are sensitive to glucose. These probes use boronic acid as a part of the fluorophore. Complexation of sugars to boron-containing fluorophores can result in changes in emission intensity [7].

*Fluorescence imaging.* Fluorescence spectroscopy-based techniques using conventional fluorimeters have been extensively applied since late 1960s to study different aspects of membrane related phenomena, i.e., relating to lipid-lipid, lipid-protein (peptide), and lipid-DNA interactions. These types of studies encompass measurements of fluorescence excitation and emission spectra, fluorescence time decays (lifetimes) and fluorescence polarization (or anisotropy) using a large variety of fluorescent probes [1].

The first experiments reporting visualization of lipid domains in bilayers by means of fluorescence microscopy provided new valuable information (such as shape and size distribution of different lipid domains), not available before in the membrane field. At the present time, there are a number of laboratories actively performing spectroscopy in a microscope for a variety of protocols and generating exciting results from studies ranging from cell physiology to the mechanics of polymer motion on surfaces [1].

The technique that is widely used for cell imaging is a multiphoton microscopy (MPM) that is based on multiphoton excitation (MPE). MPE is accomplished using longer-wavelength excitation to avoid much stronger single-photon absorption of the fluorophore, so that 2 or 3 photons are needed to reach the same energy level due to one-photon absorption. Multiphoton microscopes have been used extensively for cellular imaging. For example, MPM can be used for calcium imaging or for measurement of rapid signaling events in cells. Multiple fluorophores could be excited by MPE at a single wavelength, so it is convenient to carry out experiment labeling different regions of cell with different specific fluorophores [7].



A longstanding goal of MPM has been to obtain three-dimensional images of cells. This is possible because the localized excitation allows collection of images at various focal planes in the cell. Using these 2D images it is possible to reconstruct a 3D image [7].

Quantum dots (QDots), such as CdSe, CdS, ZnS, have the potential to revolutionize and expand fluorescence imaging and screening applications in biology and medicine [3]. Colloidal semiconductor quantum dots are single crystals a few nanometers in diameter whose size and shape can be precisely controlled by the duration, temperature and ligand molecules used in the synthesis. This process yields QDots that have composition- and size-dependent absorption and emission [9].

Over the past few years, QDots have been tested in most biotechnological applications that use fluorescence, including DNA array technology, immunofluorescence assays, and cell and animal biology. Some of the early and most successful uses of QDots have been in immunofluorescence labeling of fixed cells and tissues; immunostaining of membrane proteins, microtubule, actin, and nuclear antigens. The main advantage of QDots resides in their resistance to bleaching over long periods of time (minutes to hours), allowing the acquisition of images that are crisp and well contrasted. This increased photostability is especially useful for three-dimensional (3D) optical sectioning, where a major issue is bleaching of fluorophores during acquisition of successive z-sections, which compromises the correct reconstruction of 3D structures [9].

*Single-molecule fluorescence spectroscopy.* Single molecule spectroscopy provides an insight into the behaviour of each individual molecule. The simplest reason of using single-molecule experiments is the need to achieve very high sensitivity. Single molecule measurements represent the ultimate level of sensitivity – the ability to detect  $1.66 \cdot 10^{-24}$  mole of the object of interest (1.66 yoctomole). Sensitivity is clearly a strong driving force in applications such as pathology and diagnostic medicine in which one would ideally like to be able to detect one copy of a protein or gene that is indicative of disease. Measurement sensitivity will also play a key role in overcoming the contemporary challenges of studying and developing nanoscale devices and subsequently interfacing with them. As well as high sensitivity, single molecule measurements also provide information about the probe fluorophore local microenvironment with extremely high spatial resolution [4].

Various properties of single fluorescent probes attached to macromolecules can be exploited to provide information on molecular interactions, enzymatic activity, reaction kinetics, conformational dynamics, molecular freedom of motion, and alterations in activity and in chemical and electrostatic environment. “Native” fluorescence probes such as fluorescing products and fluorescing enzymes were successfully used to probe enzymatic turnovers of single molecules [13].

A simple, but powerful, use of single-molecule detection localizes a single fluorophore with a few tens of nanometers precision. The dimensions of a dye molecule are much smaller than the wavelength of light it emits, and therefore it acts as a point source of light. The response of the optical system to this point source is a spot of light, the center of which can be localized with great accuracy. This localization precision has been used to follow the motion of individual motor proteins, the diffusional trajectories of labeled lipid molecules in membranes, and the diffusion of molecules in gels, in

solutions, and at the liquid-solid interface. This positioning accuracy can be further exploited for colocalizing two (or more) different macromolecules. When two macromolecules are labeled with two noninteracting fluorophores that differ in their optical properties (absorption and emission spectra, fluorescence lifetime, dipole orientation), they can be colocalized with nanometer accuracy and can report on association, binding, and enzymatic-turnover events. Even higher colocalization accuracy can be obtained when the two fluorophores interact by fluorescence resonance energy transfer. This technique, capable of measuring distances on the 2- to 8-nm scale, relies on the distance-dependent energy transfer between a donor fluorophore and acceptor fluorophore. Chemical and electrostatic activity could be studied by monitoring changes in the rotational freedom of motion of a tethered fluorophore. The various interactions between the fluorophore, the macromolecule, and the surrounding solvent determine to what extent the probe is free to rotate around its tether. Changes in conformation, charge, potential, redox state, hydrophathy, local pH, steric interactions, and stability may result in changes in the fluorophore's rotational diffusion [13].

*Study of protein structure.* Fluorescence spectroscopy is one of the most important methods of study such macromolecules as proteins. For instance, solute quenching reactions provide information about the location of fluorescent groups in the examined molecular structure. A fluorophore that is located on the surface of such structure will be relatively accessible to a solute quencher. A quenching agent will quench the chromophore that is buried in the core of the molecular assembly to a less degree. Thus, the quenching experiment can be used to probe topographical features of the examined structure and to detect structural changes that may be caused by addition of external compounds or changed physical conditions [3].

Among biopolymers, proteins are unique in displaying useful intrinsic fluorescence. In proteins, the three aromatic amino acids – phenylalanine, tyrosine, and tryptophan – are all fluorescent. A valuable feature of intrinsic protein fluorescence is the high sensitivity of tryptophan to its local environment. Changes in the emission spectra of tryptophan often occur in response to conformational transitions, subunit association, substrate binding, or denaturation. These interactions can affect the local environment surrounding the indole ring. Tyrosine and tryptophan display high anisotropies that are often sensitive to protein conformation and the extent of motion during the excited-state lifetime. Also, tryptophan appears to be uniquely sensitive to collisional quenching, apparently due to a tendency of excited-state indole to donate electrons. Tryptophan can be quenched by externally added quenchers or by nearby groups within the proteins. So, the high sensitivity of the emission from tryptophan to the details of its local environment has provided numerous opportunities for studies of protein functions, folding and dynamics [7].

The method of single molecule fluorescent spectroscopy is also widely used for studying protein structure and motion [11, 12].

*Conclusion.* Fluorescence spectroscopy, taking an intensive path of development for more than a hundred and fifty years, in the 21<sup>st</sup> century has become one of the leading research methods that are applied in various branches of chemical, biological and physical sciences. Nowadays the greatest efforts for investigation of the structure and properties of biological microobjects are made, and the methods of fluorescence spectroscopy allow scientists to achieve high accuracy in the results obtained.

Fluorescence sensing and imaging allow to solve a number of important and serious problems that deal with fundamental and applied (for example, in the clinical analysis) research. Prospects of application of fluorescence spectroscopy are very large and promising.

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## **THE INDICES OF NITROGENOUS AND CARBOHYDRATE METABOLISM IN RATS WITH DIFFERENT EMOTIONAL STATUS UNDER GLYCEROL MODEL OF RHABDOMYOLYSIS**

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**Summary:** There is a clear correlation between features of metabolism and nervous and endocrine systems status of all creatures. Animals which have different levels of emotional and nervous organization can respond to the various factors in different ways. They differ in hormones and neuromediators levels, contents of free radical lipid peroxidation products and possibility to resist some pathogenic effects. All animals are conditionally divided into two groups: emotional active and passive.

There was used one of models of oxidative stress in this experiment which called rhabdomyolysis. It was caused by intramuscular glycerol administration which led to releasing

dangerous intracellular components into the blood stream and increasing reactive oxygen species (ROS) level which upset normal prooxidant/antioxidant balance in organism. Antioxidants are biologically active molecules which are able to protect organism from peroxidation, so the main purpose of this experiment is to study some possible protective mechanisms of glutathione and changes in the indices of nitrogenous and carbohydrate metabolism in rats with different emotional status under experimental rhabdomyolysis.

**Key words:** emotional status, rhabdomyolysis, prooxidant/antioxidant balance, nitrogenous and carbohydrate metabolism, glycerol, glutathione.

**Анотація:** Існує чіткий зв'язок між особливостями метаболізму та станом нервової та ендокринної систем усіх живих створінь. Тварини з різним рівнем емоціональної нервової організації можуть реагувати на різноманітні впливи по-різному. Вони відрізняються рівнем гормонів та нейромедіаторів, вмістом продуктів вільнорадикального окислення ліпідів та здатністю чинити опір деяким патогенним впливам. Усі тварини умовно поділяють на дві групи: емоціонально активні та пасивні.

В цьому експерименті була використана одна із моделей оксидативного стресу – рабдоміоліз. Він був викликаний внутрішньом'язовим введенням гліцерола, який призводив до вивільнення у кров'яне русло небезпечних внутрішньоклітинних компонентів та підвищення рівня активних форм кисню, що порушували нормальний прооксиданто-антиоксидантний баланс в організмі. Антиоксиданти – це біологічно активні молекули, що здатні захищати організм від окислення, тому головна мета даного експерименту - вивчити деякі можливі захисні механізми дії глутатіона та зміни показників вуглеводного та азотистого метаболізму у крис із різним емоціональним статусом при експериментальному рабдоміолізі.

**Ключові слова:** вуглеводний і азотний метаболізм, гліцерин, глутатіон, емоційний статус, рабдоміоліз, прооксиданти-антиоксидантний баланс.

**Аннотация:** Существует четкая связь между особенностями метаболизма и состоянием нервной и эндокринной систем всех живых существ. Животные с разным уровнем эмоциональной нервной организации могут реагировать на различные воздействия по-разному. Они отличаются уровнем гормонов и нейромедиаторов, содержанием продуктов свободнорадикального окисления липидов и способностью сопротивляться некоторым патогенным воздействиям. Все животные условно подразделяют на две группы: эмоционально активные и пассивные.

В этом эксперименте была использована одна из моделей оксидативного стресса – рабдомиолиз. Он вызывался внутримышечным введением глицерола, который приводил к выходу в кровяное русло опасных внутриклеточных компонентов и повышению уровня активных форм кислорода, которые нарушали нормальный прооксиданто-антиоксидантный баланс в организме. Антиоксиданты – это биологически активные молекулы, которые способны защищать организм от окисления, поэтому главная цель данного эксперимента - изучить некоторые возможные защитные механизмы действия глутатиона и изменения показателей углеводного и азотистого метаболизма у крыс с различным эмоциональным статусом при экспериментальном рабдомиолизе.

**Ключевые слова:** эмоциональный статус, рабдомиолиз, прооксиданто-антиоксидантный баланс, углеводный и азотистый метаболизм, глицерол, глутатион.

Features of metabolism of all creatures are associated with their nervous and endocrine system status. Animals with different emotional nervous organization differ in the level of neuromediators exchange and lipid peroxidation. Some influences of factors of physical and chemical nature lead to prooxidant/antioxidant balance changes in organism and development of oxidative stress.

There was used one of models of oxidative stress in this study - rhabdomyolysis caused by intramuscular glycerol administration.

Oxidative stress – is the process of cell damage caused by free radicals effects – reactive oxygen species (ROS). A lot of ROS are generated in the cell constantly, 5% of

oxygen which get into tissues and turns into free radicals. The level of free radicals is so low that the cell is able to inactivate them by an antioxidant system. But the level of ROS which exceeds protective opportunities of the cell can cause serious cell damages (for example, ATP exhaustion). As a result one of the least reactive ROS superoxide turns into more aggressive one which can cause oxidation and damage of membrane proteins and lipids, DNA. Cells can return into initial condition if violation is not very large. But more marked oxidative stress causes cell death. Cell membrane ruins during necrosis and cell content releases in intracellular space. It may damage surrounding cells and tissues and cause the cascade of pathological processes.

Somatic muscles are target for different damages as a result of influences of environment, metabolical changes and infection agents. Damage of muscle sarcolemma and release of potentially dangerous intracellular components into the blood stream and after-effects of these processes are forming the main point of rhabdomyolysis syndrome.

The development of acute renal deficiency and electrolytic violations such as hyperpotassiumemia and hypocalcemia appear as dominating consequences of rhabdomyolysis.

Antioxidants are biologically active molecules the main function of which is to protect the organism from peroxidation. Mechanisms of their action can be different: activation (reactivation) of antioxidant enzymes, suppression reactions in organism which lead to ROS formation, displacement of free radical peroxidation reactions to the side of less reactive compounds formation, etc.

Animals which belong even to one pure line are different from one another in their behavior, level of moving and emotional activity. Animals are divided into two groups depending on stability to emotional stress: emotionally active and emotionally passive animals. They differ in the hormones and neuromediators level, content of free radical lipid peroxidation products and possibility to resist some pathogenic effects. That is why the main purpose of this experiment is to study possible antioxidant effects of glutathione on the indices of nitrogenous and carbohydrate metabolism in rats with different emotional status under experimental rhabdomyolysis.

## **Materials and methods**

There were used 54 three month old male albino Wistar rats weighing 160-220 grams in this experiment. Animals were divided into two groups:

1. Emotionally active animals.
2. Emotionally passive animals.

There were 4 sub-groups in each group:

- a. Control group of animals which received physiological solution.
- b. Animals which received glycerol.
- c. Animals which received glutathione.
- d. Animals which received glutathione prior to glycerol administration.

After 4 hours animals were taken for the experiment under light ether anesthesia, blood was taken to obtain serum for determining glucose, urea and creatinine levels. Liver was irrigated by physiological solution. Glycogen concentration was determined by Kamp's method.

The results obtained were represented in the diagrams and tables.

The results obtained in groups with normal distribution calculated with Past program.

Glucose and urea content in blood serum and glycogen content in liver tissues of animals which belong to both groups didn't differ for certain, but they were different by the creatinine level in blood serum.

Animals with different emotional status had various reactions on the glycerol injections. The experiment showed that the glucose level increased under glycerol injections in emotionally active rats, but in emotionally passive rats - there is no reliable increasing.

Glycerol administration caused glycogen content decreasing in liver tissues of both groups of rats. Glutathione administration prior to glycerol injections prevented glycogen content decreasing.

Glycerol administration caused urea level increasing in blood serum of emotionally active and passive animals. Glutathione administration prior to glycerol injections prevented urea level increasing in blood serum of emotionally active rats.

Glutathione administration prevented glucose content increasing in blood serum of emotionally passive animals.

## **Discussion**

Emotionally active animals are distinguished by increased creatinine content in blood serum in comparison with the second group of rats. It can be explained that creatinine is a "reflection" of the moving muscle activity level. The first group of animals is emotionally active therefore they have higher moving activity.

During the oxidative stress caused by free haem accumulation the first adaptational answer of the organism is glycogenolysis activation namely disintegration of glycogen to glucose and glucose-6-phosphate which runs in liver and muscles. During this process glucose level is getting higher.

Glycogen content changes in liver and glucose in blood serum can testify to the activation of the sympatho-adrenalic system under rhabdomyolysis and adaptive reactions starting which are directed at the intensifying providing free glucose to the organism. Glucose mobilization in the early period of the stress-reaction development is provided by glycogen disintegration in liver and then by gluconeogenesis activation.

Glutathione administration prior to glycerol injection prevented its effect on the glucose content in blood serum and glucose concentration didn't differ from the control group.

Glycerol administration caused urea content increasing in blood serum of rats of both groups. Increasing of urea concentration reflects proteins disintegration intensification and activation of nitrogenous metabolism during the stress-reactions development. Transamination and desamination processes are activated, free ammonia is formed to be used in the urea synthesis process.

Preliminary glutathione administration prevented glycerol effects on the nitrogenous metabolism of emotionally active rats. Creatinine is an index which reflects the kidneys function and skeletal muscles damage. Creatinine releases from twitch cells of muscle tissue, gets into the blood, moves to kidneys, then outputs with urine. Thus creatinine content increasing in blood is an index of kidneys work disorders and renal failure.

During glycerol administration we didn't observe any significant changes in creatinine content in blood serum in both groups as to the control group. Kidney filter

violation occurs later under rhabdomyolysis, in our case after 4 hours creatinine releases from damaged muscles.

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УДК 911.3

## **SHALE GAS EXTRACTION – A GUARANTEE OF ECOLOGICAL CATASTROPHE IN THE REGION**

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**Summary:** The article analyzes the environmental consequences of the production of shale gas in the Kharkiv region.

**Key words:** shale gas, technology, field development, the danger of ecological catastrophe, chemical compounds.

**Анотація:** У статті аналізуються екологічні наслідки видобутку сланцевого газу на території Харківської області.

**Ключові слова:** сланцевий газ, технологія, розробка родовищ, небезпека, екологічна катастрофа, хімічні сполуки.

**Аннотация:** В статье анализируются экологические последствия добычи сланцевого газа на территории Харьковской области.

**Ключевые слова:** сланцевый газ, технология, разработка месторождений, опасность, экологическая катастрофа, химические соединения.

Kyiv - Kharkiv - Lviv – Shell company in the Kharkiv region leads the test boring for the future extraction of shale gas.

Whereas in the Western part of Ukraine there is still no understanding between local communities, regional councils and the American company Chevron, which plans to extract shale gas on the territory of Olesky area.

But in the West and in the East the environmentalists are against the extraction, and miners do not promulgate all the information about their technologies. The authorities are convinced that there are much more benefits from the exploitation of deposits than harm.

Should we allow Shell company to start the exploration on the territory of Kharkov region? Can we extract the gas, and what are the environmental risks of it? There are no clear answers to these questions among Kharkov scientists and ecologists. The last meeting of representatives of Shell company, local MPs and scientists in the walls of the Kharkiv regional Council confirmed this statement.

The extraction of shale gas is becoming more and more difficult. It is mostly because the population in different countries rebelled against such work on its territory. On the contrary, in the territory of Ukraine the initiative of gas extraction is picked up rapidly. The contract with a foreign Shell company has already been signed. The company has begun its activity in Kharkiv and Donetsk regions. The results of these is that almost the whole country will reap the fruits of its labor. Environmentalists are sounding the alarm about the insecurity of the technologies of extracting shale gas.

To make money at the expense of health – is a thankless and dishonourable action. All funds are subsequently used for treatment or prevention of diseases. Not everyone will agree to participate in the liquidation of Chernobyl catastrophe if he or she knows the whole truth about the consequences. For most foreigners Ukraine is associated with the area of Chernobyl. It seems that if it hadn't been for the state of emergency, quite a few people would have known about us. But the black advertising has done its job. Our country attracts foreign investors and businessmen.

Last year in autumn, there was a worldwide campaign against fracturing. People protested in the USA, Canada, Great Britain, Romania and many other countries. Their opinion is heard and measures are taken.

For example, France is recognized as the richest shale gas country in Europe. But it is strictly prohibited not only the extraction, but also the exploration of deposits of shale gas. What cannot be said about Ukraine. A small number of activists in Kyiv picketed the Ministry of Ecology. It seemed that a few people have heard about the fraction. Public organization «Green Front» conducted an explanatory work with the population. In Kharkov everybody was invited to watch the film about shale gas. In a half-empty cinema-house was showed the documentary of American filmmaker Josh Fox «Gas Land». It tells about the disastrous consequences for health and the environment in the area, where the operations were carried out concerning the extraction of shale gas. Before the first night this film was nominated for an Oscar and won many international competitions.

The politicians didn't remain silent too about impeding catastrophe. They picketed the Kharkiv regional Council. There was held the parliamentary session where the question of shale gas extraction in the region was solved once again. At the rally was heard such words:

«It is offered to extract shale gas in the territory of Ukraine, new working places are promised, it will be gas independence, but in fact by signing this agreement, the officials create the ability for them to «plunder» national goods».

A full scale preparatory work is taking place at the village of Fun, Pervomaisky district. The project depth of drilling is 5250 m. Ecologists of the whole world are



discussing the way of extraction shale gas from the bowels of the earth. At a depth of no less than 5 thousand meters the water is injected with a mixture of chemicals (more than 600 items simultaneously). Thus, there is a «water hammer».

The pressure blows up the layer and releases the gas. Chemical compounds that fall into the ground are not decomposed. They remain in the environment forever. The world practice has shown that 2% of the boreholes are the cause of thousands cases of pollution. That is why the population of the developed countries of Europe refused to have anything to do with shale gas on its territory or created boundary conditions for using it.

World practice noted negative aspects of this technology:

- fraction requires major stocks of water near the fields. For one fraction uses a mixture of water (7,500 tons), sand and chemicals. As a result, close to deposits a significant amounts of waste polluted water is accumulated which is not utilized by miners in accordance with environmental regulations;

- according to the experience of the development of Shale, shale wells have much shorter operation life than natural gas holes;

- formulae of chemical cocktail for fraction in companies which extract shale gas, are confidential. According to the reports of environmentalists, shale gas leads to significant contamination of groundwater with toluene, benzene, xylene, ethylbenzene, arsenic etc. Some companies use hydrochloric acid fluid thickened with the help of polymer, for one fracturing is used 80-300 tons of chemicals;

- shale gas has significant methane losses, which leads to the intensification of the greenhouse effect;

- shale gas production is profitable only if there is a high demand for it, and high gas prices.

According to the words of Kharkiv ecologists, deliberate injection of chemicals into the bowels of the earth is a crime. Such a procedure promises residents of the region a number of problems.

In chemistry lies the first danger of fracking: falling into water, fracking-liquid is dangerous for all living beings. It often contains such substances, as ethylene glycol (lethal dose for humans 100-300 ml), benzene (toxic, carcinogen, has a narcotic effect on the human body), methanol (strong poison, 5-10 ml causes poisoning, and 30 g - death of a person), boric acid (cellular poison, acute poisoning affects the brain, mucous membranes and skin, when using chronically - blood and reproductive cells; especially dangerous boric acid for developing the embryos – even the flow of a single non-toxic dose to the mother can cause pathological changes in the fetus), and so on. In fracking-liquid may contain more than 500 different chemical substances, not all of which have been studied enough from the point of view of danger to the human, environment, ecosystems.

The second problem of the method of gas extraction is observed from time to time the extrusion of «blue fuel» to the surface. And then the huge quantity of combustible pass by gas extractors, turning the water streams, holes and wells in detonating mixture, which can burn or even explode.

The third surprise for gasmen is the earthquake. Not strong, but frequent. Houses crack, landslides occur...

The fourth are «shanks». From the ground, except the valuable gas, come radioactive elements (radon, uranium and so on), various poisonous and toxic substances. All these «gifts» sooner or later ends up in rivers, lakes or in the fields.

Engineers of Shell company don't agree with ecologists. They are referring to the fact that the space between the pipe and the tank can be cemented. Then the threat about drinking water and environment will become irrelevant. It is difficult to assume, how the most powerful underground explosion will not destroy the cement. And is there any guarantee that artificially introduced lion's share of chemicals will not stay in the land and not subsequently infiltrate into the environment.

A detailed and reasonable description of the technology of extraction of shale gas in Ukraine is the only way to achieve mutual understanding. Yet there are no clear and intelligible answers to the arguments of environmentalists, from indifferent politicians and the population of the country. Ukrainians are faced with the fact that shale gas will be extracted here, with the help of this technology and full stop! And they didn't resist or have already got used to stand on their knees, or they didn't realize the depth of the problem and take on trust everything that is dictated from commercial TV screens.

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## **DEALING WITH CHRONIC PAIN**

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**Summary:** The article reviews the treatment of chronic pain. It describes new technologies applied by traditional medicine and also some alternative therapies that effectively help solve this problem.

**Key words:** chronic pain, non steroidal anti-inflammatory drugs (NSAIDs), transcutaneous electrical nerve stimulation (TENS), radiofrequency ablation, stress control techniques.

**Анотація:** Стаття присвячена огляду методів лікування хронічного болю. У ній описані нові технології, які застосовуються традиційною медициною, а також деякі альтернативні терапевтичні методи, які ефективно допомагають вирішити цю проблему.

**Ключові слова:** хронічний біль, нестероїдні протизапальні препарати (НПЗП), черезшкірна електронейростимуляція (TENS), радіочастотна абляція, методи управління стресом.

**Аннотация:** Статья посвящена обзору методов лечения хронической боли. В ней описаны новые технологии, которые применяются традиционной медициной, а также некоторые альтернативные терапевтические методы, эффективно помогающие решить эту проблему.

**Ключевые слова:** хроническая боль, нестероидные противовоспалительные препараты (NSAIDs), чрескожная электронейростимуляция (TENS), радиочастотная абляция, методы управления стрессом.

Today's pain specialists have sophisticated new treatments – from effective drugs to implants and electrical stimulation – to provide chronic pain relief. These advances

have emerged in the past several years, as researchers have gained a greater understanding of chronic pain and how it develops. The origins of chronic pain are all too familiar: sports injuries, back injuries, car accidents or health conditions like migraines, diabetes, arthritis, shingle and cancer. At times, however, there is no obvious cause of the chronic pain, no trauma or injury people can point to as a source of their chronic pain problem which has been frustrating for both patients and their doctors. In past generations, people often heard that chronic pain was "all in their heads". Today's pain specialists understand how the sensation of pain occurs, how the nervous system, including the spinal cord, interacts with the brain to create that sensation. Insights into the neurotransmitter system – the chemical messengers that pass nerve signals – have opened the door for important new modes of chronic pain relief. In recent years, scientists have learned how to manipulate those chemical messengers to change the way they interact with the brain's signals. That's led to the use of antidepressants and other drugs that work with specific brain chemicals that affect emotions, and help with perception of pain. And with advances in MRI imaging, researchers can clearly demonstrate that the changes are very real in the brain. Now it's possible to understand exactly where the sensation of pain is occurring in the brain when it is activated by stimuli. There is a new understanding, too, of a process called central sensitization. If initial pain from an injury is not adequately treated, those pain signals are sent repeatedly that leads to changes in the central nervous system, making it more and more sensitive. Over time, even the gentlest touch can become very painful. Pain specialists now prescribe treatments that attack moderate-to-severe chronic pain from different angles – innovative drugs, targeted nerve-zapping procedures, and drug pumps that deliver strong painkillers to the nerve root [6].

The first step in chronic pain relief is medications. When treating pain, doctors typically start with oral painkillers and non steroidal anti-inflammatory drugs (NSAIDs). These reduce inflammation and relieve pain, especially related to arthritis, tendinitis, nerve injury, mild to moderate cancer pain, and other forms of chronic pain. Finding which drugs work for chronic pain will likely be a trial-and-error process although specialists are honing in on the solutions. Individualized treatment is very important. When pain is severe, doctors turn to stronger pain relief medications – anticonvulsants. Drugs used to treat seizure disorders have been effective in chronic pain relief. It's still unclear how they control pain, but the drugs are believed to soften the effects on nerve-related pain such as post herpetic neuralgia from shingles. A new generation of anticonvulsant drugs is looking promising for chronic pain relief. There is a lot of work being done to improve these drugs, make them more convenient to take with fewer side effects.

Antidepressants will help with pain too. Low doses of common antidepressants are being prescribed for many chronic pain problems. These drugs adjust levels of brain chemicals, which are thought to be their mechanism for helping to control pain. Antidepressants often help when patients don't get complete chronic pain relief from other treatments. They relieve pain whether the person is depressed or not. The doses needed to treat pain are usually lower than doses used for depression treatment.

One of the most effective treatments for severe chronic pain is narcotic pain medications which work on the nerve cells' pain receptors. But use of narcotics has always been controversial. There's been a perception among many doctors that they will

get into legal problems if they undertreat or overtreat pain. There is a small risk of addiction, but studies show that when used appropriately, the risks are small. When prescribing narcotics, pain specialists often prescribe combinations of medications taking advantage of new extended-release antidepressants, for example. Combining medications lets them reduce the amount of narcotics and provide better pain relief, because the mechanism of narcotics is different from drugs like antidepressants and anticonvulsants. The synthetic narcotics don't have a risk of addiction. They are very effective in treating a lot of different types of pain syndromes.

One of the most famous targeted procedures to relieve pain is nerve blocks. When a group of nerves is causing pain to a specific organ or body region, the pain can be blocked with injection of a local anesthetic. Injections and nerve blocks are more effective for treating acute pain. If they're used early on for a pinched nerve, they can prevent chronic pain from developing.

Another method of pain treatment is radiofrequency ablation. In this outpatient procedure, a small area of nerve tissue is heated to decrease pain signals from that area. The procedure is conducted under guided CT imaging. A needle is inserted at the offending nerve site, and then an electrical current produced by a radio wave is used for the heat-and-destroy mission. The chronic pain relief lasts for a relatively long period, from three to six months. This is a big advance because it is a very localized, very specific pain treatment. It's not a cure-all, but it can really make a difference in specific cases [1].

Transcutaneous electrical nerve stimulation (TENS) therapy is helpful for short-term pain relief. The treatment involves a small device to deliver low-level electrical current when it's needed to help block pain. TENS is especially helpful in treating various types of muscle pain, and is often used with trigger point injections. Trigger points are painful sites in muscle or connective tissue. These trigger points can irritate the nerves around them and cause pain in other parts of the body. Extreme tenderness can also develop in nearby muscles or regions of the body. In a trigger point injection, a local anesthetic (sometimes with a steroid) is injected into trigger point to relieve the pain. It typically takes only a few treatments to resolve trigger point pain. It's a relatively simple and safe procedure [5].

Pain specialists also turn to more sophisticated technology to offer chronic pain relief. Pain pacemaker is another well-known technique, which is also called spinal cord stimulation. It involves a pacemaker-type device that is implanted in the body. The body delivers low-level electrical signals to the spinal cord or to specific nerves, which helps block pain signals from reaching the brain. The patient can adjust the on/off button and adjust the intensity of the electrical signals. Spinal cord stimulation is often used when other treatments have failed – as with failed back surgery. It is also used when cancer pain infiltrates a nerve root. When medications don't work, doctors advise patients to try the stimulator. If it works well, then they can get a permanently implanted stimulator [1].

Psychological counseling is another way to deal with chronic pain. It keeps people actively involved in their physical therapy. Such negative emotions as depression, anxiety, stress, and anger reduce the body's natural painkillers and increase the body's sensitivity to pain. With counseling, patients can learn coping skills and figure out

solutions to life problems that are causing stress or depression and regain a sense of control and pleasure in life [3].

There are also alternative treatments that depend on human. Relaxation techniques are an important part of pain treatment. Through regular practice, they help to reduce stress and promote relaxation, which helps with chronic pain relief. Deep breathing, meditation, guided imagery, hypnosis – all these allow mind to help the body. Stress makes pain worse, so learning to relax is a goal for patients. If a person is upset about something, his pain will go up several points on the pain scale, so stress control techniques can be very helpful for all types of pain [2]. Biofeedback, for example, is a process that enables an individual to learn how to change physiological activity for the purposes of improving health and performance. Precise instruments (such as electromyograph (EMG), electrodermograph (EDG), electroencephalograph (EEG), electrocardiograph (ECG) and others) measure physiological activity such as brainwaves, heart function, breathing, muscle activity, and skin temperature. These instruments rapidly and accurately 'feed back' information to the user. The presentation of this information – often in conjunction with changes in thinking, emotions, and behavior – supports desired physiological changes. Over time, these changes can endure without continued use of an instrument. Biofeedback helps people learn to train their minds to control body functions such as muscle tension, breathing, and heart rate – all of which helps reduce anxiety and stress reactions. Studies have shown that biofeedback reduces frequency and duration of headaches, and works as well as many medications in providing chronic pain relief [1].

Though many medical experts remain deeply skeptical about acupuncture, its use continues to spread – often alongside conventional medicine. Acupuncture does have real effects on the human body, which scientists are documenting using high-tech tools. A growing body of research suggests that it may have several mechanisms of action. Neuroimaging studies show that it seems to calm areas of the brain that register pain and activate those involved in rest and recuperation. It was also found that acupuncture works in part by stimulating the release of endorphins, the body's natural feel-good chemicals. It stimulates blood flow and tissue repair at the needle sites and sends nerve signals to the brain that regulates the perception of pain and reboot the autonomic nervous system, which governs unconscious functions such as heart beat, respiration and digestion. It increases the number of receptors for pain-reducing neurotransmitters, bringing patients relief. The most common uses of acupuncture are for chronic pain conditions like arthritis, lower back pain and headaches, as well as fatigue, anxiety and digestive problems, often when conventional medicine fails.

Doctors endorse the use of psychotherapy, relaxation techniques and alternative therapies, supported by growing evidence of the mind-body connection in chronic pain relief. It is an exciting time in pain management and there are more advances coming. The knowledge has increased tremendously in the last few years, though we still have a lot to learn. Research has given us clues in developing even newer treatment options.

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## STEM CELLS IN RESEARCH DIABETES TREATMENTS

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**Summary:** Different standpoints, approaches and theories concerning the usage of stem cells in diabetes treatment are considered in the presented article.

**Key words:** diabetes, pancreas, immune system, transplant, endocrine cell, gene, precursor cell.

**Анотація:** У поданій статті розглядаються різні точки зору, підходи до вивчення та теорії щодо вживання стволових клітин у лікуванні діабету.

**Ключові слова:** діабет, підшлункова залоза, імунна система, трансплантація, ендокринна клітина, ген, клітина провісник.

**Аннотация:** В представленной статье рассматриваются различные точки зрения, подходы к изучению и теории использования стволовых клеток при лечении диабета.

**Ключевые слова:** диабет, поджелудочная железа, иммунная система, трансплантация, эндокринная клетка, клетка-предшественник.

There is strong evidence that the behaviour of stem cells is strongly affected by their local environment. It is vitally important to identify the environmental signals that control stem cell expansion and differentiation in order to harness those signals to optimize delivery of stem cell therapies.

Stem cells undoubtedly offer tremendous potential to treat many human diseases, including ageing, cancer, diabetes, blindness and neurodegeneration and to repair tissue damage resulting from injury or ageing.

There are strong grounds for believing that over the next 50 years our understanding of stem cells will revolutionize medicine. In contrast to the golden era of developmental biology, one of stem cell research's defining characteristics is the motivation to benefit human health [8].

For decades, diabetes researchers have been searching for ways to replace the insulin-producing cells of the pancreas that are destroyed by a patient's own immune system.

Over the past several years, doctors have attempted to cure diabetes by injecting patients with pancreatic islet cells – the cells of the pancreas that secrete insulin and other hormones. However, the requirement for steroid immunosuppressant therapy to prevent rejection of the cells increases the metabolic demand on insulin-producing cells and eventually they may exhaust their capacity to produce insulin. The deleterious effect of steroids is greater for islet cell transplants than for whole-organ transplants. As a result, less than 8 percent of islet cell transplants performed had been successful [8].

Recently, James Shapiro and his colleagues have developed an experimental protocol (Edmonton protocol) for transplanting islet cells that involves using a much larger amount of islet cells and a different type of immunosuppressant therapy. In a

recent study, they report that, seven of seven patients who received islet cell transplants no longer needed to take insulin, and their blood glucose concentrations were normal a year after surgery. The success of the Edmonton protocol is now being tested at 10 centers around the world [4].

In humans, the pancreas develops as an outgrowth of the duodenum, a part of the small intestine. The cells of both the exocrine system – the acinar cells – and of the endocrine system – the islet cells – seem to originate from the ductal cells during development. During development these endocrine cells emerge from the pancreatic ducts and form aggregates that eventually form what is known as islets of Langerhans. In humans, there are four types of islet cells: the insulin-producing beta cells; the alpha cells, which produce glucagon; the delta cells, which secrete somatostatin; and the PP-cells, which produce pancreatic polypeptide. The hormones released from each type of islet cell have a role in regulating hormones released from other islet cells. In the human pancreas, 65 to 90 percent of islet cells are beta cells, 15 to 20 percent are alpha-cells, 3 to 10 percent are delta cells, and one percent is PP-cells. Acinar cells form small lobules contiguous with the ducts. The resulting pancreas is a combination of a lobulated, branched acinar gland that forms the exocrine pancreas, and, embedded in the acinar gland, the islets of Langerhans, which constitute the endocrine pancreas.

During fetal development, new endocrine cells appear to arise from progenitor cells in the pancreatic ducts. Many researchers maintain that some sort of islet stem cell can be found intermingled with ductal cells during fetal development and that these stem cells give rise to new endocrine cells as the fetus develops. Ductal cells can be distinguished from endocrine cells by their structure and by the genes they express. For example, ductal cells typically express a gene known as cytokeratin-9 (CK-9), which encodes a structural protein. Beta islet cells, on the other hand, express a gene called PDX-1, which encodes a protein that initiates transcription from the insulin gene. These genes, called cell markers, are useful in identifying particular cell types.

Following birth and into adulthood, the source of new islet cells is not clear, and some controversy exists over whether adult stem cells exist in the pancreas. Some researchers believe that islet stem cell-like cells can be found in the pancreatic ducts and even in the islets themselves. Others maintain that the ductal cells can differentiate into islet precursor cells, while others hold that new islet cells arise from stem cells in the blood. Researchers are using several approaches for isolating and cultivating stem cells or islet precursor cells from fetal and adult pancreatic tissue. In addition, several new promising studies indicate that insulin-producing cells can be cultivated from embryonic stem cell lines.

In developing a potential therapy for patients with diabetes, researchers hope to develop a system that meets several criteria. Ideally, stem cells should be able to multiply in culture and reproduce themselves exactly. That is, the cells should be self-renewing. Stem cells should also be able to differentiate *in vivo* to produce the desired kind of cell. For diabetes therapy, it is not clear whether it will be desirable to produce only beta cells – the islet cells that manufacture insulin – or whether other types of pancreatic islet cells are also necessary. Studies by Bernat Soria and colleagues indicate that isolated beta cells—those cultured in the absence of the other types of islet cells—are less responsive to changes in glucose concentration than intact islet clusters made up of all islet cell types. Islet cell clusters typically respond to higher-than-normal

concentrations of glucose by releasing insulin in two phases: a quick release of high concentrations of insulin and a slower release of lower concentrations of insulin. In this manner the beta cells can fine-tune their response to glucose. Extremely high concentrations of glucose may require that more insulin be released quickly, while intermediate concentrations of glucose can be handled by a balance of quickly and slowly released insulin [5].

Isolated beta cells, as well as islet clusters with lower-than-normal amounts of non-beta cells, do not release insulin in this biphasic manner. Instead insulin is released in an all-or-nothing manner, with no fine-tuning for intermediate concentrations of glucose in the blood [5]. Therefore, many researchers believe that it will be preferable to develop a system, in which stem or precursor cell types can be cultured to produce all the cells of the islet cluster in order to generate a population of cells that will be able to coordinate the release of the appropriate amount of insulin to the physiologically relevant concentrations of glucose in the blood.

Several groups of researchers are investigating the use of fetal tissue as a potential source of islet progenitor cells. For example, using mice, researchers have compared the insulin content of implants from several sources of stem cells – fresh human fetal pancreatic tissue, purified human islets, and cultured islet tissue [3]. They found that insulin content was initially higher in the fresh tissue and purified islets. However, with time, insulin concentration decreased in the whole tissue grafts, while it remained the same in the purified islet grafts. When cultured islets were implanted, however, their insulin content increased over the course of three months. The researchers concluded that precursor cells within the cultured islets were able to proliferate and differentiate into functioning islet tissue, but that the purified islet cells (already differentiated) could not further proliferate when grafted. Importantly, the researchers found, however, that it was also difficult to expand cultures of fetal islet progenitor cells in culture [5].

Many researchers have focused on culturing islet cells from human adult cadavers for use in developing transplantable material. Although differentiated beta cells are difficult to proliferate and culture, some researchers have had success in engineering such cells to do this. Fred Levine and his colleagues have engineered islet cells isolated from human cadavers by adding to the cells' DNA special genes that stimulate cell proliferation. However, because once such cell lines that can proliferate in culture are established, they no longer produce insulin. The cell lines are further engineered to express the beta islet cell gene, PDX-1, which stimulates the expression of the insulin gene. Such cell lines have been shown to propagate in culture and can be induced to differentiate to cells, which produce insulin. When transplanted into immune-deficient mice, the cells secrete insulin in response to glucose. The researchers are currently investigating whether these cells will reverse diabetes in an experimental diabetes model in mice [6].

The researchers report that these cells do not produce as much insulin as normal islets, but it is within an order of magnitude. The major problem in dealing with these cells is maintaining the delicate balance between growth and differentiation. Cells that proliferate well do not produce insulin efficiently, and those that do produce insulin do not proliferate well. According to the researchers, the major issue is developing the



technology to be able to grow large numbers of these cells that will reproducibly produce normal amounts of insulin.

Another promising source of islet progenitor cells lies in the cells that line the pancreatic ducts. Some researchers believe that multipotent (capable of forming cells from more than one germ layer) stem cells are intermingled with mature, differentiated duct cells, while others believe that the duct cells themselves can undergo a differentiation, or a reversal to a less mature type of cell, which can then differentiate into an insulin-producing islet cell [4].

Scientists reported that when ductal cells isolated from adult human pancreatic tissue were cultured, they could be induced to differentiate into clusters that contained both ductal and endocrine cells. Over the course of three to four weeks in culture, the cells secreted low amounts of insulin when exposed to low concentrations of glucose, and higher amounts of insulin when exposed to higher glucose concentrations. The researchers have determined by immunochemistry and ultrastructural analysis that these clusters contain all of the endocrine cells of the islet. Scientists are working with primary cell cultures from duct cells and have not established cells lines that can grow indefinitely. However the cells can be expanded. According to the researchers, it might be possible in principle to do a biopsy and remove duct cells from a patient and then proliferate the cells in culture and give the patient back his or her own islets. This would work with patients who have type 1 diabetes and who lack functioning beta cells, but their duct cells remain intact. However, the autoimmune destruction would still be a problem and potentially lead to destruction of these transplanted cells [3]. Type 2 diabetes patients might benefit from the transplantation of cells expanded from their own duct cells since they would not need any immunosuppression.

Some researchers question whether the ductal cells are indeed undergoing a dedifferentiation or whether a subset of stem-like or islet progenitors populate the pancreatic ducts and may be co-cultured along with the ductal cells. If ductal cells die off but islet precursors proliferate, it is possible that the islet precursor cells may overtake the ductal cells in culture and make it appear that the ductal cells are dedifferentiating into stem cells.

In theory, embryonic stem cells could be cultivated and coaxed into developing into the insulin-producing islet cells of the pancreas. With a ready supply of cultured stem cells at hand, the theory is that a line of embryonic stem cells could be grown up as needed for anyone requiring a transplant. The cells could be engineered to avoid immune rejection. There is also some evidence that differentiated cells derived from embryonic stem cells might be less likely to cause immune rejection.

Several teams of researchers have been investigating the possibility that human embryonic stem cells could be developed as a therapy for treating diabetes.

Bernat Soria and his colleagues reported using mouse embryonic stem cells that were engineered to allow researchers to select for cells that were differentiating into insulin-producing cells. They added DNA containing part of the insulin gene to embryonic cells from mice. The insulin gene was linked to another gene that rendered the mice resistant to an antibiotic drug. By growing the cells in the presence of an antibiotic, only those cells that were activating the insulin promoter were able to survive. The cells were cloned and then cultured under varying conditions. Cells cultured in the presence of low concentrations of glucose differentiated and were able to

respond to changes in glucose concentration by increasing insulin secretion nearly sevenfold. The researchers then implanted the cells into the spleens of diabetic mice and found that symptoms of diabetes were reversed [5].

Manfred Ruediger is using the approach developed by Soria and his colleagues to develop insulin-producing human cells derived from embryonic stem cells. By using this method, the non-insulin-producing cells will be killed off and only insulin-producing cells should survive. This is important in ensuring that undifferentiated cells are not implanted that could give rise to tumors. However, some researchers believe that it will be important to engineer systems in which all the components of a functioning pancreatic islet are allowed to develop [2].

Ron McKay and his colleagues performed a series of experiments, in which they induced mouse embryonic cells to differentiate into insulin-secreting structures that resembled pancreatic islets. McKay and his colleagues started with embryonic stem cells and let them form embryoid bodies—an aggregate of cells containing all three embryonic germ layers. They then selected a population of cells from the embryoid bodies that expressed the neural marker nestin. Using a sophisticated five-stage culturing technique, the researchers were able to induce the cells to form islet-like clusters that resembled those found in native pancreatic islets. The cells responded to normal glucose concentrations by secreting insulin, although insulin amounts were lower than those secreted by normal islet cells. When the cells were injected into diabetic mice, they survived, although they did not reverse the symptoms of diabetes [7].

According to McKay, this system is unique in that the embryonic cells form a functioning pancreatic islet, complete with all the major cell types. The cells assemble into islet-like structures that contain another layer, which contains neurons and is similar to intact islets from the pancreas [7].

Recent research has also provided more evidence that human embryonic cells can develop into cells that can and do produce insulin. Itskovitz-Eldor reported that human embryonic stem cells could be manipulated in culture to express the PDX-1 gene, a gene that controls insulin transcription. In these experiments, researchers cultured human embryonic stem cells and allowed them to spontaneously form embryoid bodies (clumps of embryonic stem cells composed of many types of cells from all three germ layers). The embryoid bodies were then treated with various growth factors, including nerve growth factor. The researchers found that both untreated embryoid bodies and those treated with nerve growth factor expressed PDX-1. Embryonic stem cells prior to formation of the aggregated embryoid bodies did not express PDX-1. Because expression of the PDX-1 gene is associated with the formation of beta islet cells, these results suggest that beta islet cells may be one of the cell types that spontaneously differentiate in the embryoid bodies. The researchers now think that nerve growth factor may be one of the key signals for inducing the differentiation of beta islet cells and can be exploited to direct differentiation in the laboratory [1].

Itskovitz-Eldor and his Technion colleagues further characterized insulin-producing cells in embryoid bodies [1]. The researchers found that embryonic stem cells that were allowed to spontaneously form embryoid bodies contained a significant percentage of cells that express insulin. Based on the binding of antibodies to the insulin protein, the researchers estimate that 1 to 3 percent of the cells in embryoid bodies are

insulin-producing beta-islet cells. They also found that cells in the embryoid bodies express glut-2 and islet-specific glucokinase, genes important for beta cell function and insulin secretion. Although the researchers did not measure a time-dependent response to glucose, they did find that cells cultured in the presence of glucose secrete insulin into the culture medium. The researchers concluded that embryoid bodies contain a subset of cells that appear to function as beta cells and that the refining of culture conditions may soon yield a viable method for inducing the differentiation of beta cells and, possibly, pancreatic islets.

Taken together, these results indicate that the development of a human embryonic stem cell system that can be coaxed into differentiating one and functioning insulin-producing islets may soon be possible.

Ultimately, type 1 diabetes is especially difficult to cure, because the cells are destroyed when the body's own immune system attacks and destroys them. This autoimmunity must be overcome if researchers hope to use transplanted cells to replace the damaged ones. Many researchers believe that at least initially, immunosuppressive therapy similar to that used in the Edmonton protocol will be beneficial. A potential advantage of embryonic cells is that, in theory, they could be engineered to express the appropriate genes that would allow them to escape or reduce detection by the immune system. Others have suggested that a technology should be developed to encapsulate or embed islet cells derived from islet stem or progenitor cells in a material that would allow small molecules such as insulin to pass through freely, but would not allow interactions between the islet cells and cells of the immune system. Such encapsulated cells could secrete insulin into the blood stream, but remain inaccessible to the immune system [8].

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## **DANGER OF CANCER** **Chernikov R.M. (Kharkiv)**

**Language supervisor: Zhytnytska A.A.**

**Summary:** The article is about one of the major health problems of humanity – cancer. The result of the research shows the basic concepts of what cancer is, the statistics of cancer, what causes it and why it is so hard to stop, the future of studying cancer and methods of curing it.

**Key words:** cancer, metastasis, tumor.

**Анотація:** Ця стаття про одну з головних проблем здоров'я людства - рак. Результат дослідження надає загальне поняття про таке: рак, статистику цієї хвороби, чим вона викликана, і чому її так важко зупинити. Також зображені майбутні методи лікування та вивчення раку.

**Ключові слова:** метастази, пухлина, рак.

**Аннотация:** Эта статья об одной из главных проблем здоровья человечества - раке. Результат исследования дает общее понятие про рак, статистика этой болезни, чем она вызвана, и почему ее так трудно остановить. Также изображены методы лечения и изучения рака в будущем.

**Ключевые слова:** метастазы, опухоль, рак.

What is cancer? Cancer is a condition where cells in a specific part of the body grow and reproduce uncontrollably. The cancerous cells can invade and destroy surrounding healthy tissue, including organs.

Sometimes cancer begins in one part of the body before spreading to other areas. This process is known as metastasis. There are over 200 different types of cancer, each with its own methods of diagnosis and treatment.

How common is cancer? Cancer is a common condition. In 2009, there were an estimated 12.7 million cancer cases around the world. More than one of three people will develop some form of cancer during their lifetime. This number is expected to increase to 21 million by 2030.

Every cell in our body contains DNA. It carries our genetic code and contains the instructions for all the cell's actions. If the DNA inside cells is damaged, these instructions go wrong. In fact, damage to the DNA or "mutations" as they are known, constantly occur in our cells as they divide and reproduce. Most of the time, the cells recognise that a mutation has occurred and repair the DNA, or self-destruct and die. When a number of mutations have occurred in the DNA of a cell, the control of cell growth may be lost and the cells do not die. Instead, they start to follow abnormal instructions that make them reproduce and grow, producing more and more of these mutated cells - this is the start of a cancer.

Many factors such as smoking or too much exposure to the sun can also trigger DNA damage - leading to a faster accumulation of the mutations which lead to cancer.

A family history of cancer can also increase chances of getting the disease, because it usually means that a person starts his or her life already having inherited some of the DNA mutations that take him or her down the path to cancer. Even when in remission, those who have had the disease have a higher risk of it developing again. In most cases however, the exact cause or sequence of events by which cancer develops, is not yet known [3].

A recent study has found that there are more than 80 genetic markers (i.e. mutated genes) that can increase the risk of developing breast, prostate or ovarian cancer, for

example. Scientists believe the results could soon lead to widespread use of DNA profiling for these cancers, though individual genetic testing for those likely to be at the increased risk - such as when there is a strong family history of a type of cancer - is already in use.

Why is it so hard to stop? Cancer is an extremely complex condition. Each type of cancer is biologically different from any other type. For example, skin cancer is biologically different from the blood cancer called lymphoma, of which there are then many different types.

That is then coupled with genetic differences between individuals and the often random nature of the DNA mutations that cause cancer. All this makes it difficult to identify the way the particular cancer cells are behaving and how they are likely to spread or damage the body. Without a full understanding of the physiology of the cancer, effective treatments are hard to develop.

Early surgery can remove tumours. But the cancer can return if any cells are left behind. It can also return if cells have broken away from the primary tumour and formed microscopic secondary tumours elsewhere in the body before an operation to remove the primary. And because cancer cells are our own body's cells, many treatments to destroy them also risk destroying our healthy cells. One controversial theory of why cancer is so hard to stop is that it is rooted in the ancient traits of our genes [1].

Professor Paul Davies from Arizona State University believes cancer may use tried-and-tested genetic pathways going back a billion years to the dawn of multicellular life, when unregulated cell growth would have been an advantage. He argues that this tendency was suppressed by later, more sophisticated genes, but lies dormant in all living organisms. Cancer occurs when something unlocks these ancient pathways. Other scientists disagree, saying that these pathways would not have survived millions of years of evolution.

The field of cancer research is moving away from defining a cancer by where it is in the body, as one type of breast cancer can have more in common with an ovarian cancer than another cancer in the breast.

Instead scientists are looking deeper at what is going wrong inside cancerous cell a tumour can have 100,000 genetic mutations and these alter over time. By pinpointing the mutations that can cause certain cancers, doctors hope to personalise treatment - choosing the drug most likely to work on a particular type of tumour.

Scientists are creating targeted cancer therapies using their latest insights into cancer at a molecular level. These treatments block the growth of cancer by interfering with genetic switches and molecules specifically involved in tumour growth and progression.

Clinical trials using gene therapy are also underway. This experimental treatment involves adding genetic material into a person's cells to fight or prevent disease. Scientists at Queen's University in Belfast have discovered a new way of causing breast cancer cells to self destruct. The research used a miniscule gene transport system to deliver a poison directly into cancerous cells. It is hoped the new technique could overcome the side effects of treatments such as chemotherapy and radiotherapy [2].

Using a Designer Biomimetic Vector (DBV), Dr Helen McCarthy, from Queen's School of Pharmacy, packaged a gene into a nanoparticle 400 times smaller than the

width of a human hair, allowing it to be delivered straight into breast cancer cells in the laboratory.

This meant that the gene (iNOS), which specifically targets breast cancer cells using DBV, would force the cells to produce poisonous nitric oxide. This would either kill the cells outright or make them more vulnerable to being destroyed by chemotherapy and radiotherapy.

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## **REVOLUTIONARY TECHNIQUES IN HEALTH CARE**

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**Summary:** The paper deals with the application prospects of some up-to-date technologies in medicine. The advantages and disadvantages of medical equipment use in daily life are considered. Some medical devices and their resources are described. The principle of disease diagnostics based on the measurements of the main human indicators without any direct doctor's participation is explained.

**Key words:** device, medical monitoring, wireless healthcare.

**Анотація:** Стаття присвячена розгляду перспективі використання новітніх технологій в медицині. Виявлені переваги та недоліки впровадження медичинської апаратури в побут людей, описані деякі прилади та їх можливості. Пояснюється принцип діагностики захворювань, що базується на вимірюванні важливих показників людини без безпосередньої участі лікаря.

**Ключові слова:** безпроводна охорона здоров'я, медичний контроль, прилад.

**Аннотация:** Статья посвящена рассмотрению перспективы использования современных технологий в медицине. Выявлены достоинства и недостатки внедрения медицинской аппаратуры в повседневную жизнь людей, описаны некоторые устройства и их возможности. Объясняется принцип диагностики заболеваний, основанный на измерении наиболее важных показателей человека без непосредственного участия доктора.

**Ключевые слова:** беспроводное здравоохранение, медицинский контроль, устройств.

There is a growing tendency to develop the devices which could monitor people's health providing an individual's check-up on the daily basis. These systems will enable doctors to obtain the necessary information about the patients in time to correct the treatment or to change the diet. By means of special sensors which are implanted under the skin, the patient's life may be saved and the necessary treatment may begin.

Such ambient monitoring and intervention could avert a heart attack, stroke, or other medical crisis. It could keep a person out of the hospital and save money for both the patient and the health care system.

A health-monitoring bathroom is not science fiction. This is what health care could look like within decades. Perhaps predicting such dramatic change within 10 years is overly optimistic. But the necessary technologies already exist or are close at hand, the need to reduce health care costs is real, and the current health care system demands change. What is more, a groundswell of support for wireless health care is rising from a diverse group of people and organizations.

The change is happening, a technological revolution in health care has been predicted before, but we are at an inflection point now, where wireless connectivity, personal cellular devices, pervasive sensing technologies, social networks, and data analytics are mature enough to make wireless medicine a reality. Eventually, most health care will occur not during occasional visits to doctors' offices, clinics, or hospitals but continuously, during ordinary activities in people's homes, cars, and workplaces.

A trial program developed by the U.S. Department of Veterans Affairs offered an early look at what systemic change could mean. In 2003, the VA began using simple messaging devices and occasional video conferences to let chronically unhealthy veterans stay in touch with nurses and other health care professionals. Under this program 71 000 veterans are now receiving daily monitoring for such conditions as diabetes, heart disease, and post-traumatic stress disorder.

A patient would regularly connect one or more vital-signs monitoring devices (a blood pressure cuff, for example, or a thermometer) to the Health Buddy and follow on-screen instructions to collect the data. A patient would also respond to the questions on symptoms and behavior, such as: "Have you taken your medicine?", "Are you feeling sad?" This daily assessment was automatically uploaded to a secure server, and professionals managing the patient's care then used a Web interface to look for problems. Each care coordinator was able to monitor 125 patients with this system.

The Zeo Personal Sleep Coach is a device which communicates wirelessly with a headband to monitor sleep cycles. The system scores each night of sleep and lets a person look at the detailed information online.

There is also a device which can solve serious problems. The MiniMed Paradigm Real-Time Revel System from Medtronic is the first to combine an insulin pump with regular monitoring of glucose levels for diabetes management.

Some diseases can be prevented by means of the Withings's WiFi Body Scale which uploads the weight and body-mass information to a website. Users can then track trends and print graphs to share with nutritionists or doctors.

In general, wireless glucose monitors are already on the market from companies like Medtronic and DexCom, and the latest devices may soon be paired with insulin infusion pumps, so they can automatically adjust insulin dosages in response to changes in the patient's glucose level.

This kind of system allows far closer control of diabetes than a manual self-administered system, avoiding the need to prick the skin, collect a blood sample, insert that sample into a reader, and then pick the appropriate insulin dose. And supplying exactly the right amount of insulin just when it is needed has been shown to prevent

complications, including blindness, kidney disease, and peripheral vein disease that can lead to the loss of a limb [1, p.53].

People with congestive heart failure may soon benefit from a wireless monitor being developed by CardioMEMS. This tracking method detects fluid buildup in the patient's lungs, a common complication that often leads to hospitalization. The device can detect a problem even before the patient notices major symptoms; the doctor can then adjust the patient's medication to reduce fluid levels.

There are many conditions when treatment will be improved by such monitoring tools. Similar approaches may be used to blunt the progress of chronic kidney disease and prevent hospitalizations for chronic obstructive pulmonary disease, emphysema, and pneumonia.

Thus, a number of medical conditions and physical data can be monitored by sensors and wireless communications. Increasingly, people are turning to technology to gain a more complete picture of their overall health. In the past, the only way to obtain the detailed information was through costly stays at clinics or expensive medical tests. Now, however, it is both affordable and widely available to apply some of these monitoring systems.

Even Ford is getting into the wireless health care action. In May 2011, the company announced that it is developing in-car health tracking as a part of its Sync system. The first prototype system uses Bluetooth to connect the car to a continuous glucose-monitoring device. The system gives audio updates to the user and an alarm sounds if glucose levels fall too low, a situation that could lead to a loss of consciousness or a seizure.

People who suffer severe spinal cord injuries and subsequent paralysis often lose a bladder control too. But a new electronic device may restore that bodily function. British neuroscientist James Fawcett and his colleagues have developed a neuroprosthetic device which replaces the damaged nerves that convey the bladder's sense of fullness. The device also blocks or triggers a bladder emptying on cue through electrical stimulation. Fawcett and his team successfully demonstrated the technology in rats and published their results in *Science Translational Medicine* [2].

The company GlaxoSmithKline is also aiming for something much more radical: connecting thousands of tightly packed individual nerve cells with electrodes and associated circuitry to read and interpret the “code” in the collection of nerve-cell fibers that constitute a nerve, and then modulating the code to restore a specific function to a healthy state. If researchers can tap into the nerve to either introduce or erase an action potential, they will be able to restore an organ or function to a healthy state, for example, by coaxing insulin from the pancreas to treat diabetes [3].

It seems possible to expand wireless health care capabilities. This comprehensive health monitoring and treatment system will evolve from technology that today helps family members monitor aging relatives. These sensing systems do far more than detecting a sudden fall. They monitor ordinary tasks like getting out of bed, opening the refrigerator, and walking around the house and can spot any changes that can signal a problem. For instance, an elderly person who starts to sleep later each day does not leave home, and eats less frequently may be developing complications from medications, a worsening of congestive heart failure, or depression.



While a smart medicine cabinet can check that the right medicines are moving on and off the shelves as scheduled, it cannot tell if the patient is actually consuming them. In the future, wireless technology integrated into medications will be able to confirm that the patient has ingested the medicine. Proteus Biomedical, based in California, has developed digestible computer chips with built-in wireless transmitters. Digestive fluids in the stomach activate the devices, which then create ultralow-power signals that can be picked up by a tiny recorder inserted under the skin or worn as a small adhesive skin patch. The recorder notes the date and time of the pill's activation along with other pieces of information, such as the type of drug, dose, and the place of manufacture. It also takes a snapshot of the patient's heart rate, respiratory rate, and other physiological measurements. Ultimately, such technology could be used to tailor medications to the individual.

Of course, these devices do not work alone. Somewhere the data need to be interpreted, as in the VA's telehealth program, by medical professionals. These systems will be faster and more accurate than human clinicians at spotting anomalies and function better at identifying those cases that require human consultation.

The problem of privacy must not be neglected. Health care information should be made at least as secure as a person's checking account. The necessary laws should be adopted.

Actually, a universal interface for monitoring the functioning of a human body that is as easy to understand as the gauges on a car's dashboard has not been developed yet. That is, in the same way a car's dashboard shows how much gas is left in the tank or if the engine is malfunctioning, an interface that clearly depicts health status and early warnings of disease is badly needed.

The creation of new models of care that cover a patient's entire treatment at a fixed price (instead of charging each time, a patient shows up at the doctor's office) should offer incentives to use technologies that keep patients healthy and out of the hospital. The main thing that will drive adoption of these integrated wireless systems is the data that validate their cost-effectiveness; that will require studies and trials that go far beyond what the VA has done to date.

In general, there is every reason to believe that today's trends (the expansion of tools for wirelessly monitoring and diagnosing disease, the increasing ability to remotely manage drugs and medical devices, and the growing understanding about how genetics affects susceptibilities to disease) with smart systems which learn as well as respond will be tied together. Health care could change a society as dramatically as the Industrial Revolution once did.

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# **REGRESSION OF NEOVASCULARIZATION AT THE OPTIC DISK AFTER INTRAVITREAL INJECTION OF RANIBIZUMAB IN PATIENTS WITH DIFFUSE MACULAR EDEMA AND PROLIFERATIVE DIABETIC RETINOPATHY**

**Dobritsa Y.V. (Kharkiv)**

**Language supervisor: Zubkova L.M.**

**Summary:** The article is devoted to the analysis of the effectiveness of treatment of proliferative diabetic retinopathy (PDR) and diffuse macular edema (DME) in patients with type II diabetes mellitus. As a result of research the reduction of intensity of the optic disc neovascularization from the first to the subsequent ranibizumab IVI was recorded.

**Key words:** pathological angiogenesis, proliferative diabetic retinopathy, diffuse macular edema.

**Анотація:** Стаття присвячена аналізу ефективності лікування проліферативної діабетичної ретинопатії та дифузного макулярного набряку у пацієнтів з II типом цукрового діабету. В результаті дослідження було відмічено зниження інтенсивності неоваскуляризації оптичного диска під впливом ін'єкцій ранібізумабу.

**Ключові слова:** патологічний ангиогенез, проліферативна діабетична ретинопатія, дифузний макулярний набряк.

**Аннотация:** Статья посвящена анализу эффективности лечения пролиферативной диабетической ретинопатии и диффузного макулярного отека у пациентов с II типом сахарного диабета. В результате исследований было отмечено снижение интенсивности неоваскуляризации оптического диска на фоне инъекций ранибизумаба.

**Ключевые слова:** патологический ангиогенез, пролиферативная диабетическая ретинопатия, диффузный макулярный отек.

Pathological angiogenesis in the retina and the possibility of its blockage in patients with diabetic retinopathy is actively studied in the last decade. However, biological mechanisms of the final stages of pathological angiogenesis — such as remodeling and differentiation of newly formed capillaries — are still poorly understood [3]. Moreover, the capacity for reduction of newly formed vascular network remains limited.

To increase the effectiveness of treatment of proliferative diabetic retinopathy (PDR) and diffuse macular edema (DME) in patients with type II diabetes mellitus. In pursuit of the main goal of DME reduction in patients with PDR, we noted and attempted to analyze the features of regression of neovascularization at the optic disc (OD) stimulated by intravitreal use of ranibizumab [1].

We observed 20 patients (9 men and 11 women, 22 eyes) with PDR (neovascularization at the optic disc) and diffuse DME, age ranging from 53 to 77 years, duration of type II diabetes 12 to 22 years, HbA1c level 8.8% to 13.6%, average 10.7%. For the treatment, 1 intravitreal injection (IVI) of 0.5 mg ranibizumab per month was used. The number of injections ranged from 3 to 6 for each patient during the observation period of 1.5 years. Evaluation of the effectiveness was conducted by the following criteria: the thickness of the neuroepithelium (NE) in the foveolar region according to the OCT; fundus picture obtained via ophthalmoscopy with photographic recording; the dynamics of visual acuity; fluorescein angiography of the retina (during the first 7 days and 30 days after IVI) [2].

In all cases (22 eyes), after the 1st injection of 0.5 mg ranibizumab, regression and resorption of DME were registered — namely, decrease of NE thickness in the

fovea by an average of  $464 \pm 25 \mu\text{m}$  up to  $331 \pm 32 \mu\text{m}$  ( $p < 0,05$ ) micrometers. Visual acuity in the observed patients increased by an average of  $0,2 \pm 0,05$  to  $0,4 \pm 0,05$ . In addition, we noted complete regression of neovascularization at the optic disc in 14 eyes (63%) and partial regression of neovascularization in 8 eyes. This was confirmed by the lack of visual prepapillar neovascularization under ophthalmoscopy and absence or reduction of the previously existing massive extravasal release of fluorescein from newly formed prepapillar vessels. The reduction of neovascularization at the optic disc began as early as in 20 hours after the 1st ranimizumab IVI and reached its maximum in 3–7 days (which is obviously due to the 9 days period of the drug's half life). In 26–29 days after the 1st IVI newly formed vessels reduced by ranibizumab gradually renewed their activity and in 30–35 days (according to fluorescent angiography data) extravasal output of fluorescein on the surface of the optic disc was recorded in all 22 studied eyes (100%). At the same time, increase of NE thickness in the fovea was detected only in 12 (52%) eyes, indicating a more pronounced ability of ranibizumab to decrease vascular permeability without reducing the newly formed vessels.

After the 2nd injection of ranibizumab the expected decrease in the NE thickness in the fovea was detected with OCT ranging from  $417 \pm 25 \mu\text{m}$  to  $298 \pm 27 \mu\text{m}$  ( $p < 0,05$ ) accompanied by complete repeated NVD reduction in 18 eyes (81%). In 4 cases, incomplete NVD reduction occurred. The terms of regression of newly formed vessels at the optic disc after the 2nd ranibizumab IVI reduced by 18 hours to 2–4 days. Fluorescent angiography revealed reduction or complete absence of extravasal fluorescein output at the optic disc as well as the following symptoms: increase in "hand-retina" time by (on the average of)  $21 \pm 4$  seconds to  $30 \pm 3$  ( $p < 0,05$ ) seconds; delayed choroidal filling; decrease in the caliber of the retinal veins with a slight decrease in the caliber of the arteries (the measurement was made at the optic disc and at a distance of 2–3 pd); disappearance of the contrast from previously inserted arterio-venous shunts; in 4 eyes with partial reduction of NVD decrease in functioning of newly formed capillaries at the optic disc was detected. Visual acuity of the patients remained stable. The duration of the effect of NVD reduction in our patients increased by up to 32–38 days.

After the 3rd injection of ranibizumab, along with a decrease in the NE thickness of the retina in the fovea, cessation of blood flow in the existing arterio-venous shunts in the newly formed capillaries at the optic disc in all 22 eyes in the period from 1 to 5 days was recorded. The results of fluorescent angiography showed a further increase in "hand-retina" time and consistent reduction in the diameter of retinal veins. Decrease in the tortuosity of veins, their more direct course may also be noted. The caliber of the arteries was not significantly altered. The size of the avascular zone in the macula as compared by angiograms after the 1st, 2nd and 3rd IVI did not change. Visual acuity remained within an average. After executing a sequence of 3 injections of 0.5 mg ranibizumab we conducted its repeated intravitreal injection on indications (in PRN mode). The maximum injection quantity in this group of patients was 6. The frequency of subsequent injections varied depending on NE thickness in the fovea (since our main purpose was arresting the macular edema). Observations of our patients allow us to note that after the 3rd of ranibizumab IVI the effect of NVD reduction lasted for various periods – i.e., from 2 to 4.5 months. A longer period of stable NVD reduction occurred in patients older than 65 years, which is probably due to the decrease of angiogenic

stimuli of the retina with age. Besides, the effect of NVD reduction persisted longer on the eyes which previously underwent panretinal laser coagulation of the retina (12 eyes). We managed to prevent progression of preapillary vasoproliferation by sequential administration of ranibizumab in 18 out of 22 eyes studied (81%), which helped to preserve productive central vision in our patients for the whole observation period.

Thus, VEGF is the key mediator of angiogenesis, directly and indirectly affecting all stages of formation of pathological blood vessels. The newly-formed vessels at the optic disc (according to the literature) are not a fully fledged capillary network but rather a “tubular structure” consisting of proliferating endothelial cells. Consequently, the anti-VEGF-therapy may have the potential to combat existing neovascularization at the optic disc. Our preliminary results suggest an impact made by the anti-VEGF-therapy (intravitreal injection of ranibizumab) not only on the processes of vascular permeability, but also on the final stages of pathological neovascularization (in our case, the one localized at the optic disc). We found that the intensity of the optic disc neovascularization is reduced from the first to the subsequent ranibizumab IVI. As the results of fluorescent angiography show, reduction of preapillary vasoproliferation after the introduction of ranibizumab occurs against the background of its effects on hemodynamics and microcirculatory system of the retina.

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УДК 911.3

## **TO THE QUESTION OF SPREAD OF ECOTOURISM IN AR CRIMEA**

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**Summary:** The article considers the problems of ecotourism development in the Crimea. The research identifies the factors influencing the development of ecotourism in the Crimea. The analysis of interaction of the factors influencing ecotourism is also conducted.

**Key words:** density of population, development of tourism industry, ecotourism.

**Анотація:** В статті розглядаються проблеми розвитку екотуризму в АР Крим. При проведенні дослідження виявлено чинники впливу на розвиток екотуризму в Криму, а також проведений аналіз взаємодії одного з факторів на проведенням екотуризму.

**Ключові слова:** екотуризм, щільність населення, розвиток туристичної галузі.

**Аннотация:** В статье рассматриваются проблемы развития экотуризма в АР Крым. Исследования выявили факторы влияния на развитие экотуризма в Крыму, а также показали взаимодействие разных факторов в организации экотуризма. В результате анализа данных, полученных при исследовании современной ситуации в АР Крым, определены наиболее благоприятные административные территории для занятия экотуризмом. Результатом работы является выявление наиболее благоприятных районов АР Крым по одному из параметров - плотностью населения - для занятия данным видом туризма.

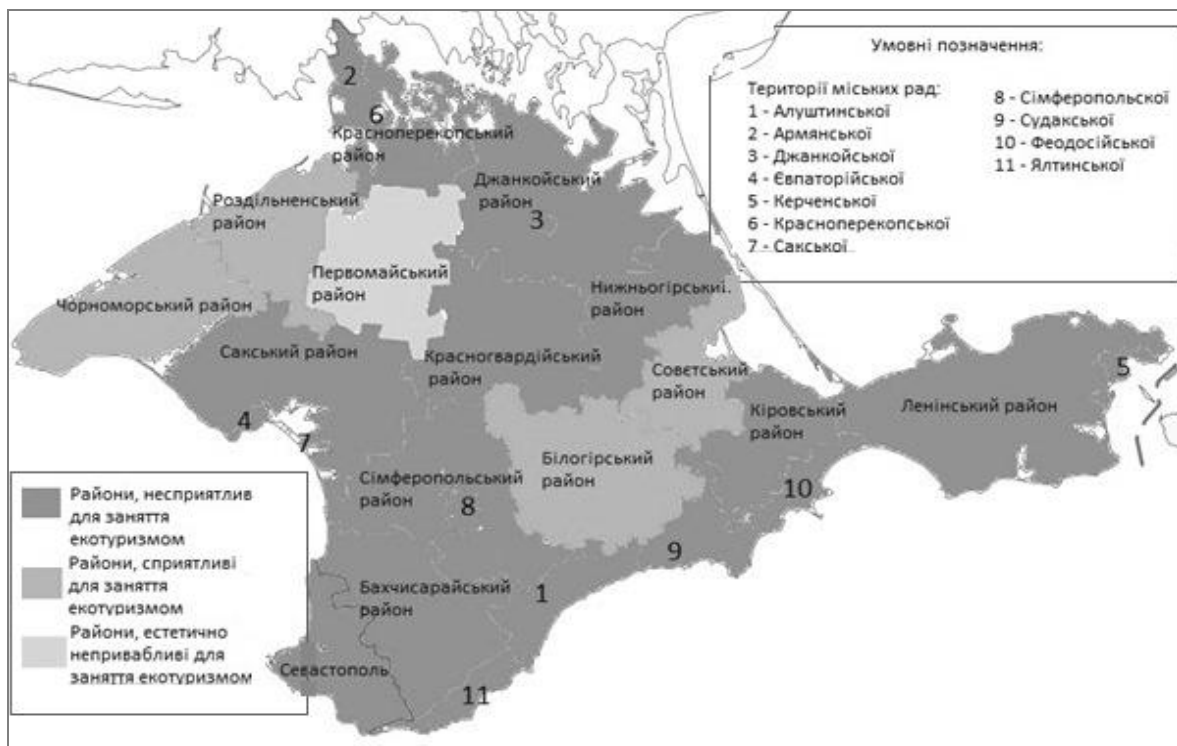
**Ключевые слова:** экотуризм, плотность населения, развитие туристической отрасли.

The Crimea is known as a famous place of tourism. It has one of the best natural environmental places for the development of eco-tourism in the region. To characterize the preconditions for the formation and development of eco-tourism, it is important to detect the phenomena of human and natural facts that affect the development of ecotourism in the Crimea. Among a number of significant factors is population density and is one of the significant factors. Tourists who think their own location in the environment of wildlife for the highest spiritual, physical and aesthetic value, it is important to determine areas that are favorable for this type of tourism.

At this stage of this progressive and modern type of tourism in the Crimea one of the most important issues is the issue of the location of the object directly in wildlife. Thus, as the peninsula is one of the most popular recreational facilities of the national and global level, in the summer season there are a number of problems for ecotourism. First, the increase of anthropogenic load in the summer, which violates the integrity of the ecosystem [3]. To anthropogenic factors include the overall density of the local population and tourists and employing traditional forms of tourism. There is a problem of waste emissions in the area [1]. Economic development also has a significant impact, because the location of industrial facilities, fields, arable land, pasture, adversely affect the general state of nature. Natural factors that have a positive impact on development of ecotourism, include climatic, landscape, hydrology, orographic and natural aesthetic factors. Differences in territories contribute to the attractiveness of the place, which is determined by the set of the factors listed above. Analysis of characteristics, such as anthropogenic and natural, for making a decision of development ecotourism needs time. The work is a very voluminous and can not be enough described in this article. It's an attempt of studying the impact factor of population density, as one of a number of factors for the development of ecotourism [2].

The phenomenon of ecotourism and the most favorable areas for its conduct in the administrative region of the Crimea on the map is demonstrated. It is possible to analyze three types of areas: areas where population density index above 30 persons/km<sup>2</sup> (according to the World wild nature of the figure is the highest population density to considered favorable territory for eco-tourism [4]). Nonfavorable territory; areas where population density does not exceed 30 persons/km<sup>2</sup> is favorable territory; as well as areas that are favorable for ecotourism by population density, but they are not subjects to this type of tourism because of the lack of natural monuments and landscapes of unique wildlife.

Picture 1. Attractiveness of the regions of the Crimea



On the territory of these areas may dominate natural or mono desert, mono steppe landscapes, and areas that are under human pressure over historical time have become monotonous modified ecosystems, which are not of significant interest for this type of tourism.

The territory of the Republic of Crimea has different conditions for spreading of ecotourism. Administrative areas with different population density and varieties, often are altered by man.

Landscapes of the most favorable areas are the Black Sea, Rozdilnensky, Sovietsky, Belogorsky areas through a large number of natural attractions and areas of natural reserve fund.

This means there are still places of unspoiled nature, natural and aesthetic resources for the spiritual and physical recreation for man among wildlife in these areas. Pervomajskiy area is favorable for the class ecotourism by population density, but not aesthetically attractive.

Republican, regional and historical monuments of local level are available. Other areas for the studied parameters are unfavorable for the class of ecotourism, particularly because of the high rate of population density and level of economic development of the territory.

So, analyzing the complex factors which carry a direct or indirect impact on the development of eco-tourism in the Crimea and considering in details effect of one of the most important ones - the density of the population, identifying the most attractive areas for this type of tourism that can improve the development of tourism and recreational potential development of routes and promotion of ecotourism.

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## NEW METHODS FOR TREATING HUNTINGTON'S DISEASE

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**Summary:** Different standpoints, approaches and new methods for treating Huntington's disease are discussed in the article. The signs, symptoms of Huntington's disease and their causes and side-effects are described and explained.

**Key words:** Huntington's disease, signs, symptoms, chorea, mutation, cytosine, adenine, guanine, neuron, defective gene, autophagy, ramification.

**Анотація:** У поданій статті розглядаються різні точки зору, підходи та новітні методи лікування хвороби Гентингтона. Ознаки, симптоми хвороби Гентингтона та їх причини і побічні наслідки описуються та пояснюються.

**Ключові слова:** хвороба Гентингтона, ознаки, симптоми, хорея, мутація, цитозин, аденін, гуанін, нейрон, дефектний ген, аутофагія, наслідки.

**Аннотация:** В представленной статье рассматриваются различные точки зрения, подходы и новые методы лечения болезни Гантингтона. Описываются и объясняются признаки, симптомы болезни Гантингтона и их причины и побочные явления.

**Ключевые слова:** болезнь Гантингтона, признаки, симптомы, хорея, мутация, цитозин, аденин, гуанин, нейрон, дефектный ген, аутофагия, последствия.

Huntington's disease is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition).

Adult-onset Huntington's disease, the most common form of this disorder, usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and problematic learning new information or making decisions. Many people with Huntington's disease develop involuntary jerking or twitching movements known as chorea. As the disease progresses, these movements become more pronounced. Affected individuals may have trouble walking, speaking, and swallowing. The people with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. The individuals with the adult-onset form of Huntington's disease usually live about 15 to 20 years after the signs and the symptoms begin.

A less common form of Huntington's disease known as the juvenile form begins in childhood or adolescence. It also involves movement problems and mental and emotional changes. Additional signs of the juvenile form include slow movements, clumsiness, frequent falling, rigidity, slurred speech, and drooling. School performance declines as thinking and reasoning abilities become impaired. Seizures occur in 30 percent to 50 percent of children with this condition. Juvenile Huntington's disease tends to progress more quickly than the adult-onset form; the individuals affected usually live 10 to 15 years after signs and symptoms appear.

Mutations in the HTT gene cause Huntington's disease. The HTT gene provides instructions for making a protein called huntingtin. Although the function of this protein is unknown, it appears to play an important role in nerve cells (neurons) in the brain.

The HTT mutation that causes Huntington's disease involves a DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, the CAG segment is repeated 10 to 35 times within the gene. In the patients with Huntington's disease, the CAG segment is repeated 36 to more than 120 times. The people with 36 to 39 CAG repetition may or may not develop the signs and symptoms of Huntington's disease, while the people with 40 or more repeats almost always develop the disorder.

An increase in the size of the CAG segment leads to the production of an abnormally long version of the huntingtin protein. The elongated protein is cut into smaller, toxic fragments that bind together and accumulate in neurons, disrupting the normal functions of these cells. The dysfunction and eventual death of neurons in certain areas of the brain underlie the signs and symptoms of Huntington's disease [1].

Although there is not yet a cure for Huntington's disease, the research being done is encouraging in terms of slowing the progression of the disease. Since Congress established the Commission for the Control of Huntington's Disease and Its Consequences in 1977, it has provided consistent support for federal research in USA. The efforts to understand and reverse Huntington's disease include the following:

<b>Current Research Efforts for Huntington's Disease</b>	
<b>Basic neurobiology</b>	Investigators in the field of neurobiology – which encompasses the anatomy, physiology, and biochemistry of the nervous system – continue to study the Huntington's gene with an eye toward understanding how it causes disease in the human body.
<b>Clinical research</b>	Neurologists, psychologists, psychiatrists, and other investigators are researching potential treatments that will then undergo clinical trials in humans.
<b>Imaging</b>	Leading-edge technologies are enabling scientists to understand how the defective gene affects brain tissue, body chemistry and metabolism.
<b>Animal models</b>	Research is being done with mice to mimic the human disease and test potential treatment modalities [3].

The study, conducted by researchers at the University of California explains a fundamental aspect of how Huntington's disease wreaks havoc within cells and provides clear therapeutic opportunities.

The implications are significant. It is a lead that can be vigorously pursued, not just for Huntington's disease, but also for similar neurodegenerative conditions like Parkinson's disease and maybe even Alzheimer's disease.



In the study, the team focused on PGC-1alpha, a protein which helps regulate the production and operation of mitochondria. Neurons have a constant, high demand for energy. They are always on the edge for maintaining adequate levels of energy production. PGC-1alpha regulates the function of transcription factors that promote the creation of mitochondria and allow them to run at full capacity.

In a mouse model of Huntington's disease, the researchers found that elevated levels of PGC-1alpha virtually eliminated the misfolded proteins that cause Huntington's disease.

PGC-1alpha in particular impacted expression of another protein that is crucial for autophagy. However, for neurons that need to last a lifetime, self-renewal is crucial for survival. Autophagy is a process whereby healthy cells degrade, recycling old, unneeded or dangerous particles and products, such as oxidative, damaging molecules generated by metabolism. Why should PGC-1alpha co-activation be linked to enhanced autophagy pathway function? Considering that PGC-1a promotes mitochondrial biogenesis and increased mitochondrial metabolic activity, the up-regulation of mitochondrial number and mass required to achieve higher energy production likely results in a proportionately greater accumulation of damaged mitochondria that need to be turned over. Consequently, enhanced autophagy-lysosome pathway function would be required to accommodate this increased need for mitochondrial turnover via autophagy, a process known as mitophagy.

PGC-1alpha drives this pathway through another protein called transcription factor EB or TFEB. Scientists were unaware of this connection before, because TFEB is a relatively new player, though clearly emerging as a leading actor. The researchers discovered that even without PGC-1alpha induction, TFEB can prevent huntingtin (Htt) aggregation and neurotoxicity.

The researchers crossbred the mice with Huntington's disease with the mice that generated elevated levels of PGC-1alpha and found that they showed significant improvement. According to the researchers, the generation of misfolded proteins was essentially eliminated and the mice behaved normally.

Both PGC-1alpha and TFEB provide two new therapeutic targets for Huntington's disease [4].

A new study published on the 26th November 2013 in the open access journal PLOS Biology, identifies a new target in the search for therapeutic interventions for Huntington's disease.

Nuclear huntingtin aggregates have been found to interfere with the transcription of many genes, and the previous work has shown beneficial effects for Huntington's disease of inhibiting a family of enzymes that are normally thought to regulate transcription – the histone deacetylases, or HDACs. However, humans have eleven different HDAC enzymes, and it has been uncertain exactly which HDAC needs to be inhibited to see these benefits.

The study has pinpointed just one of these enzymes as the target – HDAC4 – but with an intriguing twist; everything is happening in the cytoplasm, not the nucleus, and HDAC4's classic role in transcription has little to do with it.

The researchers noted that the HDAC4 protein naturally contains a region that, like mutant huntingtin, is rich in the amino acid glutamine. They show that HDAC4 can associate directly with huntingtin protein in a manner that depends on the length of the

glutamine tracts, but that this association between HDAC4 and huntingtin occurs in the cytoplasm of nerve cells in the mouse brain, and – surprisingly – not in the nucleus, where HDAC4 is known to have its transcriptional role.

Researchers did their work in an aggressive disease mouse model of Huntington's disease – the gold standard model for this type of study. They find that halving the levels of HDAC4 in the cells of Huntington's disease mice can delay the aggregation of huntingtin in the cytoplasm, thereby identifying a new route to modulating the toxicity of mutant huntingtin protein. Crucially, reducing HDAC4 levels can also rescue the overall function of nerve cells and their synapses, with corresponding improvements seen in coordination of movement, neurological performance and the lifespan of the mice. In agreement with the cytoplasmic association between HDAC4 and huntingtin, this all happens without any obvious improvement in the defective gene transcription in the nucleus.

There are currently no disease-modifying therapeutic treatment medications available for Huntington's disease. It is still very early days and it is important to note that the medical applications of any therapy arising from this study have not been studied in a clinical setting and are far from clear. However, one broad-brush HDAC inhibitor, suberoylanilide hydroxamic acid (SAHA) had previously been shown to improve movement defects in preclinical tests in this mouse model. The authors have shown in a related publication that, in addition to inhibiting HDAC enzyme function, SAHA decreases levels of the HDAC4 protein. Therefore it is hoped that the development of HDAC4-targeted compounds may be a promising strategy in improving the lot of Huntington's disease patients [5].

In another study, led by the University of Leicester in the United Kingdom, the researchers stopped the development of neurodegeneration linked to Huntington's disease by targeting a specific enzyme – kynurenine 3-monooxygenase, KMO – in fruit flies. The team directly manipulated metabolites in the kynurenine 3-monooxygenase (KMO) cellular pathway with drugs in order to manipulate the symptoms the flies displayed.

This work provides the first genetic and pharmacological evidence that inhibition of a particular enzyme – kynurenine 3-monooxygenase (KMO) – is protective in an animal model of this disease, and the researchers have also found that targeting other points in this cellular pathway can improve Huntington's disease symptoms in fruit flies.

This work provides important confirmation of kynurenine 3-monooxygenase (KMO) inhibition as a potential therapeutic strategy for these individuals. As many kynurenine 3-monooxygenase (KMO) inhibitors are available, and more are being developed, it is hoped that such compounds can ultimately be tested in clinical trials for this as well as other neurodegenerative disorders [2].

The researchers that contributed to the studies plan to continue their efforts, targeting the enhancement and development of medical intervention in Huntington's and other neurodegenerative disorders.

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## COLLIE EYE ANOMALY

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**Summary:** Collie eye anomaly (CEA) is a genetic eye disease, which affects several breeds of similar origin known since the middle of the last century. Affected individuals show a wide range of severity, ranging from chorioretinal hypoplasia and coloboma to retinal detachment and intraocular hemorrhage. Its prevalence in affected breeds is found to be very high in some breeds and quite low in others.

**Key words:** Canine inherited ocular disease, chorioretinal hypoplasia, collie eye anomaly, coloboma, genetic test.

**Анотація:** Аномалія очей коллі це генетичне захворювання очей, котре вражає декілька порід зі схожим походженням, відоме з середини минулого століття. Вражені особини демонструють широкий спектр тяжкості, що коливаються від хоріоретинальної гіпоплазії і колобоми до відторгнення сітківки та внутрішньоочної кровотечі. Її поширення дуже широке у деяких уражених породах, а у інших доволі низьке.

**Ключові слова:** Аномалія очей коллі, генетичний тест, колобома, спадкове захворювання очей собак, хоріоретинальна гіпоплазія.

**Аннотация:** Аномалия глаз колли это генетическое заболевание глаз, которое поражает несколько пород схожего происхождения, известное с середины прошлого века. Пораженные особи показывают широкий спектр тяжести, которые колеблются от хориоретинальной гипоплазии и колобомы до отторжения сетчатки и внутриглазного кровотечения. Её распространение очень широко в некоторых пораженных породах, а в других довольно низкое.

**Ключевые слова:** Аномалия глаз колли, генетические тест, колобома, наследственное глазное заболевание собак, хориоретинальная гипоплазия.

Collie eye anomaly (CEA) is a congenital inherited ocular disorder in dogs of herding and other related breeds. It is a non-progressive complex trait, the pattern of chorioretinal and scleral development disturbance of which manifests variably between individuals. It is characterized by regional hypoplasia of the choroid, and coloboma of differing severity between affected individuals.

Collie eye anomaly was first described in the middle of the twentieth century in Europe and since then its presence has been well known by breeders and researchers and quite a lot of study has gone into understanding the disease. This anomaly has historically been called posterior scleral ectasia and posterior staphylomas and still today there are differing opinions on the most correct name for this anomaly [8]. Because of the individual difference the true extent of the disease and its spread in the affected breeds has never been fully known or its significance properly acknowledged. The disease has been somewhat problematic with regards to breeding. Not only does it

cause blindness in a small number of affected individuals, but also due to the "go normal" phenomenon which causes the window to correctly diagnose the anomaly to be fairly short. Also, the fact that not all individuals are severely affected with lack or loss of vision has led some breeders and breed clubs to consider breeding restrictions to be unnecessary [2].

Even though the anomaly is named after collies, it affects not only the collie breeds. The most commonly affected by the anomaly breeds are in one or another way related, and they most likely inherited the anomaly from a common ancestor further back. The mutation prevalence varies in different breeds and the obtained from Optigen current status is: 72% in Rough Collie, 62% in Smooth Collie, 60% in Longhaired Whippet, 52% in Shetland Sheepdog, 35% in Border Collies, 30% in Lancashire Heeler, 18% in Nova Scotia Duck Tolling Retriever and 15% in Australian Shepherd [8]. The percentage includes carriers and affected dogs. The Optigen statistics includes only the dogs that were tested in their lab, but not in the others and not of the tested dogs' offspring. Thus, the real status is rather hard to find out.

CEA involves deformation of the vascular and fibrous layers of the eye and causes four different clinical manifestations (from the mildest to the most severe): chorioretinal hypoplasia, coloboma, retinal detachment and intraocular hemorrhage. Other defects were originally thought to be a part of CEA, including microphthalmia, corneal opacity and retinal folds, but have later been shown to not be a part of the anomaly [8]. These lesions are usually not symmetrical between the eyes.

Chorioretinal hypoplasia is seen in almost all cases of disease, it is present at birth, and does not change with age. Here the chorioid hasn't developed normally and gaps lacking in pigment in the chorioid can be seen, usually lateral to the optic disc; unusually formed vasculature, retinal vascular tortuosity can also be seen. Authors differ in their usage of either chorioretinal dysplasia or chorioretinal hypoplasia, dysplasia being an abnormality in development of tissue and hypoplasia is underdevelopment of tissue; experts seem to differ on this fact as it seems it is not fully understood if this is caused by underdevelopment or abnormal development. Also there are different opinions on the involvement of the retina and the names chorioidal and chorioretinal can be found in different literatures [8].

Coloboma are a genetic ocular defect characterized by maldevelopmental of the eyelid, iris, lens, retina or optic nerve. Typical colobomas develop secondary incomplete closure of the optic fissure, and atypical colobomas develop secondary to a lack of tissue induction [3]. Small coloboma do not normally give problems but big ones can give visual problems, retinal detachment and intraocular hemorrhage.

Retinal detachment results in reduced vision or even blindness. Retinal detachment can affect either a local area or the entire retina, and is then only attached at the optic disc where the optic nerve leaves the eye. This can both occur spontaneously in adults or be present at birth and the animal is blind in the affected eye [8].

Intraocular bleeding can also occur when the retina detaches, and is not considered a basic part of CEA but a result of the anomaly. Through a rupture of the small vessels of the eye the eyeball can be filled with blood. The blood is unlikely to be cleared once the bleeding has started but it will usually not result in increased ocular pressure and therefore it isn't painful for the dog [8].

The most interesting and mysterious thing about CEA is the so called 'go normal' phenomenon. This is where animals that have been diagnosed clinically affected when they are puppies appear normal when examined as adults [8]. That happens due to the pigment filling the back of a young puppy's eye and obscuring areas of choroidal hypoplasia, making the defect impossible to detect upon ophthalmic exam. Thus, the dogs who 'went normal' can give affected offspring when used in breeding.

A group of researchers at Cornell University and Fred Hutchinson Cancer Research Center took on the task of researching the genetic defect that causes Collie Eye Anomaly. Their work showed that the disease is caused by an autosomal recessive mutation on chromosome number 37. Their work further showed that both the mild and severe form stem from the same mutation in all tested cases and that all affected individuals were homozygous for the same mutant gene [7]. The reason for the difference in severity is not fully understood. It is though likely that there are other genes acting as modifiers that influence CEA gene expression [6].

The test itself is a PCR test, which stands for polymerase chain reaction. The PCR test is a fast and relatively inexpensive test that amplifies the desired DNA strand in only a few hours. With this test it is now possible to test all individuals of the affected breeds to find their genetic status which is of great help to find the affected animals that "went normal".

In Barnett's and Stade's article (1979) on CEA in the Shetland Sheepdog they found an interesting family line of Shetland Sheepdogs that had been linebred for several generations. This particular line had kept an old type appearance, having large circular eyes and a domed skull, and they had apparently no signs of CEA in any of the tested dogs, or indeed of any other ocular anomaly [8]. This does in fact pose an interesting question, is there any correlation between the preferred head and eye shape and the prevalence of CEA in the affected breeds. For the Rough and Smooth Collies and the Shetland Sheepdog their standard calls for flat skulls and a head shape resembling a blunt wedge and medium sized eyes of almond shape [4]. For the Border Collie and Australian Sheepdog their standards call for wider and more domed skulls and somewhat larger eyes [4]. So, it is possible that the preferred head and eye shape phenotype is associated with the CEA disease status.

The existence of a genetic test makes breeding of the affected breeds easier, as the knowledge of the genetic status of the breeding animals gives breeders a chance to use the information and choose accordingly which dogs to mate. In Figure 1 all possible genetic combinations are shown. It can be seen, that mating two homozygous normal, or clear (+/+), animals gives 100% clear offspring, which is an ideal situation. Unfortunately, in some breeds, like Smooth and Rough Collies, the percentage of carriers and affected animals is too high and excluding all affected animals from breeding would most likely result in a whole other batch of problems. This effect is called a genetic bottleneck and would likely result in a huge loss of valuable genetic material. Such loss of diversity might be so devastating for these breeds that they might not survive it. If its other qualities are such that they outweigh the presence of CEA it might very well be valuable to use an affected individual in breeding.

Parent I Parent II	+/+ (clear)	+/- (carrier)	-/- (affected)
+/+ (clear)	100% +/+ (clear)	50% +/+ (clear) 50% +/- (carrier)	100% +/- (carrier)
+/- (carrier)	50% +/+ (clear) 50% +/- (carrier)	25% +/+ (clear) 50% +/- (carrier) 25% -/- (affected)	50% +/- (carrier) 50% -/- (affected)
-/- (affected)	100% +/- (carrier)	50% +/- (carrier) 50% -/- (affected)	100% -/- (affected)

**Figure 1.** Possible genetic combinations

The desirable breedings are the ones which have at least one parent that is Normal by the DNA test. All other breedings are at risk of producing pups affected with CEA [6]. The FCI International Breeding Strategies states that results from DNA tests for inherited diseases should be used to avoid breeding diseased dogs, not necessarily to eradicate the disease. Dogs shown to be carriers (heterozygote) for a recessive inherited disease should only be bred to a dog that is proven not to carry the allele for the same disease' [5].

Thus, CEA has for a long time posed a challenge to breeders of the affected breeds. A big diversity of clinical manifestations along with the “go normal” phenomenon, as well as the limited number of adversely affected individuals, posed a problem with defining the mode of inheritance. Nowadays, the existence of the genetic test is an invaluable tool for breeders who can today know the genetic status of their breeding animals and all the offspring they breed. Even with what is known today there is still some way to go before all that is important about CEA is known, and there is ample room for future research into the subject.

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## **QUALITATIVE IDENTIFICATION OF COBALT (II)-ION IN A SOLUTION AND ITS QUANTITATIVE DETERMINATION WITH PERMANGANOMETRIC TITRATION**

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**Summary:** The problems of qualitative and quantitative determination of cobalt (II) in solution are discussed in this article. Relevance of the study lies in the fact that the salts of this element are highly toxic and have a carcinogenic effect, so the careful monitoring of cobalt in drinking water is necessary (MAC 0.01 g/l). The aim is to choose the most selective qualitative reactions and a method of the redox titration to detect and establish the exact concentration of cobalt ions.

**Key words:** cobalt, permanganometry, qualitative reactions, titration.

**Анотація:** В цій статті розглянуто проблеми якісного та кількісного визначення іонів кобальту (II) у розчині. Актуальність роботи полягає в тому, що солі даного елемента мають високу токсичність та канцерогенний ефект, тому необхідно проводити ретельний контроль вмісту кобальту у питній воді (ПДК 0.01 г/л). Метою роботи був підбір найбільш селективних якісних реакцій та методу окисно-відновного титрування для виявлення та визначення точної концентрації іонів кобальту.

**Ключові слова:** кобальт, перманганатометрія, титрування, якісні реакції.

**Аннотация:** В данной статье рассмотрены проблемы качественного и количественного определения ионов кобальта (II) в растворе. Актуальность работы заключается в том, что соли данного элемента обладают высокой токсичностью и имеют канцерогенный эффект, поэтому необходим тщательный контроль содержания кобальта в питьевой воде (ПДК 0.01 г/л). Целью работы являлся подбор наиболее селективных качественных реакций и метода окислительно-восстановительного титрования для обнаружения и установления точной концентрации ионов кобальта.

**Ключевые слова:** качественные реакции, кобальт, перманганатометрия, титрование.

Cobalt is one of the most important trace elements for animals and humans. In the form of vitamin B12 (cobalamin), it plays a number of crucial roles in many biological functions. Cobalamin is necessary for DNA synthesis, formation of red- blood cells, maintenance of the nervous system, growth and development of children.

But at the same time, the excess of cobalt is harmful for a human. The LD<sub>50</sub> value for soluble cobalt salts has been estimated to be between 150 and 500 mg/kg. Thus, for a 100 kg person the LD<sub>50</sub> for a single dose would be about 20 grams. However, chronic cobalt ingestion has caused serious health problems at doses far less than the lethal dose. It causes disturbance in maintenance of the cardiovascular system, the thyroid gland and the nervous system. Inhalation of dusts of this metal leads to such diseases as asthma and pulmonary edema. Cobalt compounds are carcinogenic. The MAC (maximum allowable content) of cobalt in the air is 0,5 mg/m<sup>3</sup>, in the drinking water – 0,01 mg/l.

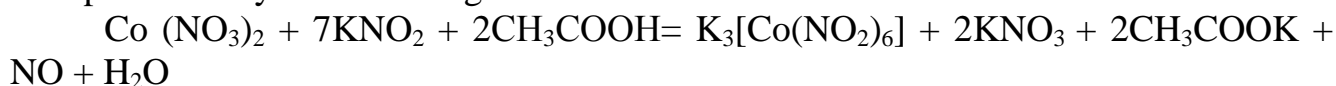
In connection with high level of the air pollution and the drinking water, especially in big cities, the control of the content of cobalt compounds is necessary.

The aim of the study is to choose the most selective and available qualitative reactions that can help to determine the abundance of permissible MAC; selection of the

method of the redox titration to detect and establish the exact concentration of cobalt ions.

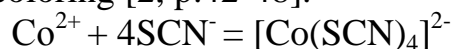
Qualitative analysis of this cation in the solution was based on choice of the most selective reaction with the formation of the characteristically colored complex. Interactions with a lot of inorganic reagents were studied, and the methods with proper sensitivity were selected.

The reaction with potassium nitrite in medium of acetic acid consists in the formation of yellow precipitate of potassium hexa-nitro-cobaltate (III)  $K_3[Co(NO_2)_6]$ . Oxidation of Co (II) to Co (III) takes place with the help of  $NO_2^-$  ions. The process can be represented by the following reaction:



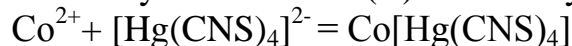
The sensitivity of the reaction is about 0,001 mg ( $Co^{2+}$ )/ml and the presence of nickel-ions is allowed. The reaction should be carried out in an acid medium (pH=3). If the medium is alkaline cobalt (II) hydroxide is precipitated, if it is more acidic – unstable compound  $H_3[Co(NO_2)_6]$  is formed. During the reaction other oxidants and reductants should not be in the solution. For example, hydrogen iodide reduces nitrite-ion to nitric oxide; free iodine is formed and the reagent destructs. Also interaction of hexa-nitro-cobaltate (III) with rubidium, cesium or ammonium ions leads to precipitation [1].

The reaction with ammonium thiocyanate is based on formation of coordination complexes as  $[Co(SCN)]^+$ ,  $[Co(SCN)_2]$ ,  $[Co(SCN)_3]^-$  and  $[Co(SCN)_4]^{2-}$ , which have blue coloring [2, p.42-48].



The mixture consisting of diethyl ether and amyl alcohol is added with the aim to increase the sensitivity of the reaction (up to 0,003 mg( $Co^{2+}$ )/ml). After shaking the organic phase solution has blue coloring that is caused by thiocyanate coordination complexes. PH of the solution should be about 4-5. The presence of  $Fe^{3+}$  leads to formation of red colored complex  $Fe(CNS)_3$ , that masks blue coloring of  $[Co(SCN)_4]^{2-}$ . So the reaction in the presence of  $Fe^{3+}$  should be carried out with adding tartaric or oxalic acid, alkali metals fluorides, sodium pyrophosphate combining with  $Fe^{3+}$  into colorless complexes. Ions of Ni (II) can be in the solution [3].

The reaction  $Co^{2+}$  with ammonium tetrathiocyanomercurate(II) is the formation of dark-blue crystals of cobalt(II) tetrathiocyanomercurate(II)  $Co[Hg(CNS)_4]$ .



The reaction is specific, only ions Fe (III) interfere with the determination, the sensitivity is 0,005 mg( $Co^{2+}$ )/ml, pH should be less than 7. If  $Zn^{2+}$  ions are added to the solution, mixed zinc-cobalt (II) precipitate is formed immediately [3, p.237-238].

Short comparative characteristic of the reactions mentioned above is given in Table 1.

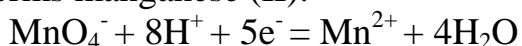


Table 1. Comparative characteristic of the qualitative reactions on cobalt(II) ion.

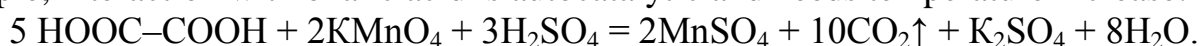
The reagent	Observations	The sensitivity, mg(Co <sup>2+</sup> )/ml	Conditions
KNO <sub>2</sub> + acetic acid	Yellow crystalline precipitation	0.001	Ni <sup>2+</sup> - ions do not interfere with the determination.
NH <sub>4</sub> CNS + diethyl ether, amyl alcohol	Blue coloring	0.003	Ni <sup>2+</sup> - ions do not interfere with the determination. Fe <sup>3+</sup> should be removed by adding tartaric or oxalic acid, fluorides of alkali metals, sodium pyrophosphate.
(NH <sub>4</sub> ) <sub>2</sub> [Hg(CNS) <sub>4</sub> ]	Yellow crystalline precipitation	0.005	Only Fe <sup>3+</sup> - ions do not interfere with the determination.

Among methods of quantitative determination of cobalt (II) ions in the solution the permanganometric titration was considered as a type of a redox titration.

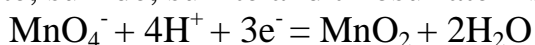
The permanganometric method is based on reduction of potassium permanganate in different mediums. In acid medium (pH<4) permanganate ion attaches five electrons and forms manganese (II):



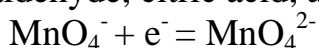
Most of the reactions have quite big velocity. But there are some exceptions, for example, interaction with oxalic acid is autocatalytic and needs temperature increase:



Potassium permanganate reduction takes place in weak acid, neutral and weak alkali mediums with attaching three electrons and formation of brown precipitate of manganese (IV) oxide. In these conditions, for example, cyanide can be oxidized to cyanate, sulfide, sulfite and thiosulfate – sulfate, hydrazine – to nitrogen.

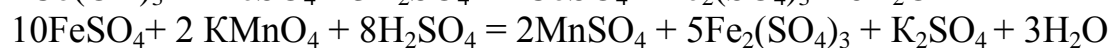
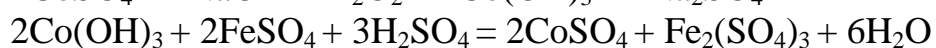
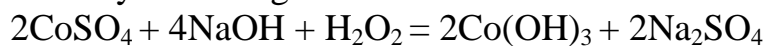


In alkali solutions permanganate-ion is reduced with the help of one electron forming manganite-ion. A lot of organic compounds, such as methanoate, formaldehyde, citric acid, acetone, can be determined by this method [4, p. 375-379].



Advantages of the method: the solution of  $\text{KMnO}_4$  can be used as a titrant in any medium; possibility of using the solution of potassium permanganate in acid medium for determination of many substances which do not interact with weaker oxidants; stoichiometry of most redox titrations; optimal velocity of reactions; opportunity of titration without an indicator; the availability of potassium permanganate. But at the same time the permanganometric method has some disadvantages: a titrant  $\text{KMnO}_4$  is prepared as a secondary standard – it is hard to obtain chemically pure potassium permanganate; reactions with  $\text{MnO}_4^-$  ions should be carried out in strictly definite conditions (pH, temperature, etc.),  $\text{Cl}^-$  ions should be removed from the solution [5, p. 297-298].

The determination of cobalt after precipitation as cobalt (III) hydroxide is based on quantitative oxidation of cobalt (II) to cobalt (III) by hydrogen peroxide in alkali medium. Excess of iron (II) is added to the solution as ammonium iron (II) sulfate and unreacted iron (II) is titrated by the solution of potassium permanganate. It is represented by following reactions:



Advantages of the method: determination of cobalt in a solution is possible in the presence of a small quantities of iron and nickel impurities; such ions as cadmium, zinc, calcium, strontium, barium, etc. do not interfere with determination; high accuracy of a titration that is conditional on Mohr's salt use (ammonium iron (II) sulfate) – its solutions are stable and are not oxidized by atmospheric oxygen; clear color change when the equivalence point is reached. Disadvantages: if the process of boiling has not been carried through undecomposed hydrogen peroxide it can react with potassium permanganate and give a significant error in the titration.

The methodology of the experiment. 10 ml of the analyzed solution of cobalt (II) sulfate with concentration 0,17 M (that corresponds to 100 mg  $\text{Co}^{2+}$  per aliquot) was selected with Mohr's pipette and was put into a conical flask of 250 ml. The solution had red coloring. 30 ml of 0,2 M solution of sodium was added – blue cobalt (II) hydroxide precipitated, and 80 ml 3% solution of hydrogen peroxide – the solution foamed and black cobalt(III) hydroxide precipitated. The solution was boiled to remove unreacted hydrogen peroxide. 30 ml of 0,1 Eq/l solution of ammonium iron (II) sulfate in 6 M sulfuric acid, 15 ml of a 5 M solution of sulfuric acid was put into the flask. Mixed. Cooled – the temperature of the solution had increased due to hydration reaction of sulfuric acid and sodium hydroxide. The solution changed its color into yellow-pink due to the presence of  $\text{Fe}^{2+}$  and  $\text{Co}^{2+}$  ions. Excess of unreacted iron (II) sulfate was titrated with 0,1 Eq/l solution of potassium permanganate until pale pink coloring was stable for 30 seconds [2].

The following results were obtained: an average volume 13.2 ml of the solution of potassium permanganate was spent on the titration of 10 ml aliquot of analyzed solution. The practical concentration of the cobalt ion was 0.168 mol/l. Relative error of the method was 1.18%.

So, various qualitative reactions were studied and the most optimal ones on such parameters as selectivity, availability of reagents and sensitivity were found –

interaction of cobalt ions with ammonium thiocyanate, potassium nitrite and ammonium tetrathiocyanomercurate (II).

The method of the permanganometric titration can be used for determination of cobalt ions in the absence of instrument (for example, for potentiometric titration, spectrophotometry). The relative error of the experiment does not exceed 1.2%. The method is selective, that allows its use for determination of the concentration of cobalt in the drinking water.

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УДК 621.865

## **MIRACLES OF MEDICINE: CAN ARTIFICIAL ORGANS REPLACE REAL BODIES?**

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**Language supervisor: Belovodskaya I.I.**

**Анотація :** Стаття присвячена розгляду переваг і недоліків використання штучних органів в сучасній медицині для збереження і продовження життя людей і забезпечення нормальної життєдіяльності, розвиток технологій створення та інтеграції штучних органів, а також наведені основні різновиди існуючих і таких, що розробляються зараз штучних органів, розглянуті перспективи і можливості подальшого розвитку даної галузі медицини.

**Ключові слова:** штучні органи , порятунок життя , штучне серце , штучні нирки , штучні легені , штучна шкіра , 3D друк штучних органів.

**Аннотация:** Статья посвящена рассмотрению преимуществ и недостатков использования искусственных органов в современной медицине для сохранения и продления жизни людей и обеспечения нормальной жизнедеятельности, развитие технологий создания и интеграции искусственных органов, а также приведены основные разновидности существующих и разрабатываемых в настоящий момент искусственных органов, рассмотрены перспективы и возможности дальнейшего развития данной отрасли медицины.

**Ключевые слова:** искусственные органы, спасение жизни, искусственное сердце, искусственные почки, искусственные легкие, искусственная кожа, 3D печать искусственных органов

**Summary:** The article deals with the advantages and disadvantages of using artificial organs in modern medicine for saving lives and ensuring a normal functioning. The development of technologies for the creation and integration of artificial organs, the main variety of existing and emerging at the moment artificial organs and prospects for further development of this branch of medicine are discussed.

**Key words:** artificial organs, saving lives, artificial heart, artificial kidney, artificial lung, artificial leather, 3D printing of artificial organs.

*Along with the shift in emphasis to developing future innovations that enhance quality of life, there is a growing need for those devices that keep patients alive. Artificial organs and organ assist devices represent such lifesaving technologies.*

*Jörg Vienken*

An artificial organ is a man-made device that is implanted or integrated into a human to replace a natural organ, for the purpose of restoring a specific function or a group of related functions so the patient may return to a normal life as soon as it is possible.

Technology has improved hugely since the Jarvik-7, which was powered by a large console that made it impossible for patients to leave the hospital. Doctors have yet to develop a true replacement for the real thing. And with the worldwide number of patients in need of a transplant far exceeding the small number of available donors, the need for a longer-lasting alternative certainly hasn't gone away. There is a considerable lack of donor organs now, and patients around the world face terrifying waitlists for organ transplants. In the USA, more than 108,500 patients with malfunctioning organs are listed on the list for organ transplantation in 2010, including heart, kidney, liver, lungs, pancreas and cornea, exceeding the number of patients on the waiting list from 1990 by 5 times. The waiting time for a liver transplant averages 26 months; for a lung, it can be nearly three years.

So, there is a number of reasons to construct and install an artificial organ, an extremely expensive process initially, which may entail many years of ongoing maintenance services not needed by a natural organ, might include:

1. Life support to prevent imminent death while awaiting a transplant;
2. Dramatic improvement of the patient's ability for self-care;
3. Improvement of the patient's ability to interact socially;
4. Cosmetic restoration after cancer surgery or an accident.

Already, researchers are developing bioartificial organs that can keep patients with serious organ failure alive and functioning for years. For now, the goal is to keep patients alive until they can receive a real organ, but one day, patients may be able to live for long periods of time with artificial hearts or kidneys.

'In the late 1990s, people started working on developing organs using a tissue-engineering approach, and everybody thought in the next 10 years we would be growing all organs,' said Dr Alex Seifalian, professor of nanotechnology and regenerative medicine at University College London (UCL), who was the scientific lead on the bionic man project.

'They were trying to simulate what nature is; trying to grow, for example, a nose or ear; trying to make exactly the same cartilage and grow cells on some bio-absorbable material that disappears to leave the cartilage, and that will be placed in the patient.' But scientists, including Seifalian, have encountered problems with this approach. 'In 1997 we had a grant to develop artificial arteries with tissue engineering,' he said. 'In animals it worked very well and then when we went to humans it just didn't work very well because the people who needed arteries were over 50 years old, their cells weren't growing, they'd get infections.' The other problem was making the technology commercially viable: growing organs in a lab is a costly, time-consuming process and Seifalian's collaborator company pulled out. So, one of the key problems with artificial

organs is ensuring biocompatibility, the ability of materials to provide a good environment for living cells to grow and function around them.

Proponents of biological organ replacements have recently been encouraged by the development of 3D tissue printing, which offers the tantalising possibility that we might build organs mechanically, layer by layer — a much faster process than growing them in the lab. But printing complex internal organs like the liver or heart is still some way off, and the technology will face similar issues to traditional tissue engineering when it comes to implanting. In the meantime, some scientists are pursuing a different approach, combining biological tissue with synthetic materials and/or mechanical and electronic components to create what could be called hybrid or even cyborg organs, which are more easily manufactured, longer lasting and more successful once implanted into the body.

Let's take a look at artificial organs you can use today, and what's in store for the future.

### Brain

"Brain pacemakers" are used to treat people who suffer from epilepsy, Parkinson's disease, major depression and other diseases. The pacemaker is a medical device that is implanted into the brain to send electrical signals into the tissue. Pacemakers may also be implanted outside the brain, on or near the spinal cord, and around cranial nerves [1].

### Ear

A cochlear implant (CI) is a surgically implanted electronic device that provides a sense of sound to a person who is profoundly deaf or severely hard of hearing. The quality of sound is different from natural hearing, with less sound information being received and processed by the brain. However, many patients are able to hear and understand speech and environmental sounds. Newer devices and processing-strategies allow recipients to hear better in noise, enjoy music, and even use their implant processors while swimming.

As of December 2010, approximately 219,000 people worldwide have received cochlear implants. The vast majority are in developed countries due to the high cost of the device, surgery and post-implantation therapy [1].

### Heart

If you want a mechanical ticker now, don't get too attached to it because it's only temporary. Internal artificial hearts such as the AbioCor exist today, but because of the tendency to form stroke-inducing blood clots, they're limited to heart patients waiting around for organ transplants.

Scientists are aiming for a miniaturized artificial heart controlled by minuscule processors that determine how quickly the heart needs to beat. It will be equipped with sensors that detect artery blockage and will notify its patient and the doctor of any impending malfunctions [3].

### Liver

Of the 16,000 people waiting for liver transplants, there are only about 6,500 transplantable livers available each year. Researchers are developing ELAD, an Extracorporeal Liver Assist Device that resides outside the body. Mimicking a normal liver, it cleanses the blood of toxins and waste, and produces albumin and clotting factors. It's not all artificial, though, with the secret sauce inside being "immortalized human liver cells," interlaced with tiny tubes through which the patient's

blood flows. The current technology offers a temporary replacement for the liver while awaiting a donor [1].

### Hand

Today's artificial hands have come a long way from the days of Captain Hook. Using what's called myoelectric linking, the prosthetic limb picks up electrical impulses from remaining muscle fibers on the arm, transmitting those impulses to articulating fingers and a thumb. They're attached to the stub by suction, belts or cuffs, and some can be expensive, costing upwards of \$35,000. More reasonably priced is the i-Limb, an \$18,000 artificial hand with articulating fingers and thumb, each with its own motor [1].

### Lungs

About the closest you'll get to an artificial lung today is a clunky heart-lung machine next to your hospital bed. These **ECMO** (extracorporeal membrane oxygenation) machines are designed for temporary use, while a patient recovers from infections or trauma.

Scientists are concentrating on a dual-function device that pumps blood and oxygenates it at the same time, similar to an internal heart/lung machine.[1]

### Skin

Artificial skin is skin grown in a laboratory. It can be used as skin replacement for people who have suffered skin trauma, such as severe burns or skin diseases, or other purposes.

Synthetic skin was invented by John F. Burke, chief of Trauma Services in Massachusetts General Hospital and Ioannis V. Yannas, a chemistry professor at Massachusetts Institute of Technology, Cambridge, Massachusetts. In the 1970s, they created a polymer with collagen fibers and sugar molecules. A small porous was formed. When the porous was placed on the wound, skin cells around it seemed to encourage a faster healing process. This allowed the healing process to continue at a much faster rate. They also created a skin from shark cartilage and cowhide. When this skin dried and was sterilized, it could be made into a thin membrane in which materials could pass through like with the original dermis. Silicon was then added to create a protective top layer to represent the epidermis.

In the late 1970s, medical researchers began experimenting with sheets of artificial skin that could be permanently grafted onto patients who have no other options. Two Boston surgeons discovered a successful new artificial skin design in 1981 that is known as Integra. Instead of replicating the function of healthy skin, Integra “tricks” real skin cells into growing a new dermis, which would replace the damaged dermis [2].

What are the future perspectives? Artificial organs will help keep patients with organ failure alive. Production of such medical devices under the premises of economy-of-scale will help make artificial organs available for larger patient cohorts as already shown for the artificial kidney. New developments on organ printing and thereby providing three dimensional arrangements of functioning tissues and blood vessels are promising techniques for further improvements. Bioengineers currently work on regenerating organs from tissue by using stem cells and appropriate 3D-biodegradable scaffolds. An organ fabricated from the recipient's own cells could be made to order and would not face the risk of immune rejection. “These organs would be available on demand and thereby overcome donor organ shortage,” says Harvard Medical School's Harald Ott.

So, the question of the development and application of artificial organs is quite controversial. There is no single point of view on this issue. No single technology of production and development in this area, which has a positive effect on the development of biological science. The question about the future of artificial organs remains controversial. But the main conclusion can be done now – the technology of artificial organs in the near future may become a serious competitor to the transplantation in the noble cause of the incurable patients' the lifesaving.

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УДК 519.83

## **BASIC FACTS ABOUT BETTING**

**Kovtun S.A. (Kharkiv)**

**Language supervisor: Nikitina L.D.**

**Summary:** The purpose of this article is to show the readers, that betting is not only one more type of entertainment, but also a difficult math model. And a player has to know it and count its peculiarities. I also mentioned a few tips for first-time gamblers, which will help them to avoid extra money losses.

**Key words:** betting chart, bets, odds, probability, tips.

**Анотація:** Мета поданої статті полягає в тому, щоб показати читачеві, що ставки на спорт це не просто ще один вид розваг, а складна математична модель, яку гравець повинен розуміти і враховувати її особливості. Також я написав декілька порад для гравців-початківців, які допоможуть уникнути додаткових грошових втрат.

**Ключові слова:** букмекерська стрічка, ймовірність, коефіцієнти, поради, ставки.

**Аннотация:** Цель данной статьи состоит в том, чтобы показать читателю, что ставки на спорт это не совсем очередной вид развлечения, а сложная математическая модель, которую игрок должен понимать и учитывать её особенности. Также я написал несколько советов для начинающих игроков, которые помогут избежать дополнительных денежных потерь.

**Ключевые слова:** букмекерская лента, вероятность, коэффициенты, советы, ставки.

Betting appeared a long time ago. People in ancient Rome bet on gladiators' fights. But even before that people had bet to win several coins or some valuable things. Sometimes other people were called upon as referees to ensure a fair play. Those middlemen received a reward for their job from the betting parties. These middlemen are called bookmakers today.

The principle idea of sport betting is quite simple. You bet at the bookmaker's office on the result of the sport event chosen by you. Every outcome has its own odds to be set in bookmakers' opinion depending on the probability of any outcome. If the bet wins you are going to receive a profit. Otherwise the profit goes to the bookmaker and you get a naught.

Many betters especially beginners consider betting to be quite simple. As a matter of fact, they are mistaken like that fact that a favorite always wins a victory over an outsider.

It should be understood that a lot of factors affect the outcome of a sport event. These factors are as follows: physical fit, their motivation, the place where the event is held (home or in guest), the weather, etc. The factors like that should be taken into consideration in sport betting by all means. Otherwise you will never do well in this field.

The Internet betting is gaining popularity today. The reason is that one doesn't have to go somewhere to bet. It is enough to register at one of numerous betting companies. Bookmakers' sites work 24 hours 7 days a week and offer a wide range of sport events to bet.

The people who are going to take betting seriously must be experts at least in one kind of sport and be able to analyze a sport event and know how to manage their money. This knowledge and these skills will ensure successful betting [1].

I would like to begin with what every gambler starts: a betting chart (a list of games and odds). The first question I had when I looked at a betting chart was how a bookmaker defines all this huge amount of odds.

The purpose of betting shops operation is only to derive profit. In spite of a widely spread opinion, the bookmaker's profit does not depend upon the amount of lost bets, but on the correctly calculated odds. What does the word "correctly" mean? It means that the bookmaker must make profit even in case of the most unexpected outcome.

Let us consider how the odds are set. First, the analytics calculate teams' chances to win or loose. This is done in numerous ways which may be divided into two sets: analytic and heuristic.

Analytic ones are mostly statistics and mathematics (the probability theory), and heuristic ones are experts' estimates. The probabilities of outcomes are defined by combining the acquired results. Let us assume that the analytics and experts got the following data:

1 <sup>st</sup> team's		2 <sup>nd</sup> team's
victory	Draw	victory
55%	30%	5%

When converting the probabilities into odds we divide 1 by the probability, e.g.  $1/0.55=1.82$ , and get the following:

V1	X	V2
1.82	3.33	6.67

These are "true chances" but these odds will never be on the betting chart, because in this case the bookmaker will not make profit. On the chart these odds will roughly look like this:

V1	X	V2
1.70	3.00	6.00



And when talking about probabilities we will have:

<b>V1</b>	<b>X</b>	<b>V2</b>
59%	33%	16%

The total sum of probabilities does not equal 100% but 108 %. This difference of 8% is the bookmaker's profit margin envisaged by him in the odds.

Starting to accept the bets on the game the bookmaker sees the betting amounts of money are divided between the three outcomes in the following way:

<b>V1</b>	<b>D</b>	<b>V2</b>
75%	15%	10%

Thus, the gamblers betted \$ 75,000.00 on the first team victory (V1), \$15,000 on the draw game, and \$ 10,000.00 on the second team victory of every \$ 100,000.00. The majority of gamblers bet on favorites compiling most of their expresses based on these prospective results. What would the bookmaker gain from each betted \$100,000 in case of various outcomes?

<b>Outcome</b>	<b>Payments of winnings</b>	<b>bookmaker's net profit</b>
V1	127 500	-27 500
X	45 000	55 000
V2	60 000	40 000

As we can see, in case of the favorite's victory to happen more often the bookmaker will suffer losses. This is totally unacceptable for business and the bookmaker must exclude even a theoretical chance of such situation.

To do this he has to arbitrarily reduce the favorite's odds. The bookmaker does not know in advance how the bets will be divided, but he is certain that the gamblers will heavily bet on the favorite. Due to this the bookmaker overrates the favorite's chances to win.

Indeed it is impossible to calculate neither the real chances nor the division of gamblers' bets. There is always a certain inaccuracy.

That is why bookmakers try to minimize the favourite's odds to guarantee their profits, i.e. they define the teams' chances and add 10-20 percent to the calculated probability of a win. And they change the odds to gain maximum profits doing this based on the bets' current distribution while the betting money arrives.

In conclusion we can say that the bookmakers' basic principle is to distribute the money among two or more gamblers in such a way that they would pay the winners at the losers' expense and leave a certain percentage of the betting money for themselves.

Very often the odds calculated this way have nothing to do with the probabilities of real events. Thus, one must have one's own system of analyzing sports events. Now I am going to give a few useful tips on betting.

- Gamblers must know their kind of sport.

One should bet on the kind of sport one knows well. It is stupid to bet without knowing the rules of the game.

- Gamblers must know their league.

There is more than one, sometimes three or four leagues in many kinds of sports. If you feel that a certain league is your cup of tea, go on and bet. Do not try and jump from league to league and "live where you feel comfortable".

- Gamblers must know their bookmakers' companies well

Learn the betting rules, find out what kinds of bets fit your kind sport best. Before choosing a bookmaker pay attention to the odds offered (high or low, kinds of sport, their cuts, etc.), payment options and only then start using their services.

- Gamblers must know their budget.

Determine the total amount you can afford to spend during the season and the amount of your bet. Remember that your budget should not exceed 5 % of your income for one season. Do not bet too high.

Do not bet somebody else's money. Before borrowing money think how you are going to pay it back.

- Before bets on real money, try to bet on virtual.

In my opinion, the best way to show you, how good you are in betting is to participate in tournament of predictors. In most cases it is free of charge and also involves valuable prizes for the best predictors [2].

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УДК 616-085: 620.3

## **NANOMEDICINE: THE USE OF NANOSCALE SCIENCE FOR THE BENEFIT OF THE PATIENT**

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**Summary:** This article provides an overview of some tools, methods and materials of nanotechnology that offer potential applications in medicine, followed by a series of examples showing applications that are already in development. The importance of these developments is discussed in their wider context.

**Key words:** nanoscale science, nanometre, LDL particles, scanning microscope, nanolevel, medical diagnostics, nano-optics, nanosensor.

**Анотація:** У статті розглядаються деякі нанотехнологічні пристрої, методи та матеріали, які можуть знайти потенційне застосування у медицині, наведено декілька прикладів пристроїв які вже є у розробці. Висвітлюється важливість цих розробок.

**Ключові слова:** нанонаука, нанометр, ліпопротеїди низької густини, растровий мікроскоп, нанорівень, медична діагностика, нанооптика, наносенсор.

**Аннотация:** В статье рассматриваются некоторые нанотехнологические устройства, методы и материалы, которые могут иметь потенциальное применение в медицине, приводятся примеры некоторых разработок. Освещается важность этих разработок.

**Ключевые слова:** нанонаука, нанометр, липопротейды низкой плотности, растровый микроскоп, наноуровень, медицинская диагностика, нанооптика, наносенсор.

In the development of modern medicine, new scientific findings and technological developments have often served as milestones for a deeper knowledge and more effective treatments: the development of the light microscope, for example, led to the discovery of bacteria as disease pathogens, which in turn provided the platform for the discovery of penicillin as a natural, antimicrobial substance that could be used to cure infections which previously could be expected to run a fatal course. As one of the newest areas of science, nanoscale science and technology are seen by many as the key technology of the 21st century, which of course raises the question as to what role this technology will play in medicine.

Nanoscale science deals with very small objects: atoms, molecules, aggregates and surfaces, for which new instruments have to be used so that these objects can be studied, ‘touched’ and structured for specific applications. The historically separate disciplines of physics, chemistry, biology and medicine meet today in realms where things are measured by the nanometre (one thousandth of a thousandth of a millimetre), making nanoscale science a uniquely interdisciplinary field [6].

The basic unit of all living organisms, the cell, is made up of numerous smaller structures, known as organelles; these consist of biomolecules that interact with one another, bringing together mechanical and biochemical functions at the nanoscale level. The molecular ‘nanomachines’ thus form the foundations of all living organisms. ‘Nano’ is thus not so much a technological invention of the modern age as a fundamental characteristic of all life. The development of nanoscale science has opened our eyes in this respect.

The possibility of visualizing nano-objects has shown that naturally occurring Nanoscale objects can be dangerous: LDL particles (which transport cholesterol), viruses and also nanoparticles in exhaust emissions lead to major and common diseases [7].

Many disease processes begin in specific cell types with a dysfunction at the level of the cell organelles and the cellular biological ‘nanomachines’. By contrast, most methods used in medicine today are either macroscopic – scalpel, radiotherapy, cardiac catheter – and thus too crude for the diseased cell, or the medicines used to ‘flood’ the body in a very non-specific way and also trigger side effects in organs that are not even involved in the disease process. It would also make sense to treat the disease processes occurring at the nanolevel in individual cells and organs by using nanoscale tools that can specifically target these cells and organs.

Modern medicine has already achieved a lot, but has still not eradicated the principal medical problems: arteriosclerosis continues to cause myocardial infarction and stroke, leading to suffering and the need for care, as well as early death; cancers are more responsive to treatment than they used to be, but often at the cost of severe side effects; infections such as malaria continue to kill a million children a year in Africa; brain disorders in many cases lead to a loss of independence and the need for care; the

incidence of diabetes is rocketing all over the world. New medical approaches for these therapeutic areas would therefore be very welcome [3].

Nanoscale science can be described through the tools, methods and materials used. These include, amongst others:

1. *Scanning microscopes – visualization and manipulation of individual atoms and molecules.*

It was the development of the Scanning Tunnel Microscope and the Atomic Force Microscope (AFM) that triggered the emergence of nanoscale science. Scanning microscopes “feel their way” over surfaces spot by spot, so that extremely high-resolution images can be created right down to the individual atom. Originally used above all for physical experiments, these methods have acquired a value in biomedical imaging. The use of AFM technology as highly sensitive sensors for processes taking place on surfaces is becoming increasingly important for medical diagnostics. The unique opportunity to ‘treat’ individual atoms and molecules mechanically using atomic force microscopes has hardly been used in medicine as yet.

- *Scanning microscopy*

Scanning microscopes allow very high-resolution images of biological preparations to be produced right down to individual molecules. Since this is possible in a physiological environment, it is even possible to obtain very high-resolution images of live objects, and using microscopic film it is even possible to observe changes over time. This complements the possibilities offered by other microscopes, such as the electron microscope, which is dependent on very thin slices and a vacuum in order to achieve a high resolution [2].

- *Catheter-based scanning microscopes*

Since the components of scanning microscopes may also be built very small, it is possible to construct very compact devices even on the tip of an endoscope that is used in medicine. This enables measurements to be made, even inside the body.

2. *Nano-optics*

Nano-optics is concerned with optical phenomena below the wavelength of light, for example the optical visualization of individual molecules. For instance, it allows us to study the interaction of two biomolecules. Of particular medical importance is the possibility of developing sensors based on nano-optics that permit the detection of very small quantities of a biomolecule.

- *Nano-mechanical sensors*

Atomic force microscopy is based on highly sensitive measurements of the deflection made by a microscopically small lever arm as a force sensor for extremely low forces. The binding of molecules to the surface of the lever arm likewise leads to forces acting on the lever arm. This instrument thus becomes a highly sensitive sensor: in the gaseous phase, this kind of nanosensor is suitable for detecting the complex ‘odour pattern’ of specific diseases in exhaled air, thus allowing a rapid diagnosis.

- *Nano-optic sensors*

Nano-optic microscopes exploit optical effects in the so-called optical near field, below the wavelength of light, in order to achieve very high resolutions. The transparent tips used for this, with their very small optical aperture, can also be used as highly sensitive sensors for biomolecules when these are furnished with a fluorescence

mechanism that can be ‘switched off’; in experiments, it is even possible to detect the pairing of individual nucleic acid strands with this concept.

### 3. *Nanomaterials and nanosurfaces*

The nanoscale structure of a material has an enormous impact on the properties of objects. The nanoscale sciences have led to the development of novel materials, such as carbon nanotubes and carbon nanoballs (fullerene) with unique properties. There has also been a substantial growth in our understanding of nanostructured objects such as nanoparticles, nanosleeves, nanocarriers and nanostructured surfaces. Improved surface properties play a key role both in the biocompatibility of implants and vehicles for medicines and also in novel medical laboratory tests.

- *Biocompatible implants*

The biocompatibility of implants is becoming an increasingly important issue in medicine: more and more patients, for example, have coronary stents, cardiac pacemakers and joint prostheses. Stents are implanted because they improve the prognosis, e.g. in coronary artery disease, by keeping the vessel dilated. But they are not perfect: in some patients, the vessel eventually closes again despite the stent, thereby necessitating a new intervention.

More recent drug-coated stents only partially solve the problem: while late occlusions now occur less often, there is evidence to suggest that acute stent closure may occur more frequently in certain patients with drug-coated stents. Improving the structural properties of these stents, e.g. by means of nano-structured surfaces, is one way of avoiding such problems in the future.

- *Nano-bio interaction*

The interaction of cells and nano-materials is an important area of current research. It works as the binding of polymeric, biocompatible and non-toxic nanocarriers to cells, their uptake in the cell and the slow release of an active substance. Data from scientific studies show that optimum biocompatibility and very low toxicity can be achieved through the selection of suitable materials for the design of such carriers. Long-term studies on the question of unexpected long-term complications, such as organ lesions, tumour development or malformations, are currently under way.

- *Targeted therapy*

One of the key weaknesses of drug therapy today is the fact that most medicines entering the body can act on all the cells and organs of the body. They may well lead to the desired therapeutic effects on the diseased cells, but can also induce side effects on cells and organs not involved in the disease process. Not only this is unpleasant or even dangerous, but it also limits the dose of medicine necessary for treating the disease. This is seen especially in cancer therapy, where the high-dose chemotherapy that is often needed to effect a cure leads to nasty side effects in the bone marrow, gut, hair and other organs [1].

- *Designer particles for molecular diagnosis and targeted therapy*

An important area of nanoscale science is therefore the development of nanostructured carriers for medical applications. The wish list of such systems is long: they should selectively home in on the cells and organs of the body that are involved in the disease process, specifically targeting their potent healing effects on these cells and organs, while sparing cells not involved in the disease process. They should be completely non-toxic, biodegradable or capable of natural excretion, not be recognized

or eliminated by the body's own immune system before they have reached their target, and not induce any allergic reactions. Ideally, they are generic, i.e. they can be 'programmed' to combat a wide variety of diseases by docking onto any target structures one chooses and being capable of carrying any medicines.

#### 4. *Nanofluidics*

Thanks to the sensitivity of new diagnostic methods based on Nanotechnology, it is possible to manage with very small sample quantities, so that a whole series of different measurements can be performed in a single drop. However, the handling of fluids in such tiny quantities calls for new methods, which fall under the heading "micro- and nanofluidics".

- *Laboratory diagnostics*

The miniaturization of diagnostic tests that are based on the measurement of substances in fluids has crucial advantages: The quantity of samples, e.g. blood samples from premature babies or patients in intensive care, can be massively reduced. At the same time, fewer reagents are needed. Tests that are run on a surface and thus depend on the diffusion of the molecules to be measured become faster because the diffusion path is shorter. Miniaturization also allows parallelization and thus simultaneous measurement of multiple parameters in the same test. A matrix immunoassay based on micro/nano-fluidics performs multiple measurements of clinically important parameters in the smallest possible space. The vision of obtaining all parameters that are relevant to a patient from a single drop of blood within minutes appears to be within reach.

#### 5. *Nanosystems, nanodevices and nanorobots*

To identify specific diseased cells in the body and to home in on them with local treatment that targets only these cells, thereby minimizing side effects while optimizing efficacy calls for nanoscale objects with complex functionality. This development of ever 'smarter' systems for combating disease at the nanolevel is inspired by biological models in the human body and is highly promising, but it is still very much in its infancy. In certain situations, it is also an advantage that there is no need for transferring genetic material or for the use of stem cells [5].

Nanomedicine as an approach to diagnosis at the molecular level offers the prospect of detecting and locating diseases such as arteriosclerosis at an early stage, which can already be done in disease models, e.g. with transgenic mice. If this is confirmed in patients, there is a possibility that severe complications such as stroke or myocardial infarction, which lead to a lot of suffering, loss of independence, a chronic need for treatment and high costs, might be avoided by means of prophylactic treatment of people at risk to make the occurrence of these far-reaching events more unlikely.

One of the characteristics of nanomedicine is the highly targeted use of very small quantities of substance both for diagnosis and for therapy; in experimental studies, for example, certain therapeutic effects have been achieved using quantities of substance a hundred times lower than with conventional medicines. The miniaturization of diagnostic tests can considerably reduce both the amount of chemical reagents needed and also the materials needed for equipment and samples. The characteristics offer huge potential for sustainable medicine.

Nanotechnology is seen by many as the key technology of the 21st century, which will not only have a major formative influence on the main foreseeable fields of application, computer technology and medicine, but will also be of fundamental

importance for national industries and economies. As a result, the major industrial nations and political unions, above all the USA, EU, Japan, Russia and China, are investing enormous funds in the development of nanotechnology and nanomedicine.

Nanomedicine is aimed at ensuring the wellbeing of the patient and society, and not simply a propagation of new technology regardless of its implications. Responsible research in nanomedicine strives to gain a broad and fundamental understanding of nanoscale scientific tools, methods and materials, as well as their interaction with biological organisms. Basic physical and chemical research in the field of Nanotechnology is of course an indispensable part of this effort. Cell culture experiments, studies in organ sections, methods of systems biology and the use of genomics and proteomics methods can answer a lot of questions and should be used wherever possible to explore the bio/nanointeraction. But before the step is taken to perform studies in humans, the responsible use of animal studies is still necessary today in order to arrive at an overall assessment of the interaction between nano-objects and the whole body and to evaluate longer-term favourable or unfavourable effects [8].

Finally, well-planned studies in humans are necessary with the promising developments of new nanomedicine-based treatment. Clinical research and the early use of new therapy in patients with otherwise untreatable diseases must not be made impossible by excessive regulatory hurdles; on the other hand, well-founded study data will, of course, be necessary for broad commercial use.

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## **BIA METHOD MEASUREMENT ERRORS AT HOME**

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**Summery:** Bioimpedance analysis of human body composition is one of the contemporary methods of morphological and functional diagnosis. It is based on measuring the impedance of the whole body or parts of the body using special devices – bioimpedance analyzers.

**Keywords:** basic metabolic rate, bioelectric impedance analysis, body cell mass, body composition, body mass index, tissue resistivity, extracellular water, fat-free (lean) mass, skeletal muscle mass, total body water.

**Анотація:** Одним із сучасних методів морфологічної та функціональної діагностики є біоімпедансний аналіз складу тіла. Він заснований на вимірюванні опору всього тіла або частини тіла за допомогою спеціальних пристроїв – аналізаторів біоімпеданса.

**Ключові слова:** безжирова (худа) маса, біоімпедансний аналіз, електропровідність біологічних тканин, загальна вода організму, індекс маси тіла, компонентний склад тіла, основний обмін, позаклітинна рідина, скелетно-м'язова маса.

**Аннотация:** Одним из современных методов морфологической и функциональной диагностики является биоимпедансный анализ состава тела. Он основан на измерении сопротивления всего тела или части тела с помощью специальных устройств – анализаторов биоимпеданса.

**Ключевые слова:** безжировая (тощая) масса, биоимпедансный анализ, внеклеточная жидкость, индекс массы тела, компонентный состав тела, общая вода организма, основной обмен, скелетно-мышечная масса, электропроводность биологических тканей.

People have been worrying about the problem of healthy weight for a long time. But weight measurement does not give an objective evaluation because it doesn't matter how much we weigh, but it is important in what proportion are muscle, water and fat mass in the body. The deviation from the norm can result in serious health problems. But there is no opportunity to weigh the parts of the body separately.

Why is the body composition so important? Fat content and liquid distribution in the body can vary essentially depending on the nature of the physical activity, nutrition, the individual characteristics of metabolism and diseases. Deviation from the standards can result in serious health problems.

It is absolutely proved that there is a link between excess in weight and terrible diseases such as coronary heart disease, hypertension, diabetes, cancers and cholelithiasis. Half of obese patients have an increase in blood pressure. Myocardial infarction is observed in 4-5 times more often for obese individuals than for people with normal weight. Diabetes leads to kidney damage, blindness, limb vessels to defeat and to gangrene [1].

2/3 of our body is water. The smallest lack of water can cause the most serious health consequences, such as blood clots. In addition, water is needed for normal digestion, absorption of nutrients in the blood and their "transportation" to all cells. Water is also a kind of "lubricant" that enables movement of the joints and organs of the abdominal cavity. Slow metabolism, increased fatigue, increased levels of uric acid in the blood which leads to the formation of kidney stones are the results of dehydration [2]. Increased water in the body can mean a delay in the output of fluid and lead to high load on the heart and kidneys. In muscles nearly 90% fat is burnt. So the more muscle tissue, the less likely that a person will get fat, and consequently get rid of problems associated with being overweight [1].

### **BIA method**

The first mention of the study of electrical conductivity of biological objects can be referred to the work by V. Tomson dated 1880. The beginning of bioimpedance analysis (BIA) for the study of human body composition is associated with the work by a French anesthetist A. Tomasset made in the early 1960s. Impedance (Z) is called the total



electrical resistance of the tissues. It is measured by passing through a biological object AC in accordance with Ohm's law:

$$Z = U / I,$$

where U – potential difference, and I – current. Impedance has the dimension [Ohm].

The method is based on measuring the impedance of the whole body or parts of the body using special devices – bioimpedance analyzers. The method uses the frequency dependence of the electrical conductivity of living tissues. Living tissues are conductors with inhomogeneous conductivity. Their electrical impedance is inversely proportional to the liquid content in the tissue. Highly hydrated and free of fat tissue has less electrical resistance than fat, bone and epithelial. The method relies on the ability of fat-free tissue to conduct electrical current. Electric current follows the path of least resistance, and resistance tissue current is directly related to their content of liquid – high hydrogenated fat-free mass is a good conductor (has a lower electrical resistance), while the bad hydrogenated fat tissue, is a good insulator. The main electrical conductors current in the body are tissues with high level of water and electrolytes dissolved in them. Resistivity differences are explained primarily by different fluid and electrolyte content in the organs and tissues.

The method of bioelectrical impedance is a common definition of the scope, the extracellular and intracellular fluid from the measured resistance.

Total body water (TBW) is the bulk of a person from 54 to 70% of weight (average value is usually used 60%) decided to subdivide the intracellular water (IW) and extracellular water (EW). IW is 2/3 of the TBWs and EW – 1/3 TBWs. Extracellular water is 16-20 % by weight of a living organism, intracellular – 38-50 % [5].

To understand how to correlate a small amount of electric current to the liquid in the body, we consider the model of an electrical cell. The first model was proposed by Fricke who described and explained the dependence of the impedance on the current frequency.

The magnitude of the impedance has two parts – an active (R) and reactance (Xc), which are related as follows:

$$Z^2 = R^2 + X_c^2$$

The basis of resistance R in a biological object is water (extracellular and intracellular). Basis reactance Xc are cell membranes.

"It was found that the high-frequency electric current passes not only through extracellular pathways and intracellular structures, making it possible to estimate fat-free mass. At the same time low-frequency current passes only through the extracellular space. As a result, numerous studies have determined that the alternating current frequency below 40 kHz is spread primarily through the vessels and interstitial crevices, thus bypassing the cell, the resistivity of which is much higher than the resistivity of body fluids. The total electrical resistance of the tissue is thus determined substantially free (extracellular). Below 20 kHz skin resistance increases above 50 kHz – increases the current passing through the cells directly. At high frequencies from 100 KHz to 1000 KHz capacitance of cell membranes do not hinder the penetration in the current cell, and its density outside and within the cell becomes comparable" [9]. Intuitively, current flows as a function of frequency can be seen in Fig. 1:

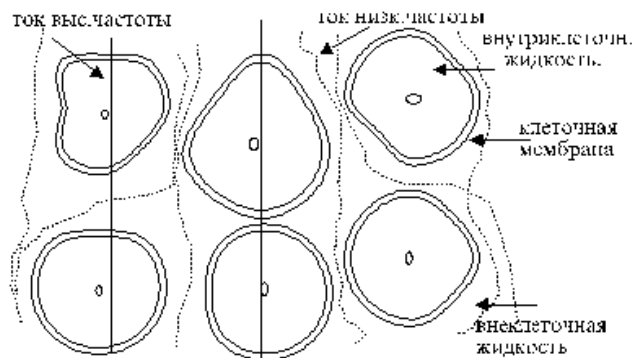


Fig. 1 shows that at low frequencies the current is on the extracellular fluid, bypassing the cell, but at high frequencies the current overcomes the resistance of the membrane and passes through the cells.

Electric and biological significance of this analysis consists in measuring the resistance (impedance) of the body's own tissues or fluids before and after exposure to an alternating current with a different frequency (from 5 to 500 kHz).

Relationship between impedance and volume of liquids are defined as not biophysical indicators, as well as the statistical dependence on the volume of fluid and impedance. Special electrical parameters of the equation are converted into the liquid. These volumes can be referred to as «electrical equivalents» fluid.

The largest resistance calculates the total water content in the body (TBW). Special equations translate electrical parameters (Z) in the volume of liquids. As an example of how to calculate the TBW we will provide some formulas:

TBW's kg =  $0.59 \times (\text{height}^2 / Z) + 0.065 \times \text{weight} + 0.04$  (author: Kushner R. F., 1992),  
 TBW's kg =  $(0.396 \times \text{height}^2 / Z) + (0.143 \times \text{weight})$  (author: Patel R., 1997),  
 wherein Z – impedance of the body.

We see an inverse relationship impedance of TBWs as mentioned above. However, the relationship between the impedance at low and high frequencies are not so simple in the body, especially in disorders of cell membrane permeability and fluid accumulation in the sectors. Therefore, there are many simple and complex models of bioelectrical impedance analysis.

To assess the suitability of bioimpedance studies obtained dependences and formulas results were compared with those made on the basis of a large number of observations using the test methods (isotopic dilution). Maximum discrepancy between the compared data is 6 %.

In determining the lean body mass in parallel densitometry (hydrostatic densitometry) and bioimpedance methods very high correlation coefficient ( $r = 0,912$ ) was obtained [4].

The simplicity of research equipment cost and comfort for the patient BIA is comparable with ECG (electrocardiogram). By informative – X-ray densitometry, hydrostatic densitometry and other bulk can be time-consuming and costly, while still having some limitations of body composition research methods.

All of the above determines the prospects for using BIA not only in medicine, but also in everyday life to track changes in body composition.

### **Guidelines on the basis of measurement of BIA**

To obtain reliable results, observe the following recommendations:

- a) the week before the survey one should refuse to receive a diuretic, which increases urine production rate and thus reduces the liquid content in the tissues;
- b) for two days – avoid alcohol, caffeine and other substances that lead to violations of water exchange;
- c) for 3-4h – refrain from strenuous exercise, receiving food and water;
- d) for 30 min before the test one should clean the bladder.

Before the measurements it is recommended to lie on a horizontal surface for 7-10 minutes. During the measurements, it is necessary to reliably isolate the subject from the surrounding conductive objects. Bioimpedance analyzer is connected to the extremities of the body, using special electrodes. Before that, the corresponding areas of the skin should be cleaned with alcohol and the electrodes coated with a thin layer of gel electrolyte, or use the disposable adhesive electrodes. Electrodes must be imposed exactly according to the instructions. Usually a standard quadruple scheme of electrodes is applied – two on the right ankle and wrist. The position of the electrodes is critical, the offset of 1 cm in the direction of the probe current results in a 2% error of the impedance measurement. The magnitude of the impedance depends on the body temperature. During the measurements, the examinee maintains a fixed position, hands and feet separated the sides at an angle of 30-45 to the axis of the body. This screening is not recommended for patients with pacemakers [3].

### **Factors leading to measurement errors**

Any examination of BIA always requires certain conditions and following recommendations in preparation for the procedure. Violation of recommendations and conditions leads to incorrect measurement of impedance of the body and calculation of the required parameters of the body (TBW, FMB – fat mass, muscle mass, bone mass).

The following factors may increase the error in obtaining the results of resistance of the body and calculations of body composition:

1. Resistance leg-foot measurement scheme include resistance only of the legs and lower abdomen, and not the entire body. However, distribution of adipose tissue in the body is uneven. The household scales foot-foot also evaluate the resistance of only one part of the body – the top. The most reliable measuring instruments are those with the principle of shin-wrist.

2. Based on the acquired resistance, parameters of interest are calculated using BL (body length, not the length of the legs, which is not constant for different people). Do not take into account wrist girth, giving data to determine bone mass (in medical institutions, this figure is introduced as the anthropometric data of the patient). Currently even ethnic characteristics are used for more accurate estimates.

3. Measurements should be a uniform distribution of the liquid lying in a horizontal position. However, they are produced in the vertical position.

4. Observe the angle between the limbs of 30-45 degrees from the axis of the body. But it is much smaller. Distance between the feet of a man measuring his testimony on household balance is 20 cm leg length for example (usually equal to the length of the legs approximately half the length of the body) – 90cm. For calculating the angle between the limbs, we present the isosceles triangle, which is based on a line between the centers of the feet and its sides. And use the law of cosines:  $c^2 = a^2 + b^2 - 2a * b * \cos\gamma$ ;  $\cos\gamma = (a^2 + b^2 - c^2) / (2ab)$ ;  $\cos\gamma = (90^2 + 90^2 - 20^2) / (2 * 90 * 90)$ ;  $\cos\gamma = (16200 - 400) / 16200$ ;  $\cos\gamma = 15800/16200$ ;  $\cos\gamma = 0.975$ . So the angle  $\gamma \approx 13$  that's

much closer than the recommended angle. Calculate the length of the legs which would satisfy the requirements for the location of the body and the angle between the limbs equal to 30 degrees.  $c^2 = a^2 + b^2 - 2a * b * \cos\gamma$ ; Let  $a = b = x$ :  $c^2 = x^2 * (2 + 2 * \cos\gamma)$ ;  $x^2 = c^2 / (2 + 2 * \cos\gamma)$ ;  $x = \sqrt{(c^2 / (2 + 2 * \cos\gamma))}$ ;  $x = \sqrt{(202 / (2 + 2 * \cos 30))}$ ;  $x = \sqrt{(400 / (2 + 2 * 0.866))}$ ;  $x = \sqrt{(400 / 3.74)}$ ;  $x = 20 / 1.9$   $x \approx 10.5$  cm so we can say that 10.5 cm is the length of imaginary legs, which is the best for measurement by scheme leg-leg.

5. Often diet is not observed (two days before the measurement are necessary to abandon the reinforcing dehydration products – coffee, tea, watermelon, etc. and products that contribute to water retention – salty food, spices), which leads to a decrease or increase in the PSB and consequently increases or decreases the impedance.

6. Electrodes should be covered with gel – electrolyte for better conductivity and improved contact with the skin, which is not even mentioned in the instructions.

7. The ambient temperature must be between 22-27 degrees Celsius which is not always feasible.

### **Conclusion**

The method relies on the ability of a fat-free tissue to conduct electrical current. A measured resistance allows us to estimate total body water, not fat mass. The values of fat and muscle tissues are calculated on the basis of total body water.

Measurements may not be accurate for several reasons:

1. Wiring diagram electrodes foot-foot gives an estimate of resistance only of the lower part of the body, and not the entire body. But the distribution of fat on the body surface is uneven;

2. The measurement in an upright position carries the resistance measurement error because of uneven distribution of liquid;

3. Failure to comply with the angle between the limbs. Recommended angle is 30-45 degrees. When you make measurement by home scales the angle is only nearly 15 degrees, depending on the length of the legs;

4. Rating not all individual data;

5. Non-compliance with diet which leads to a change in hydration of the body and the resistance measurement error.

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## **SUSTAINABLE TOURISM & GLOBALIZATION: CAN TRAVEL BE SUSTAINABLE IN SPITE OF GLOBALIZATION?**

**Lisovenko D.A. (Kharkiv)**

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**Summary:** This article is devoted to the role of ecotourism at the present stage of human development. Basic principles of ecotourism, its possible impact on sociosphere and ecosystems are presented.

**Keywords:** ecotourism, sustainable tourism, minimizing impact, conservation, ecological thinking.

**Анотація:** В даній статті розглядається роль екологічного туризму на сучасному етапі розвитку людства. Окреслюються основні принципи екотуризму, представлені його можливі впливи на соціосферу та екосистеми.

**Ключові слова:** екологічне мислення, екологічний туризм, збереження навколишнього середовища, мінімізація впливів, сталий туризм.

**Аннотация:** В данной статье рассматривается роль экологического туризма на современном этапе развития человечества. Рассматриваются основные принципы экотуризма, представлены его возможные влияния на социосферу и экосистемы.

**Ключевые слова:** минимизация влияний, сохранение окружающей среды, устойчивый туризм, экологическое мышление, экологический туризм.

Tourism is one of the fastest growing sectors of global economy. Non industrialized countries are attempting to cash in on this expanding industry in an attempt to boost foreign investment and financial reserves. While conceding that the uncontrolled growth of this industry can result in serious environmental and social problems, the United Nations contends that such negative effects can be controlled and reduced.

Perhaps, ecotourism is the most over-used and miss-used word in the travel industry. But what does it mean? Ecotourism Society defines it as "responsible travel to natural areas which conserves the environment and improves the welfare of the local people". Tourism and travel, as global industries, have a profound impact on the environment and cultures of the world. Fragile natural resources like forests can be damaged or depleted by too many visitors or irresponsible use. Animal habitats can be devastated by visitors and ecosystems altered forever. A walk through the rainforest is not eco-tourism unless that particular walk somehow benefits that environment and the people who live there. A rafting trip is eco-tourism only if it raises awareness and/or funds to help protect the watershed. A loose interpretation of this definition allows many companies to promote themselves as something they are not. If true eco-tourism is important to a person it is necessary, ask plenty of questions to determine if the trip will help "conserve and improve" the places you visit.

Nature tourism or ecotourism, recreational and educational travel based on natural attractions is a promising means of advancing social, economic, and environmental objectives in developing countries. It offers countries new opportunities for small-enterprise investment and employment, and increases the national stake in protecting their biological resources. However, making ecotourism a positive economic and environmental tool requires policies that foster responsible nature tourism development, broad-based and active local participation in its benefits, and conservation of developing countries' biological heritage.

Wildlife and its habitats in developing countries are becoming increasingly popular attractions for international tourism. Many of the biologically richest areas, are in the developing world. Growing numbers of ecotourists are flocking to the mountains of Nepal and Madagascar, the tropical forests of Costa Rica and Thailand, and the beaches of Belize and Sri Lanka. Nature tourists bring with them money to spend, money that creates jobs and incomes for households and communities in and around national parks and other protected areas. Ecotourism enterprises, tour agencies and guide services, lodges and private reserves as well as such satellite activities as crafts industries and transportation and food services, also generate revenues and foreign exchange. Governments can use this income in operating and protecting natural habitats.

Ecotourism is about uniting conservation, communities, and sustainable travel. This means that those who implement and participate in ecotourism activities should follow the following ecotourism principles:

- Minimize impact.

Tourism causes damage. Ecotourism strives to minimize the adverse affects of hotels, trails, and other infrastructure by using either recycled materials or plentifully available local building materials, renewable sources of energy, recycling and safe disposal of waste and garbage, and environmentally and culturally sensitive architectural design. Minimization of impact also requires that the numbers and mode of behavior of tourists should be regulated to ensure limited damage to the ecosystem;

- Build environmental and cultural awareness and respect.

Ecotourism means education, for both tourists and residents of nearby communities. Well before departure the tour operators should supply travelers with reading material about the country, environment and local people, as well as a code of conduct for both the traveler and the industry itself. This information helps prepare tourists as Ecotourism Societies guidelines state, "to learn about the places and peoples visited and to minimize their negative impacts while visiting sensitive environments and cultures". Ecotourism projects should also help educate members of the surrounding community, schoolchildren and the broader public in the host country. To do so they must offer greatly reduced entrance and lodge fees for nationals and free educational trips for local students and those living near the tourist attraction.

- Provide positive experiences for both visitors and hosts.

Ecotourism helps raise funds for environmental protection, research and education through a variety of mechanisms, including park entrance fees, tour company, hotel, airline and airport taxes and voluntary contributions;

- Provide financial benefits and empowerment for local people.

National Parks and other conservation areas will only survive if there are "happy people" around their perimeters. The local community must be involved with and receive income and other tangible benefits (potable water, roads, health clinics, etc.) from the conservation area and its tourist facilities. Campsites, lodges, guide services, restaurants and other concessions should be run by or in partnership with communities surrounding a park or other tourist destination. If ecotourism is to be

viewed as a tool for rural development, it must also help shift economic and political control to the local community, village, cooperative, or entrepreneur. This is the most difficult and time-consuming principle in the economic equation and the one that foreign operators and "partners" most often let fall through the cracks or that they follow only partially or formally;

- Respects local culture.

Ecotourism is not only 'greener' but also less culturally intrusive and exploitative than conventional tourism. Ecotourism strives to be culturally respectful and have a minimal affect on both the natural environment and the human population of a host country. This is not easy, especially since ecotourism often involves travelling to remote areas where small and isolated communities have had little experience interacting with foreigners. And like conventional tourism, ecotourism involves an unequal relationship of power between a visitor and a host and modification of the relationship through exchange of money. Part of being a responsible eco-tourist is learning the local customs beforehand, respecting dress codes and other social norms and not intruding on the community unless either invited or as part of a well organized tour.

- Supports human rights and democratic movements

Although tourism is often glibly hailed as a tool for building international understanding and world peace, this does not happen automatically; frequently in fact tourism bolsters the economies of repressive and undemocratic states. Mass tourism pays scant attention to the political system of the host country or struggles within it, unless civil unrest spills over into attacks on tourists. Ecotourism demands a more holistic approach to travel, one in which participants strive to respect, learn about and benefit both the local environment and local communities;

However it does give a base of ideas to work from when looking into whether or not something is or isn't ecotourism. Properly understood, the emphasis in ecotourism is on a set of principles and how to put them into practice; on what ecotourism stands for and how these standards are being implemented.

The main ecotourism impacts on local communities can be determined in Table 1 [1].

Table 1

Framework for determining the impacts of ecotourism initiatives on local communities [1].

Economic empowerment	Ecotourism brings lasting economic gains to a local community. Cash earned is shared between many households in the community. There are visible signs of improvements from the cash that is earned (e.g. improved water systems, houses made of more permanent materials).
Psychological empowerment	Self-esteem of many community members is enhanced because of outside recognition of the uniqueness and value of their culture, their natural resources and their traditional knowledge. Increasing confidence of community members leads them to seek out further education and training opportunities. Access to employment and cash leads to an increase in status for traditionally low-status sectors of society e.g. women, youths.
Social empowerment	Ecotourism maintains or enhances the local community's equilibrium. Community cohesion is improved as individuals and families work together to build a successful ecotourism venture. Some funds raised are used for community development purposes, e.g. to build schools or improve roads.
Political empowerment	The community's political structure, which fairly represents the needs and interests of all community groups, provides a forum through which people can raise questions relating to the ecotourism venture and have their concerns dealt with. Agencies initiating or implementing the ecotourism venture seek out the opinions of community groups (including special interest groups of women, youths and other socially disadvantaged groups) and provide opportunities for them to be represented on decision-making bodies.



So, ecotourism is more than a catch phrase for nature reserving travel and recreation. Eco-tourism is consecrated for preserving and sustaining the diversity of the world's natural and cultural environments. It accommodates and entertains visitors in a way that is minimally intrusive or destructive to the environment and sustains & supports the native cultures in the locations it is operating in.

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## **USING CANNABINOIDS IN CANCER THERAPY**

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**Summary:** The article describes the results of laboratory tests on the use of cannabinoids as one of the possible ways of cancer treatment. It shows the effects of certain cannabinoids on the receptors that prevent the spread of cancer cells, which opens a prospect for their using in clinical trials.

**Key words:** Cancer, cannabinoids, cannabinoid receptor CB1 and CB2, delta-9 tetrahydrocannabinol(THC), methanandamide (MET) and JWH-015.

**Анотація:** У статті описані результати лабораторних дослідів по застосуванню канабіноїдів як одного з можливих методів лікування раку. Показано вплив певних канабіноїдів на рецептори, які перешкоджають розмноженню ракових клітин, що відкриває перспективу їх застосування в клінічних випробуваннях.

**Ключові слова:** рак, канабіноїди, delta-9 тетрагідроканнабінол (THC), метанандамід (MET) і JWH-015, рецептори CB1 і CB2.

**Аннотация:** В статье описаны результаты лабораторных опытов по применению каннабиноидов как одного из возможных методов лечения рака. Показано влияние определенных каннабиноидов на рецепторы, которые препятствуют размножению раковых клеток, что открывает перспективу их применения в клинических испытаниях.

**Ключевые слова:** рак, каннабиноиды, delta-9 тетрагидроканнабинол (THC), метанандамид (MET) и JWH-015, рецепторы CB1 и CB2.

Nowadays, one of the most dangerous diseases is cancer. It is a class of diseases characterized by uncontrolled cell growth. It can be treated by surgery, chemotherapy, radiation therapy, immunotherapy, monoclonal antibody therapy or other methods. The choice of therapy depends upon the location and grade of the tumor and the stage of the disease, as well as the general state of the patient (performance status). A number of experimental cancer treatments are also under development. Complete removal of cancer without damage to the rest of the body is the goal of treatment. That is why scientists are looking for new ways for cancer therapy.

Humans have been using cannabis plants for medicinal and recreational purposes for thousands of years, but cannabinoids themselves were first purified from cannabis plants in the 1940s. There is no doubt that cannabinoids – both natural and synthetic – are interesting biological molecules. Hundreds of scientists around the world are investigating cannabinoid potential in treating cancer and other diseases – as well as the

harms they can cause. Researchers in Spain have published results showing that certain cannabinoids – molecules so-called because they were originally found in cannabis – could hold promise for treating some types of cancer.

There are different types of cannabinoids. Certain cannabinoids, such as delta-9 tetrahydrocannabinol (THC) that was discovered in the 1960s, the main active ingredient in cannabis, have well-documented mind-altering properties. But other cannabinoids have been known for some years to have biological effects elsewhere in the body. Of most interest to cancer researchers is the evidence showing that cannabinoids can slow down the growth and spread of cancer cells, or even kill them. For example, Professor Chris Paraskeva in Bristol, is investigating the anti-cancer properties of cannabinoids, as part of his research into the prevention and treatment of bowel cancer. It needs to be stressed that these studies have all been done with purified cannabinoid chemicals – not cannabis itself, which contains cannabinoids along with a cocktail of other chemicals. Cannabinoids affect cells' behaviour by sticking to receptor molecules on their surface, and triggering a cascade of events within them. There are two main types of cannabinoid receptor, known as CB1 and CB2, although researchers think there may be others out there. CB1 is mainly found on nerve cells in the brain – so it is likely to be the important one when it comes to the mind-altering effects of cannabis. CB2 is mainly found elsewhere in the body, and is the prime suspect for controlling the other effects of cannabinoids on the body. Professor Ines Diaz-Laviada and her team studied the effects of two cannabinoids – named Methanandamide (MET) and JWH-015. These are synthetic chemicals that do not occur naturally in cannabis, although they are similar to compounds found in the plant. The researchers tested the chemicals on different human prostate cancer cell lines grown in the lab, and found that they could slow down their growth and trigger cell death. By using drugs that block either one receptor or the other, or a genetic technique called RNA interference to 'knock out' CB1 or CB2 in turn, the scientists found that the anti-cancer effects of MET and JWH-015 were brought about by CB2. This is an important finding, because it tells us that it should be possible to develop drugs that target CB2, which will have an anti-cancer effect, but which crucially won't have the mind-altering effects of many cannabinoids. As a last step, the researchers tested the effects of JWH-015 on mice that had been transplanted with human prostate cancer cells. The chemical helped to slow down the growth of tumours, compared with a saltwater control. And blocking the CB2 receptors with a highly-specific drug called SR2 wiped out the effect of JWH-015, proving that it works through the CB2 pathway. Although this work is still at an early stage, it provides a tantalising suggestion that drugs that activate the CB2 receptor could be useful for treating prostate cancer. There is still more research to be done to show if MET or JWH-015 are suitable for testing in clinical trials involving patients.

As part of this research, the scientists also investigated the cellular pathways that cannabinoids activate (or block) when they bind to CB2 receptors on prostate cancer cells. By understanding these cellular responses in greater detail, they might discover new targets for cancer treatment.

And now we will speak about clinical research involving people with cancer? Results have been published from only one clinical trial testing whether cannabinoids can treat cancer in patients, led by Dr Manuel Guzman and his team in Spain. Nine people with advanced, terminal glioblastoma multiform – an aggressive brain tumour –

were given highly purified THC through a tube directly into their brain. Eight people's cancers showed some kind of response to the treatment, and one didn't respond at all. All the patients died within a year, as might be expected for people with cancer of this advanced degree. The results from this study show that THC given in this way is safe and doesn't seem to cause significant side effects. But because this was an early stage trial, without a control group, it is impossible to say whether THC helped to extend their lives. And while it is certainly not a cure, the trial results suggest that cannabinoids are worth pursuing in clinical trials.

A handful of other clinical trials of cannabinoids are currently being set up. One early-stage trial testing a synthetic cannabinoid called dexanabinol in patients with advanced cancer will be recruiting in Leeds and Newcastle. Most research has been focused on THC, which occurs naturally in cannabis plants, but researchers have found that different cannabinoids seem to work better or worse on different types of cancer cells. Lab experiments have shown promising results with THC on brain tumour and prostate cancer cells, while CBD seems to work well on breast cancer cells. Then there is the problem of the psychoactive effects of THC, particularly in high doses, although this can be counteracted by giving it together with CBD. Because of this problem, synthetic cannabinoids that don't have these effects might be more useful in the long term. There are also big questions around the best way to actually get the drugs into tumours. Because of their chemical makeup, cannabinoids neither dissolve easily in water, nor travel very far in our tissues. This makes it hard to get them deep into a tumour, or even just deliver them into the bloodstream in consistently high enough doses to have an effect. The clinical trial in Spain involved directly injecting cannabinoids into patients' brains through a small tube. This isn't an ideal method as it is very invasive and carries a risk of infection, so researchers are investigating other delivery methods such as tablets, oil injections, mouth sprays or even microspheres. They also do not know whether cannabinoids will help to boost or counteract the effects of chemotherapy, nor which combinations of drugs might be good to try. And there are currently no biological markers to help doctors identify who might benefit from cannabinoids and who might not.

The biggest issue is that there isn't enough evidence to show that cannabinoids can treat cancer in people, although research is still ongoing around the world. And it is not clear which type of cannabinoid – either natural or synthetic – might be most effective, what kind of doses might be needed, or which types of cancer might respond best to them. So far there have been intriguing results from lab experiments with prostate, breast, lung cancer, skin, bone and pancreatic cancers, glioma brain tumours and lymphoma. But the take-home message is that different cannabinoids seem to have different effects on various cancer types, so they are far from being a 'universal' treatment. None of these issues are deal-breakers, but these questions need answering if there is any hope of using cannabinoids to effectively and safely treat cancer patients. There are hundreds of exciting potential cancer drugs being developed and tested in university, charity and industry labs all over the world. Cannabinoids are merely a small part of a much larger picture.

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## **THE EXTERNAL ECONOMIC ACTIVITY OF THE CHUGUYEVSKY REGION OF THE KHARKOV AREA: CURRENT STATE, PROBLEMS AND DEVELOPMENT PROSPECTS**

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**Summary:** The article is devoted to consideration of features of foreign economic activity of Chuguyev district of Kharkov region, and also to the identification of problems and prospects for further development. It was revealed that in Chuguyev area the export-import balance is positive, and the unstable economic situation in the country is one of the most important problems.

**Key words:** barter, economy, export, import, investments, foreign economic activity, trade.

**Анотація:** Стаття присвячена розгляду особливостей зовнішньоекономічної діяльності Чугуївського району Харківської області, а також виявленню проблем і перспектив для подальшого розвитку. У результаті дослідження було виявлено, що в Чугуївському районі позитивне експортно-імпортне сальдо, а серед проблем найбільш важливою є нестабільна економічна ситуація в країні.

**Ключові слова:** зовнішньоекономічна діяльність, економіка, експорт, інвестиції, імпорт, товарообмін, торгівля.

**Аннотация:** Статья посвящена рассмотрению особенностей внешнеэкономической деятельности Чугуевского района Харьковской области, а также выявлению проблем и перспектив для дальнейшего развития. В результате исследования было выявлено, что в Чугуевском районе положительное экспортно-импортное сальдо, а среди проблем наиболее важной является нестабильная экономическая ситуация в стране.

**Ключевые слова:** внешнеэкономическая деятельность, инвестиции, импорт, товарообмен, торговля, экономика, экспорт.

One of the main directions of social and economic development of our region in modern economic – geographical space is activization of mutually beneficial relations with other countries on the basis of accumulation of export-import potential, i.e. foreign economic activity.

One of the main concepts of this subject is the concept of «foreign economic activity». The Doctor of Economics, professor of T. Shevchenko Kiev National university S. I. Doroguntsov gives the following definition of this concept: “foreign economic activity of regions is the set of their concrete forms, and also the system of the

legal, organizational administrative financial and economic possibilities providing effective interaction of national economic complexes with business structures abroad to accelerate the development of productive forces of the region and the country and to increase socio-economic indexes of life of its citizens [2].

Ukrainian scientists pay much attention to the problems of foreign economic activity of Kharkov region. In particular, they are analyzed in works of S. I. Doroguntsova, L. V. Deyneko, V. N. Mosin, B. M. Mochalov, Ya. B. Oleynik, V. A. Smirnov, L. G. Chernyuk, V. S. Yatskova and L. N. Nemets and others [1, 2].

Despite the high level studying the matter of nation-wide character, there is a need of their profound studying at regional levels as it allows to analyse the current state, to allocate the main problems of foreign economic activity and to define further priorities in the context of sustainable development. The purpose of the article is to carry out the analysis of foreign economic activity of Chuguyev region of Kharkov area, and also to identify problems and prospects of its development. The general investment and practical interest among foreign investors, the close neighbour of Chuguyev area is Russian Federation (one of the main trade partners). The favorable geopolitical location, the developed infrastructure, an industrial zone in the settlement Malinovsky – all this promotes foreign economic activity of the area. Nowadays such types of foreign economic activity are widespread in Chuguyevsky area:

1. export and import of goods, capitals;
2. rendering services (production, forwarding, insurance, consulting, marketing, export, intermediary, legal entities) by subjects of foreign economic activity of Ukraine;
3. scientific and technical, research and production, educational and other cooperation with foreign subjects of economic activity;
4. joint business activity between foreign economic structures and local enterprises, including creation of joint ventures of different types and forms;
5. the organization and active implementation in the field of carrying out auctions, conferences, symposiums;
6. goods exchange (barter) [1].

The foreign trade turnover in the area as in 2012 made 22,9 million USA dollars. Excess of export over import provided positive export-import balance in the sum of 8,3 mln. dollars of the USA. The volume of export of goods by producers of the area following the results of 2011 makes 15,6 mln. dollars of the USA, import volume - 7,3 million USA dollars. USA. On export and import operations of the enterprises the area cooperates with 42 countries of the world. Export of goods was carried out to 33 countries of the world. Exporting enterprises are:

- JSC «KG & C» (aluminum caps – Russia, Moldova, Turkey, Bulgaria);
- GP «New Pokrovsk KHP» (bran granulated – Switzerland, Great Britain, The USA, Canada; flour – Panama, Georgia, Azerbaijan, Great Britain, Moldova, Nigeria, Africa, Kazakhstan, Turkmenistan, Armenia, The United Arab Emirates, Cyprus, Singapore, semolina – Georgia, Belarus, Russia);
- JSC «LVZ PRIME» (alcoholic beverages – Iraq, Latvia, Lithuania, Azerbaijan, Switzerland, Armenia, Israel, Lebanon, Georgia, Russia, The United Arab Emirates, Turkey, Jordan, Germany, Mexico, Bulgaria, Abkhazia, Chile, the USA, Estonia, Moldova, Vietnam, Panama);

- JSC «Malinovsky glass plant» (bottles for drinks and alcohol products – Russia and the USA);

- JSC «Stankoremontny plant» (the metalworking equipment – Russia);

- JSC Rovere (timber of strong breeds - Italy).

GP «New Pokrovsk KHP» – 47,7% has the greatest share in the total amount of export of the area [3].

Goods from 15 countries of the world imported to the area imported. Import operations were performed by the enterprises

- JSC «KG & Co» – with Russia, Germany, Belarus, Italy, Great Britain, Switzerland, Thailand and Bulgaria (sheets, laying, granulates, spare part batchers, glue);

- JSC «Malinovsky glass plant» – with Russia, Germany, the Czech Republic, – cotton wool, France, Switzerland, Great Britain, Korea, China, Austria, India (forms for producing bottles, spare parts for the equipment, sensors, raw materials);

- JSC «LVZ PRIME» – with Belarus (corking metalpolymeric devices);

- JSC «Stankoremontny Plant» – (the metalworking equipment - Germany) [3].

Today Chuguyev area takes the second place in the Kharkov region on growth rates of direct foreign investments (after Balakleysky). The sum of investments in the area in 2011 made 288 million USA dollars. The result is reached by the industrial group of plants «Malinovka» which realizes a number of investment projects of the enterprises: JSC «KG & Co», JSC «Malinovsky glass plant» and JSC «Likero-vodka distillery PRIME» every year. They produce different output of high of fool technological cycle. The share of the area in the total amount of investments in Kharkov region makes 11,6%. The most considerable volumes of direct foreign investments is enclosed by investors from Cyprus, Great Britain and Denmark (98% of all foreign investments into the area). Today direct foreign investments are put into 5 enterprises of the area: JSC «Harkovsky likero-vodochny zavod plus» – 26,2%, JSC «Malinovsky glass plant» – 45,3%, JSC «Golden Kross» – 0,8%; CIAO «KG & Co» – 12%, JSC «Bikorm» – 15,7%.

For the purpose of improvement the indicators of foreign trade and investment activity authorities of the region and heads of the industrial enterprises take measures to export and import activity. The problems of more active use of an export potential consists in increasing incomes of local people by 2015. Realization of the strategic tasks stated above has to get more than 50 mln. dollars of the USA in the region. Due to its export-import operations, investment activity with foreign countries in the area some European standards have been reached. Modernized economy, foreign investments and the latest technologies are attracted, competitiveness of a domestic producer is increased, the entry into the world markets is carried out. But there are also many problems. They are difficult economic situation in the country, insufficient efforts on attraction of external investments, imperfection of legislative base, wear of fixed assets at the separate enterprises, absence of the markets of innovative and financial services.

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## **VIRTUAL REALITY TECHNOLOGIES FOR RESEARCH AND EDUCATION IN OBESITY AND DIABETES: RESEARCH NEEDS AND OPPORTUNITIES**

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**Summary:** Virtual reality technologies are the main point for consideration in the presented article. The particular attention is paid to the application of virtual reality technologies in preventive health and chronic disease management.

**Key words:** virtual reality technology, haptic systems, diabetes risk, diabetes management, three-dimensional, body mass index, virtual environment, standard of care.

**Анотація:** У поданій статті розглядаються технології моделювання віртуальної реальності. Особлива увага приділяється застосуванню технологій моделювання віртуальної реальності у профілактиці та управлінні перебігом захворювань.

**Ключові слова:** технологія моделювання віртуальної реальності, сенсорні системи, ризик захворювання на діабет, управління перебігом захворювання, тривимірний, індекс маси тіла, віртуальне середовище, міра піклування.

**Аннотация:** В представленной статье рассматриваются технологии моделирования виртуальной реальности. Особое внимание уделяется вопросу применения технологий моделирования виртуальной реальности в профилактике и управлении течением заболеваний.

**Ключевые слова:** технология моделирования виртуальной реальности, сенсорные системы, риск заболеть диабетом, управление течением заболевания, трехмерный, индекс массы тела, виртуальная среда, мера заботливости.

The rising rates, high prevalence, and consequences of obesity and diabetes call for new approaches to the complex behaviors needed to prevent and manage these conditions. Treatment and prevention strategies for diabetes and obesity typically include appropriate energy intake for weight loss or weight maintenance, suitable dietary macronutrient distribution, physical activity, medication, improved sleep habits, and in some cases bariatric surgery. Successful implementation requires sustained behavioral changes, a high level of self-monitoring, and adherence to medication if prescribed. This is difficult, however, to achieve. Moreover, socioeconomic and educational issues pose additional barriers. For example, successful glycemic control requires considerable text literacy (reading), numerical literacy (numeracy), and health literacy skills that many patients may not have. Overall, the learning and application of complex information, time and cost constraints, psychosocial factors, educational skills, and other issues make adoption of recommended behaviors and treatments challenging for health care providers, patients, and healthy individuals who wish to lower their risk.

Virtual reality (VR) technology allows the creation of controllable, multisensory, interactive, three-dimensional (3D), stimulus environments, within which human performance can be motivated, recorded, and measured, and offers clinical assessment and intervention options that are not possible using traditional methods. Much as an aircraft simulator can serve to test and train piloting ability under a variety of controlled stimulus conditions, virtual reality (VR) can be used to create relevant simulated

environments that allow the assessment and treatment of cognitive, emotional, and motor functioning. However, virtual reality (VR) is not defined or limited by any technological approach or hardware set-up. The creation of a virtual reality user experience can be accomplished using combinations of a wide variety of interaction devices and sensory display systems, and in the design of content presented in a computer-generated graphic world [7].

For example, immersive virtual reality (VR) combines computers, head-mounted displays (HMDs), body-tracking sensors, specialized interface devices, and real-time graphics to immerse a participant in a computer-generated simulated world that changes in a natural way with head and body motion. In these systems, one of the key aims is to replace the outside world perceptually with that of a simulated environment (delivered within a head-mounted display (HMD)) to create a specific user experience. Immersive virtual reality (VR) has been most commonly employed in applications where a controlled stimulus environment is desirable for constraining a user's perceptual experience within a specific synthetic world. This format has been used often in clinical virtual reality (VR) applications for anxiety disorder exposure therapy, analgesic distraction for patients suffering from acutely painful medical procedures, and in the cognitive assessment of children with attention deficit hyperactivity disorder within a virtual classroom to measure performance under systematically delivered task challenges and distractions. Some applications take advantage of simulated online worlds with functional representations (avatars) of humans and animals.

By contrast, nonimmersive virtual reality (VR) is commonly experienced using modern computer and console games systems. This format presents a 3D graphic environment on a flatscreen monitor or television (no real-world occlusion) within which the user can navigate and interact. Albeit delivered on a less immersive display, such graphic worlds are still essentially a virtual reality environment. Though less immersive, virtual environments (VEs) presented on widely available commodity display systems have the capacity to provide the user with significant options for interaction with dynamic digital content using traditional computer and game interface devices (e.g., keyboard, mouse, game pads, joysticks, etc.). The use of such ubiquitous display and interface devices has promoted widespread access to this form of nonimmersive inter-active media, mainly in the domain of entertainment. Moreover, researchers have investigated the value and usability of commercially available interaction devices and methods that can be used with flatscreen-delivered virtual environments (VEs) that can allow users to interact with digital content using more naturalistic body actions beyond what is possible with traditional game interfaces. Virtual reality gaming technologies are now also being applied to preventive health and chronic disease management [1].

Virtual reality technology might prove a useful tool for producing sustainable behavior change to manage weight. However, with the exception of one laboratory's work on clinical eating disorders (anorexia, binge eating), virtual reality (VR) applications for common weight control factors such as food selection, portion control, and cued eating represent a nascent research area. More work has been done on virtual reality (VR) as a modality to encourage physical activity for children and in the rehabilitation setting. The technology could be used to complement motivational interviewing, enhance motivation, assess emotional states of readiness for behavioral



change, and help subjects manage their emotional reactions to food choices. Visual presentations could assist subjects in adjusting distorted assessments of portion sizes, correcting unrealistic expectations of the rate of weight loss, managing adverse sensory experiences from behavior change (such as hunger from altered consumption patterns or delayed muscle soreness from unaccustomed exercise), and navigating complex food environments such as grocery stores, restaurants, and household food pantries. Reinforcement and encouragement of the positive aspects of food choice and eating behaviors represent another potentially useful venue for virtual reality (VR). Virtual reality could also be used as part of patient visits to personalize treatment and improve adherence to diet, exercise, medication, and self-monitoring regimens [3].

Virtual reality technology also presents new opportunities to apply advances in sleep research in relation to obesity and diabetes risk. Insufficient sleep (sleep deficiency) and poor sleep behaviors, including sleep-disordered breathing, have been causally linked with disordered endocrine and appetite regulation and with risk of metabolic syndrome, diabetes, hypertension, and clinical cardiovascular disease. On average, U.S. adults and teens fall 2–3 hours short of their physiological requirements of 8 and 9 hours, respectively. Thus, many people are functioning in a chronic state of sleep-deprivation and circadian phase misalignment, akin to self-induced jet lag. Virtual reality could be used to evaluate individual sleep and alertness status objectively, deliver personalized guidance on healthy sleep behaviors, and implement and assess outcomes of physician-recommended treatments such as positive airway pressure devices and light therapy. Sleep parameters amenable to study with virtual reality (VR) include sleep duration, timing, and quality; physical, perceptive, and affective aspects of sleepiness (e.g., cognizance of sleepiness and fatigue, self-monitoring of sleep habits, ocular markers of sympathetic tone); and sleep deprivation consequences (slower reaction times and impairments in memory, cognition, emotional processing, judgment, and decision-making) [2].

Virtual reality has unique and valuable characteristics as a research tool. One advantage is that the virtual reality (VR) approach can simultaneously deliver an intervention and collect data on how it is utilized, particularly with regard to the cognitive and emotional processes involved. The virtual environments can be designed to address specific hypotheses, and detailed data on the study of a participant's response to the intervention can be collected without additional intrusiveness. Virtual reality environments can be used to study cue responsiveness and extinction through virtual exposure, which has been used in the study of phobias and addictions. Visual presentations can be tailored to the user, along with therapeutic guidance to modify affective reactions and choices, and can prepare the user for future real-world encounters, thus making virtual reality (VR) suitable for role-playing and training. Performance feedback, an essential component of learning and skill acquisition, can occur in real time; thus, virtual reality (VR) can be used as a teaching tool and also to study cognitive processing of information presented in increasingly complex (hierarchical) environments, a research approach that typically is impractical in real-world settings. Also, the capability to distribute identical virtual environments across multiple locations gives new meaning to the concept of multisite data collection. For virtual reality (VR) applications addressing issues of dietary assessment and metabolic

risk management are of vital importance. A particular challenge is the lack of food and nutrient databases with suitable accessibility, information content, and programming architecture [5].

The possibility that virtual reality (VR) versions of traditional interventions may reinforce and enhance motivation for treatment, particularly among adolescents and young adults, since virtual reality (VR) provides an opportunity to match interventions to various “ages and stages”. Systems that encouraged goal-setting, monitored behavior, and provided regular feedback and rewards were considered important for motivating behavior change. Weight management education could potentially be embedded in existing video games and other consumer-based virtual reality (VR) products.

Virtual reality has been studied in patients with eating disorders to modify distorted perception of body image and could be used similarly in obesity. Virtual reality could also provide a virtual support system to those with obesity and/or diabetes via virtual social networks, including children with diabetes who feel isolated and different because of their disease. Virtual reality could encourage family interactions in an environment where parents and children could more easily work on diabetes management concerns. Social network environments could provide credits for healthy eating and engaging in regular physical activity and other health-enhancing behaviors (such as smoking cessation and good sleep habits). These virtual social networks were considered to be applicable to extending health care provider services. In addition to using virtual reality (VR) to train health care providers in weight and diabetes management, virtual reality (VR) social networks could be used by subjects and providers to deliver interventions between visits and in a more accessible manner, particularly for those patients with transportation or mobility barriers. Using similar methodology as that used for anxiety disorders and substance abuse, virtual reality (VR) cue exposure could be used to evaluate the effects of various cues on perceived hunger, food intake, and physical activity, and retrain the emotional and behavioral responses to these cues [6].

Virtual reality applications need to be easy to use and intuitive, even for older populations or for those with low vision and other sensory/physical disabilities. Technologies should accommodate user populations and study participants having low health literacy; virtual reality (VR) is potentially a useful approach for understanding how health and nutrition information is processed and used by these groups. Cautions include the need to minimize the possibility that messages embedded in the technology might appear manipulative, controlling, or prescriptive, rather than facilitative. In addition, the potential for adverse effects (such as lack or loss of social skills through displacement to virtual reality (VR) or dysfunctional avatar transference) needs to be understood. Usage costs such as purchase and maintenance expenses and time burden (amount of time spent in use, convenience of scheduling of interventions or sessions) need to be evaluated in various settings (research or private use; home, health care facility, school). Participants specifically noted the difference between television screen time, in which eating and drinking are common, and virtual reality (VR) screen time, in which hand controls minimize opportunities to eat [2].

The computer gaming industry was noted to be a rapidly advancing, economically robust sector with enormous potential for health-related research and behavior change. Researchers need to document and evaluate currently available off-the-shelf programs

because many projects can be conducted that take advantage of already existing tools, games, and software.

Priority topics for research and technology development and evaluation identified by the workshop discussion groups include studies on the use of virtual reality (VR) to develop and enhance individual, family, and community-level skills that foster desirable eating, physical activity, and other health-related behaviors; the representational capacity of virtual reality (VR) to enhance motivation and learning and to serve as a teaching tool; the social networking capabilities of virtual reality (VR); virtual reality (VR) as a modality to train and extend availability and capacity for physicians and other health care providers; and pain distraction, motivation enhancement, and balance training using immersive visual environments, haptic systems (simulated tactile feedback), and other virtual reality (VR) modalities in supervised rehabilitation exercise therapy [5].

There has been very little development of virtual reality (VR) as a modality for obesity and diabetes studies. For example, the National Institutes of Health (USA) has supported only a relatively small number of research projects using VR technologies, primarily for studies in neuroscience, mental health, sensory deficits, post-stroke rehabilitation, and use of online worlds for diabetes management. The Department of Defense (USA) has more developed virtual reality (VR) portfolio particularly in treatment of posttraumatic stress disorder and post-amputation rehabilitation. Progress in the field will be enhanced by multidisciplinary collaborations between the technology industry and academia, and among researchers with diverse expertise in biomedical sciences (such as endocrinology, nutrition, and exercise physiology), behavioral sciences, pedagogical disciplines, and computer sciences. There is a need for both developmental research leading to new technologies and potentially commercializable products as well as research that provides a venue for well-powered effectiveness trials of new interventions.

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## PROGRAMMED CELL DEATH: AT THE BEGINNING OF THE PATH

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**Summary:** The article deals with the process of apoptosis or programmed cell death. This phenomenon is necessary for normal development and homeostasis of multicellular organisms. Any defect in its mechanism may result in a tumor formation. Hence clinically many diseases are the ultimate result of either deficient apoptosis or excessive apoptosis.

**Key words:** apoptosis, etiology of diseases, necrosis, procaspases.

**Анотація:** Стаття присвячена розгляду процесу апоптозу або запрограмованої смерті клітини. Це явище необхідне для нормального розвитку і гомеостазу багатоклітинних організмів. Будь-який дефект в його механізмі може призвести до утворення пухлини. Тому клінічно багато захворювань є кінцевим результатом або недостатнього апоптозу, або надмірного апоптозу.

**Ключові слова:** апоптоз, етіологія захворювань, некроз, прокаспазы.

**Аннотация:** Статья посвящена рассмотрению процесса апоптоза или запрограммированной смерти клетки. Это явление необходимо для нормального развития и гомеостазу многоклеточных организмов. Любой дефект в его механизме может привести к образованию опухоли. Поэтому клинически многие заболевания являются конечным результатом или недостаточного апоптоза, или чрезмерного апоптоза.

**Ключевые слова:** апоптоз, некроз, прокаспазы, этиология заболеваний.

The first modern usage of the term apoptosis came from a 1972 edition of the British Journal of the Cancer. Scientist John Kerr used the word (which in ancient Greek means “to prune” or “the falling of leaves”) to describe an unusual form of a cell death he encountered while studying acute liver injury in rat models during the early 1960s. Dr. Kerr first called the phenomenon “shrinkage necrosis” because the dying cells somehow convert themselves into small round masses of cytoplasm, often containing tiny specks of condensed nuclear chromatin. These masses have their organelles intact and are eventually phagocytized and eaten by nearby cells, leaving no trace of the inflammation that accompanies classic necrotic cell death. The cells simply fold up and die, seemingly of their own accord.

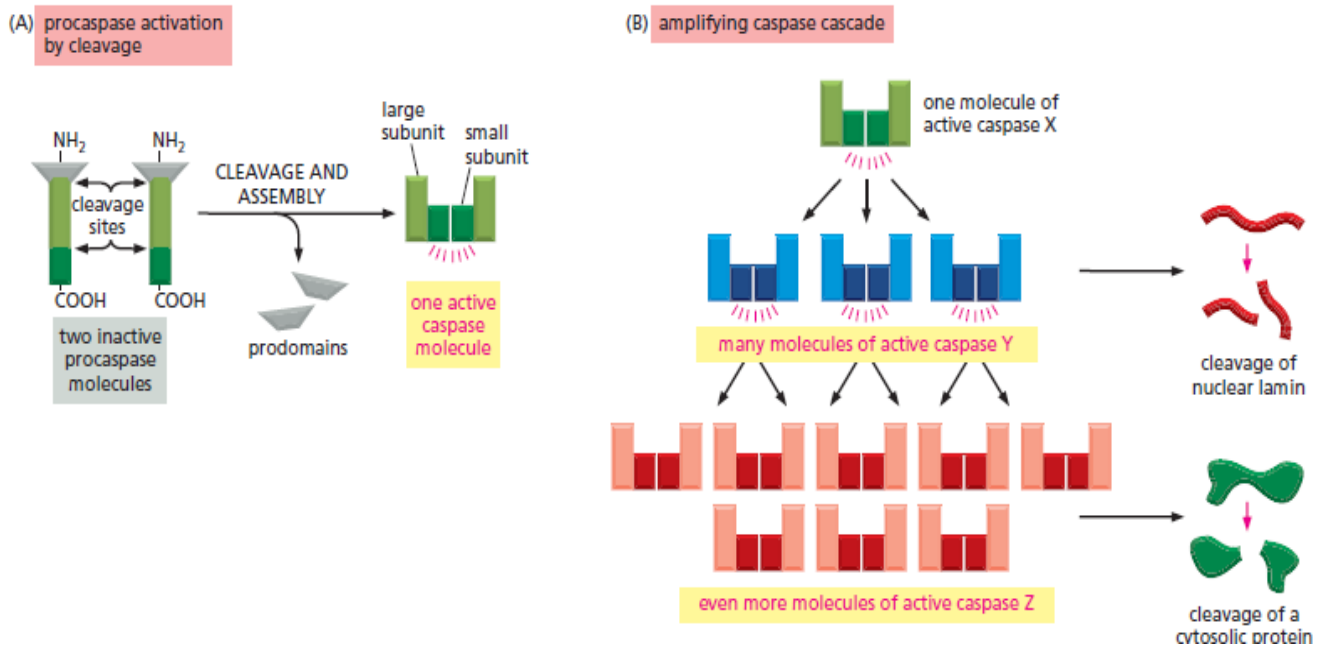
Today, apoptosis sometimes called programmed cell death is one of the hottest areas of study in cellular biology. Although there are countless ways to kill healthy functioning cells, in apoptosis, many of the most universal pathologies act through common pathways to do so. This raises the hope that by modulating apoptosis and the common pathways that lead to it, a wide variety of diseases such as auto-immune disorders, cancer, neurodegenerative diseases and more may be treated [3].

Apoptotic process consists of three phases. During the first phase cell detachment occurs from its substratum and adjacent cells with the loss of microvilli and desmosomes. DNA is fragmented by specific endonucleases and gets packed into vesicles. The change in DNA includes strand breakage (karyorhexis) and condensation of nuclear chromatin (pyknosis). The endoplasmic reticulum swells and the cell becomes denser as the cytoplasm shrinks and involutes. In the second phase the cell produces “buds” which breaks off into multiple membranes and forms an “apoptotic body”. In the third phase the cell membrane becomes permeable to dyes (e.g. Trypan blue). The apoptotic body is then phagocytosed. This entire process occurs within a short span of 15-20 minutes [4].

The machinery that is responsible for apoptosis seems to be similar in all animal cells. It involves the caspase family of proteases, the members of which are made as inactive precursors called procaspases. Procaspases are typically activated by proteolytic cleavage in response to signals that induce apoptosis. The activated caspases cleave, and thereby activate, other members of the procaspase family, resulting in an amplifying proteolytic cascade (*fig. 1*). An initial activation of a small number of protease molecules can lead, via an amplifying chain reaction (a cascade), to the explosive activation of a large number of protease molecules. Some of the activated caspases then break down a number of key proteins in the cell, such as nuclear lamins, leading to the controlled death of the cell. They also cleave other key proteins in the cell. One of the caspases, for example, cleaves the lamin proteins, which form the nuclear lamina underlying the nuclear envelope; this cleavage causes the irreversible breakdown of the nuclear lamina. In this way, the cell dismantles itself quickly and cleanly, and its corpse is rapidly taken up and digested by another cell. Activation of the apoptotic program, like entry into a new stage of the cell cycle, is usually triggered in an all-or-none fashion. The proteolytic cascade is not only destructive and self-amplifying but also irreversible; once a cell reaches a critical point along the path to destruction, it cannot turn back. Thus, it is important that the decision to die is tightly controlled [2].

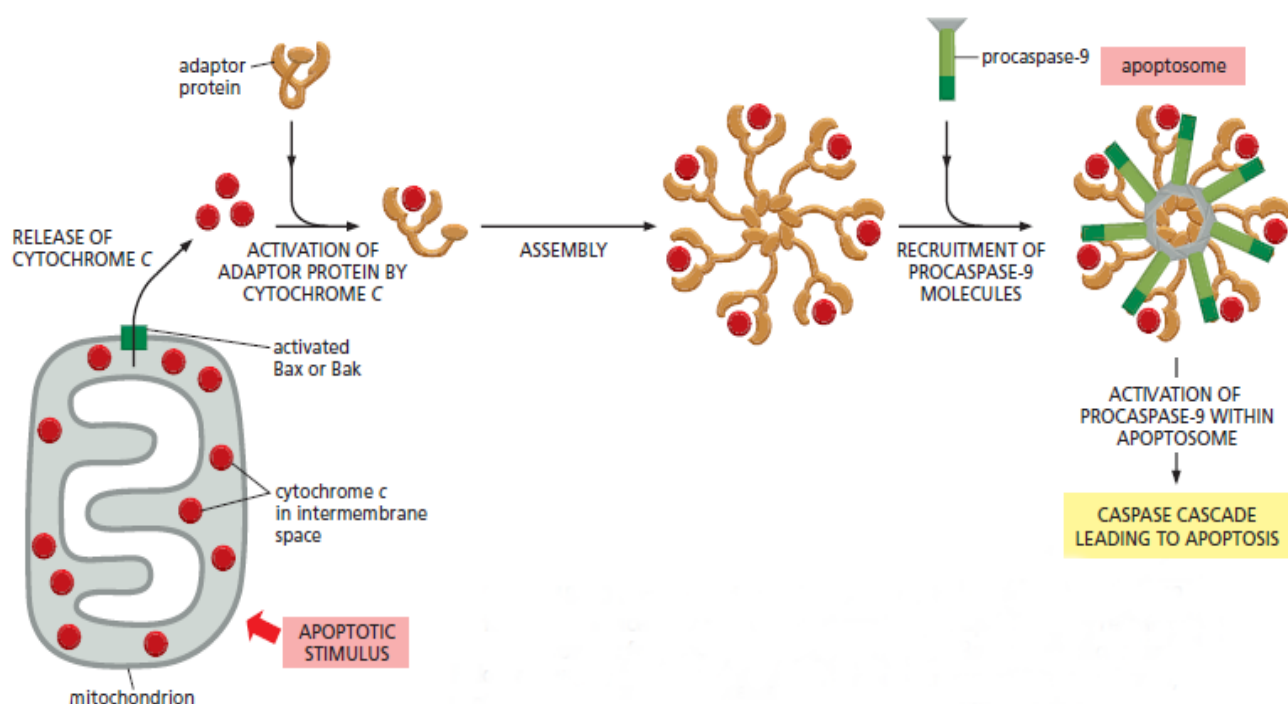
All nucleated animal cells contain the seeds of their own destruction: in these cells, inactive procaspases lay waiting for a signal to destroy the cell. It is therefore not surprising that caspase activity is tightly regulated inside the cell to ensure that the death program is held in check until it is needed.

*Fig. 1. Apoptosis is mediated by an intracellular proteolytic cascade. (A) Each suicide protease (caspase) is made as an inactive proenzyme, a procaspase, which is itself often activated by proteolytic cleavage by another member of the same protease family: two cleaved fragments from each of two procaspase molecules associate to form an active caspase, which is formed from two small and two large subunits; the two prodomains are usually discarded. (B) Each activated caspase molecule can then cleave many procaspase molecules, thereby activating them, and these can activate even more procaspase molecules.*



The main proteins that regulate the activation of procaspases are members of the Bcl2 family of intracellular proteins. Some members of this protein family promote procaspase activation and cell death, whereas others inhibit these processes. Two of the most important death-promoting family members are proteins called Bax and Bak. These proteins activate procaspases indirectly, by inducing the release of cytochrome-C from mitochondria into the cytosol. Cytochrome-C promotes the assembly of a large, seven-armed pinwheel-like structure that recruits specific procaspase molecules, forming a protein complex called an apoptosome. The procaspase molecules become activated within the apoptosome, triggering a caspase cascade that leads to apoptosis (fig. 2).

*Fig. 2. Bax and bak are death-promoting members of the bcl2 family of intracellular proteins that can trigger apoptosis by releasing cytochrome-C from mitochondria. When Bak or Bax is activated by an apoptotic stimulus, it aggregates in the outer mitochondrial membrane, leading to the release of cytochrome c by an unknown mechanism. Cytochrome-C then binds to an adaptor protein, causing it to assemble into a seven-armed complex. This complex then recruits seven molecules of a specific procaspase (called procaspase-9) to form a structure called an apoptosome. The procaspase-9 proteins become activated within the apoptosome and now activate different procaspases in the cytosol, leading to a caspase cascade and apoptosis.*



Bax and Bak proteins are themselves activated by other death-promoting members of the Bcl2 family, which are produced or activated by various insults to the cell, such as DNA damage.

Other members of the Bcl2 family, including Bcl2 itself, act to inhibit, rather than promote, procaspase activation and apoptosis. One way in which they do so is by blocking the ability of Bax and Bak to release cytochrome c from mitochondria. Some of the Bcl2 family members that promote apoptosis, including a protein called Bad, do so by binding to and blocking the activity of Bcl2 and other death-suppressing members of the Bcl2 family. The balance between the activities of pro-apoptotic and anti-apoptotic members of the Bcl2 family largely determines whether a mammalian cell lives or dies by apoptosis.

The intracellular death program is also regulated by signals from other cells, which can either activate or suppress the program. Indeed, cell survival, cell division, and cell growth are all regulated by extracellular signals, which together help multicellular organisms control cell number and cell size [2].

A number of techniques are usually employed in the study of apoptosis. Light and electron microscopy are two of the classical techniques for the study of this process. Because of the lack of cellular synchronisation in apoptosis and of the fact that the apoptotic cell is rapidly disposed of through phagocytosis, study methods based on morphologic criteria are adequate for the demonstration of the process, but are not useful for quantifying it.

Further to these procedures, the study of DNA fragmentation in agarose gels has been considered to be indicative for apoptosis. A number of techniques take advantage of this DNA fragmentation for labelling the fragments and thus for quantifying the proportion of apoptotic cells. Each DNA fragment has a 3'OH terminal portion. This terminal fragment can be labeled in various ways (for instance, with the help of a modified terminal deoxynucleotidyl transferase), a standard technique takes advantage of the changes in the membrane phospholipids that occur early in apoptotic

cells. The negatively charged membrane phospholipids exposed to the external environment by the apoptotic cell are labeled with fluorochrome-conjugated molecules, and the percentage of fluorescent cells can be easily quantified [1].

There is now a long list of diseases associated with altered cell survival. Increased apoptosis is characteristic of AIDS; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis; ischaemic injury after myocardial infarction, stroke, and reperfusion; and in autoimmune diseases such as hepatitis and graft versus host disease. Decreased or inhibited apoptosis is a feature of many malignancies, autoimmune disorders such as systemic lupus erythematosus, and some viral infections.

The role of apoptosis in cancer has probably received the greatest research effort. Observations that patterns of spontaneous and induced apoptosis differ between the small and large intestine that has led to a plausible explanation for the differences in incidence of cancer between these two sites. Studies in null mice show an increased preponderance of premature tumours and offer strong evidence that such apoptotic related genes are pivotal to development of tumours [4].

In addition, tumours develop methods to evade elimination by the immune system; one such mechanism involves tumours expressing Fas, which enables them to delete

(by apoptosis) antitumour lymphocytes. This phenomenon is known as the “tumour counterattack”. There is also an increasing evidence that systemic stimuli such as insulin-like growth factor I (anti-apoptotic) and insulin-like growth factor binding protein 3 (pro-apoptotic) may influence the development and progression of many common cancers [5].

It is now known that many existing drugs (for example, non-steroidal anti-inflammatories) act by altering the levels of apoptosis. Virtually all cytotoxic drugs and radiotherapy programmes induce apoptosis in tumour cells, and resistance to apoptosis is associated with treatment failure. These therapies also induce apoptosis in normal cells, and side effects on bone marrow, gut, and oral mucosa limit the dose that can be used. Many more new treatment strategies are currently in preclinical trials and show promise.

There is a large number of studies demonstrating that cell apoptosis plays a relevant role in the aetiology of many diseases, and that a wide range of pharmacologic agents (cytotoxic agents, hormones, antiinflammatory drugs) are effective through inducing apoptosis of target cells. Nevertheless, it appears to be evident that the future of such studies should be aimed both at documenting new associations between apoptosis and disease and at developing new therapies based on the modulation of apoptosis. In this context, it appears to be obvious that diseases such as cancer, autoimmune disorders or viral infections may derive immediate benefit from such studies, although in the intermediate and long term the regulation of apoptosis emerges as one of the most promising tools in Medicine. If future clinical studies are fruitful, this translation from basic science to clinical practice will be unique as it will affect not just one, but a broad range of disorders – and many patients will benefit.



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УДК 611.73

## **COMPUTER SIMULATION OF CORRELATED AND UNCORRELATED CONTRACTIONS OF HUMAN BRACHIORADIAL MUSCLE**

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**Summary:** The spectral characteristics of isometric muscle contractions of human brachioradial muscle were investigated. The spectra of correlated and uncorrelated muscle contractions received by means of a spectral Doppler musculoskeletal ultrasound method were compared with those received by means of computer simulation and also with the predictions of the previously developed theoretical model. The physical mechanisms which are capable to explain the observed differences between experimental and simulated spectra of muscle contractions at the low-frequency band were discussed.

**Key words:** actin, muscle, physical mechanisms, sarcomere, spectra.

**Анотація:** У роботі досліджені спектральні характеристики ізометричних м'язових контракцій плече променевого м'яза передпліччя людини. Отримані методом ультразвукової доплерівської міографії спектри корельованих і некорельованих м'язових скорочень порівнюються з передбаченнями теоретичної моделі та із результатами проведеного комп'ютерного моделювання. Обговорюються фізичні механізми, що можуть пояснити спостережувані відмінності експериментальних та модельних спектрів м'язових контракцій у низькочастотній області.

**Ключові слова:** актин, м'язи, фізичні механізми, саркомера, спектри.

**Аннотация:** В работе исследованы спектральные характеристики изометрических мышечных контракций плечелучевой мышцы предплечья человека. Полученные методом ультразвуковой доплеровской миографии спектры коррелированных и некоррелированных мышечных сокращений сравниваются с предсказаниями теоретической модели и с результатами компьютерного моделирования. Обсуждаются физические механизмы, которые могут пояснить наблюдаемое отличие экспериментальных и модельных спектров мышечных контракций в низкочастотной области.

**Ключевые слова:** актин, мышцы, физические механизмы, саркомера, спектры.

Human fulfils all kinds of movements due to the muscles. All voluntary movements - walking, facial expressions, eye movement, swallowing, breathing, etc. are carried out at the expense of skeletal muscles. Involuntary movements (except heartbeat) - peristalsis of the stomach and intestines, changes in blood vessel tone, maintaining the tone of the bladder – are due to smooth muscle contractions. The work of heart is provided by contractions of the cardiac muscle. The three types of muscle (skeletal, cardiac and smooth) have significant differences. In skeletal muscle, contraction is stimulated by electrical impulses transmitted by the nerves, the motoneurons in particular. Cardiac and smooth muscle contractions are stimulated by

internal pacemaker cells which regularly contract, and propagate contractions to other muscle cells they are in contact with. However, according to the generally accepted sliding filament theory, all three use the movement of actin against myosin to create contraction.

All muscle cells are composed of a number of actin and myosin filaments in series. The basic unit of organisation of these contractile proteins in striated muscle cells (i.e., the cells that compose cardiac and skeletal muscle, but not in smooth muscle tissue) is called the sarcomere. It consists of a central bidirectional thick filament flanked by two actin filaments, orientated in opposite directions. When each end of the myosin thick filament ratchets along the actin filament with which it overlaps, the two actin filaments are drawn closer together. Thus, the ends of the sarcomere are drawn in and the sarcomere shortens [1].

Due to the extremely important role of the muscles in the vital activity, it is necessary, inter alia, to develop and improve the methods of the diagnosis of neuromuscular diseases. Symptoms of muscle diseases may include weakness, spasticity, myoclonus and myalgia. Diagnostic procedures that may reveal muscular disorders include testing creatine kinase levels in the blood and various kinds of myography. For example, ultrasonic Doppler technology has shown to be highly effective and have been used in clinical practice for the diagnosis of the cardiovascular system [2]. Such a method can be used also to record and display the isometric contractions of skeletal muscles.

### **Materials and methods**

The main objective of the present work is the experimental study of the spectra of correlated and uncorrelated isometric muscle contractions and their comparison with model spectra obtained on the basis of the previously developed theoretical model.

The registration of the local isometric contractions of muscle fibers by Doppler myography was carried out on human brachioradial muscle, *m. flexor digitorum profundus*, which performs the function of bending the phalanxes of fingers. Experiments have been carried out using an ultrasound system which allows to register micrometer tissue displacements using a phase fluctuation method.

At the beginning, signals of uncorrelated isometric muscle contractions received from the muscle fiber in a relaxed state without load were recorded for further spectral processing. In addition, correlated and uncorrelated isometric muscle contractions arising under a constant load on the muscle of 5 kg were recorded and measured. In the experiment, measurements were carried out for two totally healthy volunteers.

The length of recording of isometric muscle contractions was about 4s. The amplitude-frequency characteristics of measured local displacements were calculated using the fast Fourier transformation algorithm. Then spectra were averaged on the results of more than 100 samples of the length of 256 points with sampling period of about 4 ms. The same procedure was used to calculate model spectra [3].

As it was mentioned above, the interaction between two filaments causes a muscle contraction. The mechanism of the muscle contraction is that of projections of myosin filaments could attach themselves to the actin filaments, forming so-called cross-bridges, and propel the thin filaments to new position. From this point of view, a simple physical model of the contractions was used to describe the experimentally obtained spectra. The model considers only the force of viscous friction, which leads to

inhibition of the relative motion of actin and myosin filaments, and ignores the elastic properties of muscle fibers. Hence the description of the  $i$ -th sarcomere's contraction and the computer simulation of it were based on a simple motion equation of the form:

$$m \frac{d^2 x_i}{dt^2} + \frac{F_{max}}{v_{max}} \frac{dx_i}{dt} = Q_i(t) = p[(N)_0 - N_i(t)]$$

where  $m$  – some effective mass associated with the sarcomere,  $p$  – the force generated by a cross-bridge,  $N_i(t)$  – the current number of bridges in each of the two areas of overlap in the sarcomere,  $N_0$  – equilibrium value of the number of bridges,  $F_{max}$  and  $v_{max}$  – the parameters of the model, having the dimensions of force and velocity, respectively.

Directly from the first equation, after the Fourier transform, we can arrive to the following expression for the power spectrum of displacements originated at each individual sarcomere. In particular, if the fluctuation of the number of bridges in the sarcomere  $\Delta(t) = (N_0 - N_{ik}(t))N_0^{-1}$  is a white noise, for which  $\Delta(\omega) = const$ , we can write simply

$$s(\omega) = \frac{C}{\omega^2[\omega^2 + \gamma^2]}$$

To compare the experimental measurement with the results of the mentioned model a simulation was carried out. Within the simulation task for the description of sarcomere's motion right side of the equation of motion was chosen as the sequence of pulses:

$$Q_i(t) = P\tau \sum_{k=0}^{\left[\frac{t}{\tau}\right]} \frac{N_0 - N_i(k\tau)}{N_0} \delta(t - k\tau) = P\tau \sum_{k=0}^{\left[\frac{t}{\tau}\right]} \Delta_i(k\tau) \delta(t - k\tau)$$

where  $\delta(t)$  – the delta function,  $P = pN_0$  – the value of the mean external load on each chain of sarcomeres and, accordingly, on each sarcomere in the chain,  $\left[\frac{t}{\tau}\right]$  – the integral part of the value  $\frac{t}{\tau}$ ,  $k$  – integer,  $\tau$  – the characteristic period of the cross-bridges excitation determined by the mechanochemical cycle of sarcomeres,  $P\tau$  – the average impulse developed by sarcomere's cross-bridges under an external load  $P$ . For modeling in accordance with this expression it was assumed for simplicity that the bridge excitation occurs within periods of time substantially less than the period of excitation and that the magnitude of the force depends on the external load.

## Results

Computer simulation was performed for a chain of 1000 sarcomeres. The values of characteristic decay time of a single contraction were chosen accordingly to the information about the mechanochemical cycle of correlated and uncorrelated sarcomere's contraction.

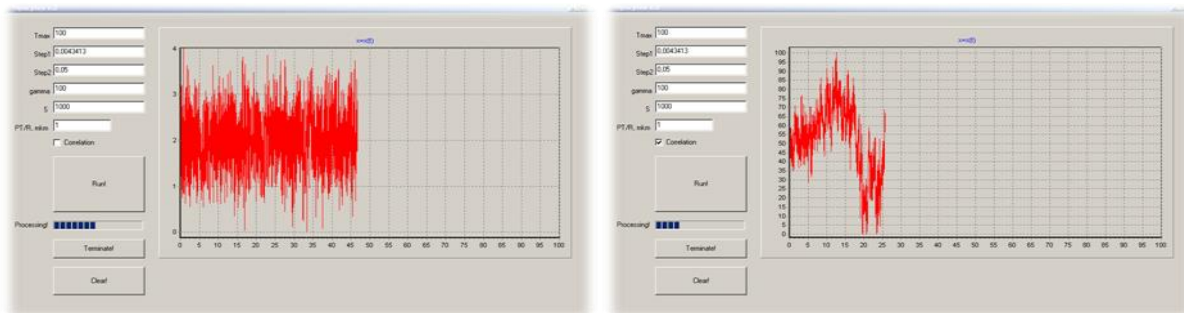


Figure 1. Computer simulation.

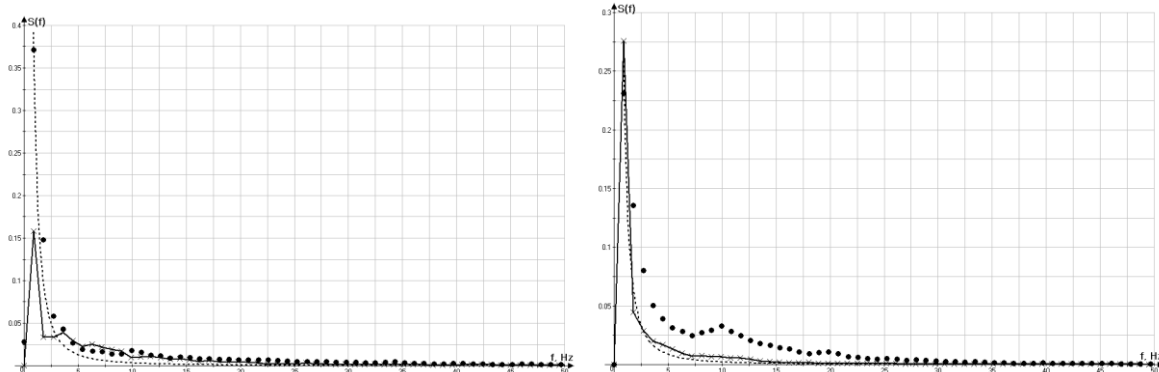


Figure 2. Displacements power spectrum of uncorrelated muscle contractions under an external load of 5 kg (40 years, left) and of correlated muscle contractions under an external load of 5 kg (21 years, right).

## Discussion

Theoretical curves (dashed lines) and the results of simulation (solid lines) aptly describe the qualitative experimentally observed strong decrease in the power spectra of displacements with the frequency, which suggests the developed fluctuation model of isometric muscle contractions to be adequate.

Despite the assumptions and simplifications in the model, computer simulation and numerical approximation of the spectral characteristics of muscle contractions indicate a general applicability of the theoretical model to explain the observed data.

Discrepancies between the model and experimental spectra can be related to two factors. First, fluctuations in the number of bridges in the sarcomere are not, obviously, white noise, and should reflect the spectral characteristics of the signals controlling their work. Secondly, in the present form of the model does not account for the elastic properties of the muscle filaments. Further research is needed to determine the contribution of these mechanisms in the spectral characteristics of the muscle contractions.

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## PERSPECTIVES OF USING CORD BLOOD IN MEDICINE

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**Summary:** The article deals with the data on the composition and use of cord blood in regenerative medicine compared with the bone marrow. Regenerative potential of cord blood, its low molecular components as well as some prospects of using its stem cells in cell therapy has been considered. The necessity of increasing the number of cord blood banks has been proved.

**Key words:** cord blood, low-molecular fraction, stem cells.

**Анотація:** Стаття присвячена розгляду даних про склад і застосування кордової крові в регенеративній медицині. Розглядається регенераційний потенціал кордової крові, її низькомолекулярних компонентів, а також деякі перспективи використання її стовбурових клітин в клітинній терапії. Обґрунтовується необхідність збільшення кількості банків кордової крові.

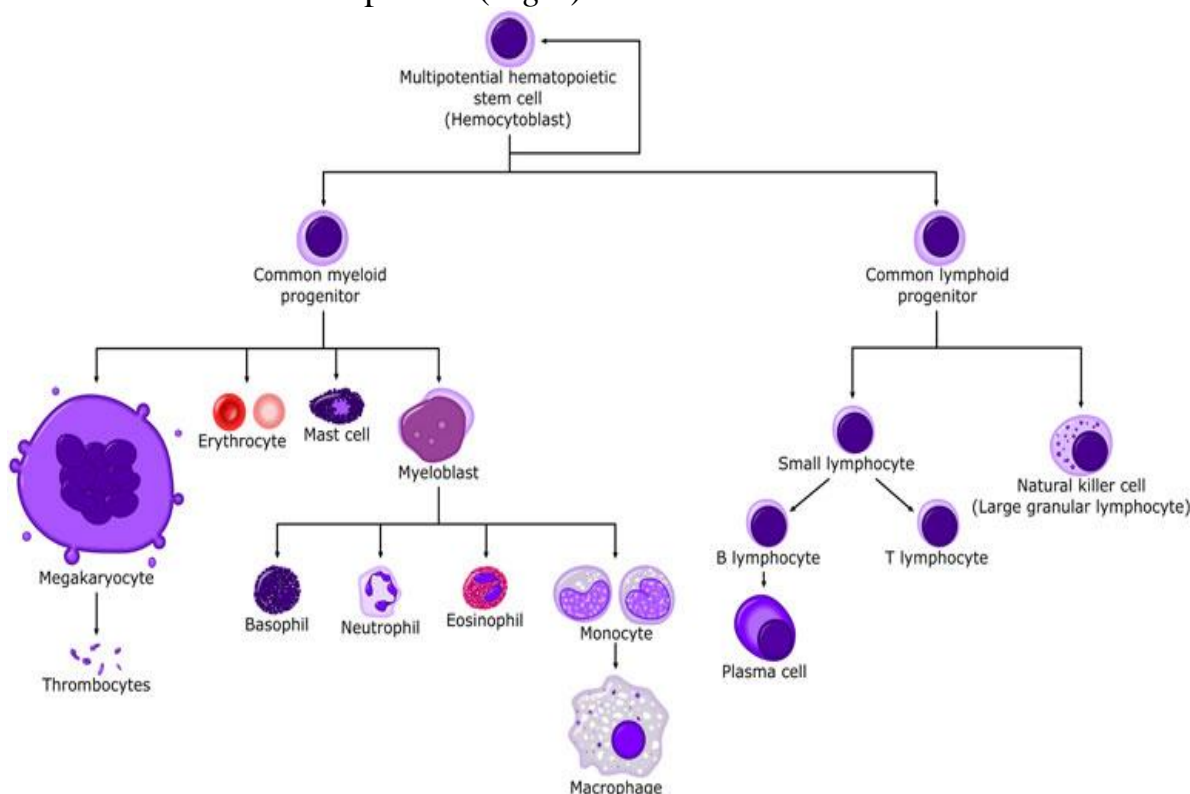
**Ключові слова:** кордова кров, стовбурові клітини, низькомолекулярна фракція.

**Аннотация:** Статья посвящена рассмотрению данных о составе и применении кордовой крови в регенеративной медицине. Рассматривается регенерационный потенциал кордовой крови, ее низкомолекулярных компонентов, а также некоторые перспективы использования ее стволовых клеток в клеточной терапии. Обосновывается необходимость увеличения количества банков кордовой крови.

**Ключевые слова:** кордовая кровь, стволовые клетки, низкомолекулярная фракция.

Cord blood (placenta, umbilical cord, fetal) is the blood that remains in the vessels of the placenta and the umbilical cord after the birth of a child and its separation from the mother. Umbilical cord blood (UCB) has an abundant source of stem cells.

The term "stem cell" was introduced in 1910 by a professor of Military Medical Academy (St. Petersburg) A. A. Maksimov to define a hematopoietic cell from the bone marrow, which he considered the forerunner of all cellular elements of blood. The modern scheme of hematopoiesis (*Fig.1*) confirms it.



**Fig.1.** Scheme of hematopoiesis

The main function of blood stem cells (BSC) is daily production of  $10^{11}$  new cells of all kinds. The research of BSC began in the 60s of the last century, when it became possible to identify common phenotypic properties of bone marrow cells that can self-renew and form other cellular elements. More than 50 years' experience in the study of BSC of bone marrow has confirmed their usage for the treatment of various pathologies of the hematopoietic system. It is known that bone marrow (BM) is a source of hematopoietic progenitor cells (HPC) used to reconstitute blood cells in a number of malignant and nonmalignant blood diseases. BM transplantation was first performed in the 1960s and currently is the main treatment for more than 15,000 patients worldwide each year [4].

New sources of stem cells that can replace lost or diseased cells of the body are being sought due to the tight government restrictions, availability, and ethical considerations regarding the usage of embryonic and fetal tissues. In turn the transplantation of BM also has a number of problems. The most notable BM transplantation disadvantages include: 1) only 30% of eligible patients can use donor's bone marrow (a large amount of time from the beginning of the donor search to the procurement of BM cells and the treatment) 2) a high probability of rejection. So the search for an alternative source of stem cells is being carried on. Nowadays all over the world the scientists are examining the properties and characteristics of human cord blood (HCB) [2, 6].

The enthusiasm over UCB began when it was found that UCB contains a large population of hematopoietic stem cells compared to adult sources. It is known, that cord blood contains a variety of specific placental proteins, growth hormones and hemopoietic factors, immunomodulators and enzymes. UCB is not immunogenic. Due to its unique composition UCB possesses a high bioactivity [10].

Some studies have shown that cord blood differs from donor one by a number of indices of the coagulation system, oxygen transport, the immunological and rheological properties, the hemopoiesis system indices and the content of protein components [2].

UCB could help to avoid some BM transplantation complications. UCB was used successfully for the first time for cell transplantation in 1988 for the treatment of a 5-year-old child afflicted with Fanconi anemia [5]. Subsequently more than 6,000 UCB transplantations have been performed all over the world, most of them with unrelated donors.

UCB's relative cellular immaturity compared to adult cells suggests a potentially unrivaled degree of plasticity. Its usage as an alternative to BM transplantation is growing as the researchers have better understanding of its composition, mechanisms of action, and broad therapeutic capacity.

Currently there are some advantages of using UCB in comparison with bone marrow cells and peripheral blood of an adult human [8]. They are:

- No risk or discomfort to donors;
- Low incidence of viral contamination (38.2%) compared to BM [8];
- There is a high immune tolerance of UCB cells because they are unable to generate cytotoxic T-Lymphocytes, which respond to allogenic antigens [2];
- Procurement and use are not associated with the same ethical considerations as embryonic and fetal tissues;

- Cord blood cells were shown to be more resistant to damaging cryopreservation factors unlike mature cells of adult donor blood [8].

Many scientists around the world are sharing the latest results of preclinical and clinical studies on the usage of cord blood to treat diseases for which hitherto treatments have not been existed.

Main clinical applications of UCB have been focused on hematologic diseases. But a large number of studies have confirmed that UCB cells may differentiate into osteoblasts, chondroblasts, adipocytes, and even neurons and astrocytes [1]. The most notable example of the multifaceted therapeutic effects of UCB has been shown on the model of embolic stroke. In this model it has been demonstrated that an intravenous administration of cord blood in 48 hours after a stroke onset can reverse the impending cell death [7].

The data obtained by some Ukrainian scientists have testified an anti-virus effect of cord blood manifested as the absence of dystrophic and necrotic injuries, the maintenance of cell structures in organs of immune system and lungs of virus-infected animals.

It has been shown that the usage of the medications based on cord blood in combination with traditional treatments make it possible to avoid reproductive losses and to lower a number of complications during the pregnancy.

The efficacy of application of the cellular elements, plasma, serum and individual macromolecular substances of cord blood has been confirmed in clinical practice [1]. However, the studies on the biological activity of low-molecular components of CB are rare. In vivo experiments have shown that the low-molecular fraction (below 5 kDa) of cord blood has a strong immunomodulatory and reparative action.

The effect of low-molecular fraction (below 5 kDa) of cord blood in the field of ophthalmology has been studied. In particular, the influence of a low-molecular fraction (below 5 kDa) of human cord blood used as an eye gel component on cornea regeneration has been examined in the experimental model of a mechanical damage. Histomorphological analysis has testified that the gel accelerates cornea healing. The data obtained require further investigations of mechanisms of HCB action as the eye gel component on reparative processes in a damaged cornea to create new ophthalmologic methods and approaches for a cornea defect treatment, which could prevent development of inflammatory complications and blindness [3].

Today in Ukraine at least 1500 patients need hematopoietic stem cell transplantation and at the same time, about 50 tons of cord blood which is a rich source of these cells are just discarded. Though currently, for the practical implementation of cellular technologies some methods of UCB cryo storage have been developed.

Consequently, UCB provides an arsenal of therapeutic effects that no pharmacological drug could possess. Thus it is necessary to increase the number of cord blood banks all over the world and in our country in particular.

Undoubtedly unique properties of the cord blood could revolutionize medicine, but further investigations are badly needed.

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## ENVIRONMENTAL PROBLEMS IN THE TERRITORY OF UKRAINE

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**Summary:** The article is devoted to consideration of main ecological problems in different regions of Ukraine territory. As a result of research there were revealed some ecological environmental versions of Ukraine. The most important aspects of pollution in all possible fields were considered. Comparisons of research results between regions of Ukraine were also made.

**Key words:** environment, negative impact, pollution, ecology, noise, biosphere, health.

**Анотація:** Стаття присвячена розгляду основних екологічних проблем у різних регіонах території України. У результаті дослідження було виявлено основні різновиди екологічного забруднення навколишнього середовища України. Було розглянуто найважливіші аспекти забруднення в усіх можливих середовищах. Також зроблені порівняння результатів досліджень між регіонами України.

**Ключові слова:** навколишнє середовище, негативний вплив, екологія, шум, біосфера, здоров'я.

**Аннотация:** Статья посвящена рассмотрению основных экологических проблем в разных регионах территории Украины. В результате исследования были выявлены основные разновидности экологического загрязнения окружающей среды Украины. Были рассмотрены важнейшие аспекты загрязнения во всех возможных средах. Также сделаны сравнения результатов исследования между регионами Украины.

**Ключевые слова:** окружающая среда, негативное влияние, экология, шум, биосфера, здоровье.



A person, his or her life and health, safety are determined as the highest social value in Ukraine.

Ukraine is a developed industrialized state where heavy equipment industry dominates. High specific density of resource and energy intensive technologies are common to Ukraine's economy, it's implementation and extension were carried out in the "cheapest" way - without any construction of appropriate treatment facilities. These and other factors such as low society environmental consciousness of levels led to significant environmental degradation of Ukraine, excessive pollution of surface and groundwaters, air and land, accumulation of harmful, as well as highly toxic reclamation materials in very large quantities.

Exceptional features of the ecological situation in Ukraine are acute local environmental situations that are due to large regional crises. Chernobyl disaster with its long-term medical, biological, economic and social consequences caused the situation in Ukraine, which is getting close to the level of global ecological catastrophe.

Ukraine is among those countries which have a high level of negative environmental impacts on industrial activity and, therefore, the issue of environmental protection is of utmost importance. This is due to needs to eliminate some negative anthropogenic effect on human health.

#### Sources and ecological effects on air pollution

Open air is a natural gas mixture of a surface layer that had been formed during the Earth evolution. Open air is inexhaustible resource, but in some regions it falls under strong anthropogenic influence that a problem of the composition of qualitative atmosphere arises.

Main anthropogenic sources of air pollution include heat and power equipment, enterprises, agriculture, transport. Ukraine has significant air pollution, especially in some industrially developed areas.

Main pollutants are carbonic oxide, sulfur compounds, nitrogen compounds and others, they lead primarily to the decrease in atmospheric transparency and people's poor health.

In recent years the dynamics of certain hazardous substances' emissions can be explored using Table 1.

The dynamics of certain pollutants' emissions into atmosphere can be explored from stationary sources in Ukraine

*Table 1*

	1990	1995	1997	2000	2003	2006
Sulfur compounds	2824	1656	1144	1033	984	990
Sulfur dioxide	2782	1639	1132	1023	976	983
Nitrogen compounds	685	437	380	341	328	336
Nitrogen oxide	760	423	369	332	320	328
Carbonic oxide	3273	1478	1371	1278	1230	1270
Carbohydrates	261	235	218	179	179	276
Light organic compounds	200	313	243	247	263	232

According to the table, main atmospheric pollutants are carbonic oxide and sulfur compounds, including sulfur dioxide.

A comprehensive analysis of chemical pollution in different regions of Ukraine was carried out and air pollution maps were made. The map is constructed according to the hygienic evaluation of air pollution that contains indicators: specific gross substance emission and its average value for the certain period of time (t/km), the annual average concentration of pollutants calculated on the basis of the daily and monthly average concentrations (in mg/m and ng/m for 3,4 benzopyrene); the total contamination rate (TCR) with a mixture of substances (dust, sulfur dioxide, nitrogen dioxide, carbonic oxide); the level of risk of air basin of a person.

The map chart shows that the most polluted air is that of the Donetsk, Luhansk, Dnipropetrovsk Regions (the leaders in mining metallurgy), and also that of the territory of some specific cities – the centers of industrial production (Kharkiv, Odessa, Poltava, etc.)



The Donetsk, Dnepropetrovsk, Lugansk Regions get the largest amount of emissions due to the location of large industrial enterprises of ferrous metallurgy and mining in those areas.

#### Water resources contamination

Water is the only natural fluid that exists in the biosphere in large quantities.

The factors of water pollution are:

- 1) Organoleptic criterion - smell, taste, color, foamability, temperature, these are different manifestations of water pollution;
- 2) Sanitary - toxicological criterion reflects the impact of chemicals on human health.
- 3) General sanitary criterion reflects the state of the biological balance of aquatic environment and chemical factors influence on the process of self-purification of water body through the criterion of velocity of organic oxidation.

Ukraine is among those countries that are poorly provided with water resources, besides the fact that they are unequally located around its territory.

The main problem of internal waters of Ukraine is pollutants spews by many industrial enterprises and those of agriculture. For instance, in 2003 the companies of the Kharkiv Region dropped into the inland waters so many contaminants to dilute 9.2 cubic km of clean water, which is several times more than the average annual runoff volume of Seversky Donets.

#### Contamination of land with solid wastes

Recently there has appeared a problem of contamination by physical factors of urban environment and occurrence, in this connection, of a number of environmental issues that affect the population's health, spread of diseases.

The first physical factor of urban environment pollution is solid wastes, the main source of cluttering and littering urban and suburban landscapes. They consist of industrial wastes, construction and housing maintenance and utilities.

Now in Ukraine the growth rate of household wastes is up to 10 % per year. This is, particularly, the market saturation of consumer goods and the general supply of imported goods in new packaging materials, first of all.

The problem of solid waste recycling increases, mainly because the most of consumer goods are doomed to a short service for people. In general, they are bought, consumed and thrown away without any proper treatment to their final value.

In the urban economy at the present stage the problem of solid waste ordering is at the foreground. It is proved that in the presence of chutes in residential buildings, the amount of all household wastes increases by about 20-25 %, mainly by eliminating fugitive garbage and food emissions into the sewerage system. Municipal landfills become a dangerous source of soil, air and ground water contamination.

Wastes from manufacturing enterprises which accumulate their wastes (including

Influence on the person	dB	Noise source
Organs of hearing are exposed to	150	Jet take-off

toxic)  
are a  
great  
problem.  
Among  
the  
most  
contaminated

ed areas are the Dnipropetrovsk, Donetsk, Luhansk and Zaporozhye Regions, the most developed industrial regions of the country. The most polluted areas of the Kharkiv Region are the Kharkiv, Kupyansk, Balakleya and Zmiev Districts, due to the location of industrial enterprises, population concentration.

#### Noise, a kind of physical pollution

One of the forms of physical pollution is noise. Noise is all unpleasant and unwanted sounds or their combinations which interfere normal work and rest, perceive normal sounds. It occurs as a result of condensation and dilution of air mass, that is, fluctuated changes in air pressure. There is continuous, non-continuous, fluctuating, intermittent, impulsive noise. We know now that sounds have harmful impact on human health, they reduce it's capacity to work, cause diseases of acoustic organs (deafness), the endocrine, nervous, cardiovascular systems. The adaptation of organisms to noise is virtually impossible that is why the

regulation and limitation of noise pollution, of environment are the important and mandatory events. The surrounding environment noise is equal to 30-60 decibels. The occupational transport noise, the level of which is often higher than standards, is added to this natural background in modern conditions. Noise levels are given in Table 2.

#### The levels of noise, dB

Table 2

the strong negative influence	140	
	130	The modern electromusic
Threshold of pain	120	Thunder noise
	110	Plane noise
	100	Noise of the train
Noise threshold of the beginning of a discomfort	90	Maximal noise of production
	80	Intensive noise on the highway
	70	
Noise level causing complaints	60	Noise on the street
Border behind which the stress begins	50	
Border of a noise fatigue	40	
Sound comfort	30	Norm of loudness at night
	20	House sound comfort
	10	Whisper
	0	The complete silence

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УДК 615.38

## **PERSPECTIVES OF STEM CELL THERAPY**

**Panashchenko R. (Kharkiv)**

**Language supervisor: Sergeeva O.A.**

**Summary:** Different standpoints, approaches and theories of aging are considered in the article. The most prominent characteristics of each theory are elucidated.

**Key words:** aging, cellular senescence, chromosome, DNA, senescence.

**Анотація:** У статті розглядаються різні точки зору, підходи до вивчення та теорії старіння. Висвітлюються найбільш яскраві характеристики кожної теорії.

**Ключові слова:** біологічне старіння, ДНК, старіння, старіння на клітинному рівні, хромосома.

**Аннотация:** В статье рассматриваются различные точки зрения, подходы к изучению и теории старения. Освещаются наиболее яркие характеристики каждой теории.

**Ключевые слова:** биологическое старение, ДНК, старение, старение на клеточном уровне, хромосома.

Stem cell therapy is an intervention strategy that introduces new adult stem cells into damaged tissue in order to treat disease or injury. Many medical researchers believe that stem cell treatments have the potential to change the face of human disease and alleviate suffering. The ability of stem cells to self-renew and give rise to subsequent generations with variable degrees of differentiation capacities offers significant potential

for generation of tissues that can potentially replace diseased and damaged areas in the body, with minimal risk of rejection and side effects.

A number of stem cell therapies exist, but most are at experimental stages, costly or controversial, with the notable exception of bone-marrow transplantation. Medical researchers anticipate that adult and embryonic stem cells will soon be able to treat cancer, Type 1 diabetes mellitus, Parkinson's disease, Huntington's disease, Celiac disease, cardiac failure, muscle damage and neurological disorders, and many others.

Stem cells may also be used to treat brain degeneration, such as in Parkinson's and Alzheimer's disease. Pharmacological activation of an endogenous population of neural stem cells/neural precursor cells by soluble factors has been reported to induce powerful neuroprotection and behavioral recovery in adult rat models of neurological disorder through a signal transduction pathway involving the phosphorylation of STAT3 on the serine residue [3, p. 1094].

The development of gene therapy strategies for the treatment of intracranial tumors offers much promise, and has shown to be successful in the treatment of some dogs; although research in this area is still at an early stage. Using conventional techniques, brain cancer is difficult to treat because it spreads so rapidly. Researchers at Harvard Medical School transplanted human neural stem cells into the brain of rodents that received intracranial tumors. Within days, the cells migrated into the cancerous area and produced cytosine deaminase, an enzyme that converts a non-toxic pro-drug into a chemotherapeutic agent. As a result, the injected substance was able to reduce the tumor mass by 81 percent. The stem cells neither differentiated nor turned tumorigenic [5].

A team of Korean researchers reported on November 25, 2003, that they had transplanted multipotent adult stem cells from umbilical cord blood to a patient suffering from a spinal-cord injury and that following the procedure, she could walk on her own without difficulty. The patient had not been able to stand up for roughly 19 years. For the unprecedented clinical test, the scientists isolated adult stem cells from umbilical cord blood and then injected them into the damaged part of the spinal cord [3, p. 1096].

Stem cell therapy for treatment of myocardial infarction usually makes use of autologous bone marrow stem cells (a specific type or all); however other types of adult stem cells may be used, such as adipose-derived stem cells. Adult stem cell therapy for treating heart disease was commercially available in at least five continents since 2007.

Possible mechanisms of recovery include:

- Generation of heart muscle cells
- Stimulation of growth of new blood vessels to repopulate damaged heart tissue
- Secretion of growth factors
- Assistance via some other mechanism

It may be possible to have adult bone marrow cells differentiate into heart muscle cells.

The first successful integration of human embryonic stem cell derived cardiomyocytes in guinea pigs (mouse hearts beat too fast) was reported in August 2012. The contraction strength was measured four weeks after the guinea pigs underwent simulated heart attacks and cell treatment. The cells contracted

synchronously with the existing cells, but it is unknown if the positive results were produced mainly from paracrine as opposed to direct electromechanical effects from the human cells. Future work will focus on how to get the cells to engraft more strongly around the scar tissue, whether treatments from embryonic or adult bone marrow stem cells will prove more effective remains to be seen [2, p. 14].

Fully mature human red blood cells may be generated *ex vivo* by hematopoietic stem cells (HSCs), which are precursors of red blood cells. In this process, HSCs are grown together with stromal cells, creating an environment that mimics the conditions of bone marrow, the natural site of red-blood-cell growth. Erythropoietin, a growth factor, is added, coaxing the stem cells to complete terminal differentiation into red blood cells. Further research into this technique should have potential benefits to gene therapy, blood transfusion, and topical medicine [2, p. 10].

Hair follicles also contain stem cells, and some researchers predict research on these follicle stem cells may lead to success in treating baldness through an activation of the stem cells progenitor cells. This treatment is expected to work by activating already existing stem cells on the scalp. Later treatments may be able to simply signal follicle stem cells to give off chemical signals to nearby follicle cells, which have shrunk during the aging process, which in turn respond to these signals by regenerating and once again making healthy hair. Most recently, Dr. Aeron Potter of the University of California has claimed that stem cell therapy led to a significant and visible improvement in follicular hair growth [4].

Stem cells have resulted in significant locomotor improvements in rats with an Amyotrophic lateral sclerosis-like disease. In a rodent model that closely mimics the human form of ALS, animals were injected with a virus to kill the spinal cord motor nerves, which mediate movement. Animals subsequently received stem cells in the spinal cord. Transplanted cells migrated to the sites of injury, contributing to regeneration of the ablated nerve cells and restoring locomotor function [3, p. 1095].

Human embryonic stem cells may be grown in cell culture and stimulated to form insulin-producing cells that can be transplanted into the patient.

However, clinical success is highly dependent on the development of the following procedures:

- Transplanted cells should proliferate
- Transplanted cells should differentiate in a site-specific manner
- Transplanted cells should survive in the recipient (prevention of transplant rejection)
- Transplanted cells should integrate within the targeted tissue
- Transplanted cells should integrate into the host circuitry and restore function [1, p. 985]

Stem Cell Educator Therapy induces immune balance by using Cord Blood-Derived Multipotent Stem Cells (CB-SCs). A closed-loop system that circulates a patient's blood through a blood cell separator, briefly co-cultures the patient's lymphocytes with adherent CB-SCs in vitro, and returns the educated lymphocytes (but not the CB-SCs) to the patient's circulation. The clinical trial reveals that a single treatment with the Stem Cell Educator provides lasting reversal of autoimmunity that

allows regeneration of islet beta cells and improvement of metabolic control in subjects with long-standing type 1 diabetes.

Both patient groups with and without residual beta cell function achieved an improvement of C-peptide levels, a decrease of the median glycated hemoglobin A1C (HbA1c) values, and a reduction of the median daily dose of insulin. After treatment, the increased expression of co-stimulating molecules (specifically, CD28 and ICOS), increases in the number of CD4+CD25+Foxp3+Tregs, and restoration of Th1/Th2/Th3 cytokine balance indicate this therapy reverses autoimmunity and induces tolerance without showing any adverse effects so far.

The human trial is actually continued as a Phase II study that is still recruiting participants.

Successful immune modulation by cord blood stem cells and the resulting clinical improvement in patient status may have important implications for other autoimmune and inflammation-related diseases without raising safety and ethical concerns [6, p. 518].

Stem cells can also be used to stimulate the growth of human tissues. In an adult, wounded tissue is most often replaced by scar tissue. In the case of wounded fetal tissue, however, wounded tissue is replaced with normal tissue through the activity of stem cells. A possible method for tissue regeneration in adults is to place adult stem cell 'seeds' inside a tissue bed 'soil' in a wound bed and allow the stem cells to stimulate differentiation in the tissue bed cells. This method elicits a regenerative response more similar to fetal wound-healing than adult scar tissue formation. Researchers are still investigating different aspects of the 'soil' tissue that are conducive to regeneration [4].

Culture of human embryonic stem cells in mitotically inactivated porcine ovarian fibroblasts (POF) causes differentiation into germ cells (precursor cells of oocytes and spermatozoa), as evidenced by gene expression analysis.

Human embryonic stem cells have been stimulated to form Spermatozoon-like cells, yet still slightly damaged or malformed. It could potentially treat azoospermia.

In 2012, oogonial stem cells were isolated from adult mouse and human ovaries and demonstrated to be capable of forming mature oocytes. These cells have the potential to treat infertility [5].

The use of stem cells for the treatment of liver disease in both humans and animals has been the focus of considerable interest. The liver has some natural regenerative properties, but is often insufficient to deal with the extent of some liver diseases. Hepatocytes have been formed from some sources of MSC, but currently they have not been applied clinically. There is a large effort to create stem cells differentiated along the pancreatic line as a possible cure for diabetes, but no line has been well established.

Mesenchymal stem cells are currently under clinical trials as a possible treatment for graft versus host disease and graft rejection after experiments on various animals showing that allogenic stem cell treatments were not rejected and showed no difference in healing capabilities compared with autologous stem cells. This is being further researched for creating off-the-shelf allogenic stem cell treatments for various aspects in regenerative veterinary medicine. Clinical trials are underway to explore the low immunogenic properties of stem cells and their possible use for treatment of problems with an overactive immune system seen with allergies and autoimmune disorders.

In recent years, US based stem cell clinics have emerged that treat patients with their own bone marrow or adipose derived adult stem cells as part of clinical trials or FDA authorized same day outpatient IRB programs, most notably for athletes to recover from osteoskeletal (bone, joint and connective tissue) related injuries. The long term impact of these treatments will need to be examined outside of their contribution to medicine.

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## **BACTERIAL GROWTH DYNAMICS IN A BATCH CULTURE**

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**Summary:** A lot of different bacteria species can be isolated from the medium and examined in the laboratory, also many microorganisms can be cultivated for industry. Given facts determine the importance of microbiological cultures which are used in biotechnology. Studying such processes as kinetics and physiology of bacterial growth leads to new discoveries in biotechnology. This paper considers information about the dynamics of bacterial growth, short description of processes happened during different growth phases in a batch culture.

**Key words:** bacterial growth, bacterial population, batch culture, phases of growth.

**Аннотация:** Множество различных видов бактерий может быть выделено из среды и изучено в лаборатории, также большое количество микроорганизмов культивируется для промышленности. Данные факты определяют важность микробиологических культур, которые используются в биотехнологии. Изучение таких процессов, как кинетика и физиология бактериального роста приводит к новым открытиям в биотехнологии. Данная статья рассматривает информацию о динамике бактериального роста, содержит краткое описание процессов, происходящих во время различных фаз роста во временной культуре.

**Ключевые слова:** бактериальная популяция, бактериальный рост, периодическая культура, фазы роста.

**Анотація:** Багато різних видів бактерій може бути виділено з середовища та вивчено в лабораторії, також велика кількість мікроорганізмів культивується для промисловості. Дані факти визначають важливість микробиологічних культур, що використовуються в біотехнології. Вивчення таких процесів, як кінетика та фізіологія бактеріального росту приводить до нових відкриттів у біотехнології. Ця стаття розглядає інформацію про динаміку бактеріального росту, містить стислий опис процесів, що відбуваються під час різних фаз росту у тимчасовій культурі.

**Ключові слова:** періодична культура, популяція бактерій, ріст бактерій, фази росту.



During batch culture, a typical bacterial growth curve shows five distinct phases of growth: lag phase, the delay before the start of exponential growth; exponential phase, where cell division proceeds at a constant rate; stationary phase, when conditions become unfavorable for growth and bacteria stop replicating(1,2,4); death phase, when cells lose viability; and, finally, long-term stationary phase, which can extend for years (5). Different scientists can point out more than five phases of growth, but they are an intermediate between main phases.

FIG1: Growth of *Salmonella typhimurium*. (A) Growth curve showing lag phase in the experimental culture flask. Lag time was determined to be 2.09 h (n 3). Viable count data for the first 5 h are shown in an inset. (B) Plot of culture pH in the experimental culture. (C) Plot of dissolved oxygen tension in the experimental culture. Oxygen concentrations during the first 5 h are shown in an inset. (D) Cell length in the experimental culture. Statistically significant increases in cell length compared to those in the standardized inoculums (t test; P 0.0001) are shown with an asterisk.

### Lag phase

It has been assumed that lag phase allows the adaptation required for bacterial cells to begin to exploit new environmental conditions (2). This process could include the repair of macromolecular damage that accumulated during stationary phase (3) and the synthesis of cellular components necessary for growth. Also transcription of different operons and regulons takes place during lag phase. Autoinducers are secreted into a cultural medium (3). However, these remain hypothetical possibilities, as the available physiological data simply show that lag phase bacteria are metabolically active (6). Consequently, there are currently no physiological or biochemical criteria to define lag phase. The physiology of bacterial lag phase remains a mystery, but microbiologists have devoted a great deal of effort to measure, model and predict the duration of bacterial lag time.

The duration of lag phase depends on many factors but it is known some common regularities.

1. Lag phase is more prolonged for species which grow slowly.
2. Lag phase prolongation depends on physiological activity and age of inoculated material.
3. Lag phase prolongation drops with amplification of inoculum.

### Exponential phase

After the lag phase, the culture enters the log phase via a short accelerating log phase. During this phase culture exists in a quasi-stationary condition. Exponential growth can occur with a *Typhimurium* and requires a number of factors to be present in excess in the growth medium, including sources of carbon, nitrogen, phosphate, and certain trace elements, such as iron. The physiology of exponential bacterial growth and replication involves multiple rounds of DNA synthesis, coupled with transcription and translation, to synthesize necessary macromolecules. These crucial events are controlled by a variety of gene regulatory processes.

Avalanche-like growth of cell amount is determined by the following relation:

$x = x_0 e^{\mu t}$ , where  $\mu$  - maximum specific growth rate and  $x_0$  – initial amount of cells.

During this phase the microorganisms grow at maximum rate possible given their genetic potential and the growth conditions. Their rate of growth is exponential during this phase i.e. they divide and double in numbers at regular time intervals.

FIG2: Growth of a microbial culture during log phase as obtained on arithmetic plot.

### Stationary phase

In a batch culture, the exponential growth phase is limited. This is because an essential nutrient of the culture medium has been used up and a few waste products (which could be toxic also) have been produced by the microorganisms inhibiting their further growth. Although growth usually does not take place during this phase, many cell functions such as energy metabolism and some metabolic processes do continue. It has been found that some organisms continue to grow at a slow rate during this phase but there is no net increase in cell number because while some cells in the population grow, others die, and the two opposite processes balance each other out. This growth phenomenon is known as cryptic growth. The size of most bacteria is considerably reduced upon entry into stationary phase. This size reduction is the result of two discrete processes referred to as reductive division and dwarfing.

### Bacterial cell age and death

A philosophically interesting peculiarity of exponentially growing bacterial populations is that there is no adult form of bacterial cells and the population is not age structured. The reason is that binary fission proceeds in a symmetrical fashion with a nonconservative dispersion of both undamaged and damaged constituents. This has led to the conclusion that bacteria are essentially immortal. In other words, their capacity for reproduction appears limitless as long as the environment supports growth. However, the statement that prokaryotes are examples of organisms that have evolved in definitely long life spans is misleading because it can be argued that the bacterium as an individual ceases to exist when cytokinesis is completed. Thus, we can logically analyze and discuss an exponentially growing cell's generation time, but the concept of a life span for such dividing individual bacteria is obscure.

On the other hand, the terms life span, longevity, and bacterial age can be useful when considering cells entering the stationary phase. Progressive physiological alterations can be followed as a function of the chronological age of individual stationary-phase cells, and the life span of such cells is far from indefinitely long. For example, the average life span, measured as the time of sustained reproductive ability, of stationary-phase *E.coli* cells is around 3 to 5 days when starved for exogenous carbon. This loss in plating efficiency has been described in microbial textbooks as the death phase of the bacterial growth cycle, and such death has been argued to be the nearest bacteria come to a "natural" death of the kind familiar to higher organisms. Even so, it is important to stress that it is a form of accidental death conceptually distinct from mandatory aging in higher organisms. Therefore, the term conditional senescence was proposed to make such a distinction.

### Death phase

If the cells are allowed to grow beyond stationary phase, then while some cells may remain alive and continue to metabolize, they will eventually die. During this death phase, the cell population continuously decreases with time and the population is said to have entered into death phase of the growth cycle. The reason of this process is apoptosis or cell death or external injuring factor. In some cases, the death of microorganisms is accompanied by cell lysis, a phenomenon in which the internal contents of the cell are leached out of the cell.

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## **MEASUREMENTS OF BODIES TEMPERATURE AND ACCELERATION INFLUENCE ON THEIR WEIGHT**

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**Language supervisor: Nemchonok S.L.**

**Summary:** A brief review of experimental effects, which have general physical reason connected with weight change. This reason is dependent of body acceleration or its microparticles thermal movement. Researches of acceleration influence and test mass temperatures were shown.

**Keywords:** acceleration, gravitational force, impact, temperature, weight.

**Анотація:** Короткий огляд експериментальних ефектів, які мають загальну фізичну причину, пов'язану зі зміною ваги, яка залежить від прискорення тіла або теплового руху його мікрочастинок. Показані дослідження впливу прискорення і температури тестової маси.

**Ключові слова:** вага, вплив, гравітаційна сила, прискорення, температура.

**Аннотация:** Краткий обзор экспериментальных эффектов, которые имеют общую физическую причину, связанную с изменением веса, который зависит от ускорения тела или теплового движения его микрочастиц. Показаны исследования влияния ускорения и температуры тестовой массы.

**Ключевые слова:** вес, воздействие, гравитационная сила, температура, ускорение.

Deep interrelation of electromagnetic and gravitational forces can and must be manifested in experiments with exact weighing of test bodies moving with acceleration under action of elastic forces. For a long time attention having been paid to this problem was not enough but this attention was in part promoted by theoretical concepts of general relativity theory as to fictitiousness of «gravitation force» concept. Meanwhile, a number of experimental measurements tested acceleration influence of external elastic forces on acceleration value of gravity as it will be shown in the present paper. We propose to characterize this influence in the following way. If a test body under action of external elastic forces moves upwards with acceleration value an increment of the gravitational acceleration will occur, which is given in a first linear approximation like.

Similarly, if a body is accelerated downwards under of external forces action, then an increment of the gravitational acceleration will occur with a different sign, given by

In equation 1 and equation 2 dimensionless factors and characterize a degree of interaction of elastic and gravitational forces. Vertical harmonious oscillations of a test body with weight  $p$  will therefore lead to an average weight given by

where  $m$  is body mass, standard acceleration due to gravity,  $A$  amplitude, and circular frequency of oscillations. The experiment will give an answer to the question whether factors are different from zero, and what their ratio is.

The simple way of difference estimation value is based on weighing of a rotor of a mechanical gyroscope with a horizontal rotation axis. The role of elastic forces is played here by centripetal forces. It is possible to show that weight  $P$  of the rotor in form of a cylinder with radiuses and is equal to

where is the angular speed of rotation. That experiment was executed in 1999 – 2000 at Saint Petersburg. In this case, we weighed a pair of coaxial rotors rotating in opposite directions for compensation of the container total angular momentum ( $=15$  mm,  $=25$  mm,  $M=250$  g), as shown in figure 1. The obtained experimental dependence is shown in figure 2.

**FIGURE 1.** The container device.

1 – electric coils of gyroscope engine,  
2 – a massive cylindrical part of a rotor,  
3 – a case of the first gyroscope, 4 – plugs of power supplies of engines of gyroscopes, 5 – a case of the second gyroscope (it is shown without section), 6 – container case.

**FIGURE 2.** Mass difference of a horizontal and a vertical rotor.

At rotation velocity of 18.6 thousand rev/min relative reduction of rotor weight was equal to . The estimated value of is near to . The factor alone was evaluated by precision measurements for the restitution coefficients of an elastic impact of a ball against a massive metal plate. In these experiments a plate (and a ball trajectory) took horizontal and vertical positions. Acceleration of the ball during impact duration exceeded of . Difference of restitution coefficients in vertical and horizontal quasi-elastic impacts of the ball is shown in figure 3.

**FIGURE 3**

Experimental dependence of restitution coefficient; the top line , a bottom line . Factor value order can be estimated by the formula

The ball velocity before impact is approximately , which gives that is unexpectedly large. Qualitative results obtained by M. Tajmar's group in experiments with a rotating superconductor probably have a physical nature close to that being discussed in the present work.

Actually, if there is acceleration influence of elastic (electromagnetic in nature) forces on gravitation, then there will be temperature dependence of body weights due to thermal movements inside the body. Microparticles acceleration in their thermal movement directly depends on their energy, and therefore from absolute temperature of a body. It is possible to show that in a classical approximation at temperatures higher than Debyetemperature, body weight temperature dependence is described by formula

where  $C$  is a factor dependent on physical characteristics (including density and elasticity) of bodies and  $T$  is the absolute temperature. According to equation (6), an increase in absolute body's temperature will cause reduction of its weight. Such an effect was surely observed in exact weighing of metal samples from nonmagnetic

materials heated with ultrasound. Layout of a hermetically sealed container is shown in figure 4. A sample weight experimental dependence in the process of its heating and cooling is shown in figure 5.

**FIGURE 4.** Layout of hermetically sealed container.

- 1 – Dewar flask; 2 – metal rod;
- 3 – holder support;
- 4 – electroacoustic transducer (PZT);
- 5 – gaskets (foam plastic);
- 6 – holder base (ebonite);
- 7 – cold welding.

**FIGURE 5.** Change in mass of a brass rod.

Ultrasound frequency is. Touch lines indicate the moments when the ultrasound was switched on and off.

Various samples made of lead, copper, brass, titan and duralumin weight temperature dependence was measured. Some measurements results are shown in Table 1.

**TABLE 1**

Samples characteristics and Measurement results, where and temperature factor .

During weighing, some physical factors were considered: convection, buoyancy, heat action and ultrasound on balance, magnetic and electric fields influence, and other factors. According to quantitative estimations, the accuracy of the temperature factors was approximately 20–25 %.

The authors also constructed a thermo-physical reduction model of apparent weight with non-uniformly heated samples the model of which agree well with the experiment. It is typical that negative temperature dependence of body weight is always observed, with the greatest factor values are obtained for samples made of light and elastic materials. Yet us note that for the first time weight negative temperature dependence of bodies was actually observed in experiments of Show and Davy described in 1923; however, the authors did not dare to insist on their results at that time.

An elementary analysis shows that microparticles acceleration of a test body in their thermal movement is directly proportional to  $\frac{1}{V}$ , where  $c$  is elasticity factor and  $\mu$  is particles mass. If  $V$  is elastic longitudinal waves velocity in a body being considered and body is material density, then the following ratio is true

equal (7) consequence must be the weight dependence of an anisotropic crystal on its orientation.

If the velocities  $V_1$ , of longitudinal waves in a crystal for orthogonal directions noticeably differ, then while constant crystal temperature the relative difference of its weight is measured in two positions "1" and "2" which is equal to

Measurement experimental results of weight differences in a rutile crystal is measured at its mutual - perpendicular positions which given in figure 6.

**FIGURE 6**

Weight differences of rutile crystal are measured at its mutually perpendicular positions; one division of a ordinate-scale corresponds to; results of four series of measurements are shown. Sample average weight is, velocities of longitudinal sound waves are and . Weights relative difference is equal to  $\frac{\Delta W}{W}$  with root-mean-square deviation

of . Big fluctuations of measured differences of weights are caused by temperature regimes instability of weighing. Nevertheless, there prevails regular inequality weight character being observed in case of anisotropic crystal the sign of which corresponds to ratio in equal (8).

So, the described experiments show that body accelerated movement caused by action of elastic (electromagnetic in nature) forces influences its gravitational interaction force with others, conditionally motionless, bodies. Indirectly, such influence causes negative temperature dependence of body weight that has a big practical value for precision gravimetry, for fundamental problems of physics of gravitation, and also for some astrophysics interpretation phenomena.

In the years to come it seems necessary to conduct the following experimental researches:

- precision measurement of various materials physical temperature weight dependence in a wide range of temperatures,
- dynamic measurements of bodies weight under condition of elastic effects: acoustic (including, ultrasonic and hypersonic) influence and impact, and also their oscillatory and rotary movements,
- mutual attraction forces measurement of accelerated moving weights under lowest temperatures.

Experimental and theoretical problems research of acceleration and gravitation interaction, and also the gravitation forces temperature dependence problems connected with them, are of great value both for gravitation physics development and for future technologies.

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# THE DETERMINATION OF THE DIFFERENTIAL RATE LAW AND THE EFFECT OF A CATALYST FOR THE REACTION

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**Summary:** The article deals with the ways to determinate the differential rate law, which depends on the concentration of this solution, for the reaction between iodide and hydrogen peroxide in an acidic environment and determination of the effect of a catalyst on the rate of reaction. The results of the study are as follows: even if one solution rises its concentration the rate of the reaction begins to quicken; with adding the determined amount of a catalyst the rate also quickens.

**Key words:** differential law, acidic environment, concentration, catalyst, temperature.

**Анотація:** Стаття присвячена методам визначення відмінної швидкості для реакції, котра залежить від концентрації речовини, між йодидом та пероксидом водню у кислому середовищі та визначенню впливу каталізатора на швидкість реакції. У результаті було визначено, якщо хоч одна сполука підвищує свою концентрацію – реакція починає прискорюватися. З додаванням визначеної кількості каталізатора реакція також починає прискорюватися.

**Ключові слова:** відмінна швидкість, кисле середовище, концентрація, каталізатор, температура.

**Аннотация:** Статья посвящена методам определения отличительной скорости для реакции, которая зависит от концентрации вещества, между йодидом и пероксидом водорода в кислой среде и определению влияния катализатора на скорость реакции. В результате проведения ряда экспериментов было выявлено, что даже если одно соединение повышает свою концентрацию – реакция начинает ускоряться. При добавлении определённого количества катализатора реакция так же начинает ускоряться.

**Ключевые слова:** отличительная скорость, кислая среда, концентрация, катализатор, температура.

## Determination of the Rate Law

Firstly, we should determine what the reaction rate is. The rate of reaction is an amount of elementary acts that take place in a unit of time. Also we can say that the reaction rate is defined as how fast or slow a reaction takes place. In our case, the rate law for the reaction between iodide ions and hydrogen peroxide can be determined by carrying out series of experiments in which the concentrations of iodide and peroxide are varied from one experiment to another [1, p. 192]. We will consider the following reaction and data for the understanding this determine:  $A + B = C$  Rate =  $k[A]^n[B]^m$

Experiment	[A] <sub>0</sub>	[B] <sub>0</sub>	Initial rate (M/s)
1	0.10	0.10	0.45
2	0.20	0.10	0.90
3	0.10	0.20	1.80

For this reaction, doubling the initial concentration of reactant A doubles the initial rate of reaction (experiments 1 and 2). This relationship corresponds to  $n=1$ . Alike, doubling the initial concentration of B has the effect of quadrupling the initial rate (experiments 2 and 3). This corresponds to  $m=2$ .

According to it, we can write the differential rate law for this reaction as: rate =  $k[A][B]^2$ .

The order of the reaction is 3, because this reaction is said to be first order in A and second order in B.

The value of the rate constant  $k$  can be determined by using the known values of

$$n \text{ and } m: k = \frac{\text{Rate}}{[A][B]^2}.$$

According to it, we can use the given initial concentrations and initial rate for each experiment and determine the value of  $k$  for each experiment. For the study we perform the reaction between iodide and hydrogen peroxide, but we have several experimental requirements:

- 1) The first is that the acidity of the solution must be maintained at a constant level so that the concentration of  $H^+$  is constant.
- 2) The second remark is the temperature of the reactants must be the same for all runs, because the rate constant depends on the temperature of the solution. Since the heat of a reaction is relatively small for this reaction the temperature should remain relatively constant throughout the process. If this were not the case we would need to place the reaction in a constant temperature bath.
- 3) Finally, the reverse reaction must be suppressed.

Forward reaction:  $2I^- + 2H^+ + H_2O_2 = I_2 + 2H_2O$

Reverse reaction:  $I_2 + 2H_2O = 2I^- + 2H^+ + H_2O_2$  (negligible)

- 4) We need a method to accurately measure the rate of reaction, so the addition of thiosulfate ions allows an accurate measurement of the rate at which the peroxide-iodide reaction is taking a place. Suppose that you add a small and known amount of thiosulfate ion to the original solution of peroxide and iodide. Iodine is produced slowly by the reaction between peroxide and iodide ions and the thiosulfate ions immediately react with the iodine as it is produced [4, p. 2].

As long as thiosulfate ions are present in the solution, no free iodine can accumulate because it is immediately turned into iodide ions which are colorless.

The thiosulfate ions are limited reagent, so if all the thiosulfate ions are consumed, iodine starts to form in solution. Iodine has a pale yellow color. But if starch is added to the solution then a more dramatic blue solution is formed by the complex of starch-iodine. The changing of color is sharp, and the time elapsed to this point is determined simply by use of a timer. The time from the addition of the peroxide solution to the appearance of the blue color is the difference between the addition and the appearance of blue color for the reaction. It is not very difficult to calculate how many moles of peroxide were reduced in the known interval of time. The average rate

can be calculated by this formula:  $\text{Rate} = - \frac{\Delta[H_2O_2]}{\Delta t}$ , where  $\Delta[H_2O_2]$  is a change in peroxide concentration, that can be calculated from known amounts of reactants. And difference of time is a change in time measured with a stopwatch.

For the peroxide-iodide reaction the average rate of the reaction over the period taken for the measurement is a good approximation of the initial reaction rate.

An additional and helpful consequence of the iodine-thiosulfate is that the concentration of iodine ion in the solution remains constant at its original value. Even though the peroxide-iodine reaction tends to consume iodide ions, the thiosulfate ion immediately returns the iodine to the iodide ion form.



As long as there are excess thiosulfate ions present, there is no change in the molarity of the iodide ion. This means that the rate of the reaction will change only if the concentration of the  $\text{H}_2\text{O}_2$  decreases [4, p. 3].

If the amount of  $\text{H}_2\text{O}_2$  which reacts during the period taken for the measurement is sufficiently small, no significant change in concentration of the  $\text{H}_2\text{O}_2$  will occur. Because of these conditions, the average rate of the reaction determined for this period will be a close approximation of the reaction rate corresponding to the initial concentration of reactants which is the initial rate of the reaction:

Initial rate =  $k' [\text{I}]_0^n [\text{H}_2\text{O}_2]_0^m$ , where  $[\text{I}]_0^n$  = initial concentration of iodide and  $[\text{H}_2\text{O}_2]_0^m$  = initial concentration of hydrogen peroxide.

#### The temperature-Dependence of the Rate Constant

With rising temperature the rate of reaction generally increases. It caused not by rising speed of molecules, but it caused by increasing the number of particles energy of which exceeds the energy of activation.

According to the empirical Van't-Hoff's rule with rising the temperature the rate of the reaction begins to increase, and for the homogeneous systems with heating for every ten degree the speed of reaction increases two or four times. And we can say that with rising temperature in arithmetical progression the reaction rate rises in geometrical progression. It seems that this dependence is related with increasing the number of molecular impact. But it is wrong. It was proved that the main number of molecular impacts with rising temperature by ten degrees increases only on several percentages, when the number of the molecules reacted increases in two or four hundred percentages.

To explain the observing discrepancies Arrhenius was the first, who showed, that the influence of temperature brings to the increasing of the number of active molecules. Active molecules are the molecules, that at the moment of impacting own the energy that is not less than the energy of activation for this reaction [2. p. 134].

The activation energy is some excess amount of energy that is necessary for the beginning of the reaction between the molecules. Also we can say that activation energy is the critical amount of energy to make the reaction proceed is called the Activation.

According to the Arrhenius theory the rate constant depends on the temperature exponentially. The relationship between the rate constant and temperature is reflected in the Arrhenius equation:  $k = Ae^{-E_a/RT}$ , where  $k$  is the rate constant,  $A$  is called the Arrhenius pre-exponential constant,  $E_a$  is the activation energy.  $R$  is a gas constant, and  $T$  is a temperature (in units of Kelvin). Not all molecules that have energy greater than or equal to  $E_a$  will lead to a reaction, because they must have a collision. The reaction rate must include the collision frequency somewhere, even for reactions in solution. The factor  $A$  includes the collision frequency, which must be multiplied by the fraction of collisions with sufficient energy to get an estimate of the reaction rate [2, p. 135].

Thus under the constant temperature the rate of a reaction is determined by  $E_a$ . The bigger  $E_a$ , the smaller the number of active molecules and more slowly the reaction is. The rate increases with decreasing  $E_a$ . And with  $E_a = 0$  a reaction passes immediately.

The main significance of the Arrhenius equation is that the rate constant depends on the value of the activation energy and on the temperature. The activation energy can be thought of as a barrier to the formation of the products and its value is useful in understanding the energetics of the reaction. We can find the value of the activation

energy by measuring the value of the rate constant at several measured temperatures. Also we can do it experimentally.

### The Effect of Catalyst

Catalysts can greatly influence the energy of activation. But what is a catalyst? A catalyst is any substance that works to accelerate a chemical reaction. The process by which this substance speeds up a reaction is called catalysis. Without the help of a catalyst, chemical reactions might never occur or take a significantly longer period of time to react. During the reaction this substance does not change and is not a part of the end result. So it is another way to increase the rate of a reaction despite of temperature or concentration. Catalysts operate by decreasing the value of the activation energy for the reaction. An effective catalyst exists for the reaction of iodide with hydrogen peroxide. The catalyst is iron (II) ions dissolved in the reaction mixture. By adding these ions to the reaction mixture we can increase the rate of the reaction.

We can consider the dependence of the rate from catalyst. If you want to increase the rate of a reaction, you need to rise the number of molecule collisions. One of many ways is to provide an alternative way for the reaction to happen which has a lower activation energy. Adding a catalyst has exactly this effect on activation energy. Also a catalyst can provide an alternative route for the reaction. That alternative route has lower activation energy. So we need less time for passing of the reaction and we can see the result sooner [4].

Thus, to determine the rate for a reaction we should know the concentrations of the compounds, the order of a reaction and the value of the rate constant. We can find the rate constant by carrying out the experiment, because we will know the concentrations of the compounds and the rate of the reaction. Likewise, we can determine the temperature dependence of the rate constant by using the Arrhenius equation and Van't-Hoff's rule. In conclusion, we can say that the certain catalyst can influence the reaction, because it can speed up and also it can make the reaction more slowly. All in all it is possible to say that concentration, temperature and catalyst can influence the rate of a reaction.

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### **RNA transport and human SIDT1 PROTEIN**

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**Summary:** The article deals with the problem of the RNA transport. The possible physiological role of SIDT1 protein is discussed. The sequence analysis of this protein revealed two potential

cysteine-based conservative heme-binding sites. Heme is predicted to play a role in the regulation of the RNA transport.

**Key words:** heme, RNA, RNA transport, SIDT1 protein.

**Анотація:** У статті розглядається проблема транспорту РНК, а саме за участю білку SIDT1. Обговорюється ймовірна фізіологічна роль транспорту РНК за допомогою цього протеїну. Базуючись на аналізі послідовності білка, було виявлено два консервативні потенційні гем-зв'язуючі мотиви, що мають цистеїн у своєму складі. Припускається, що гем є регулятором транспорту РНК.

**Ключові слова:** білок SIDT1, гем, РНК, транспорт РНК.

**Аннотация:** В статье рассматривается проблема транспорта РНК, а именно при помощи белка SIDT1. Обсуждается физиологическая роль транспорта РНК при помощи данного белка. На основе анализа последовательности данного белка было выявлено два потенциальных гем-связывающих цистеин содержащих мотива, которые являются консервативными среди позвоночных. Предполагается, что гем регулирует процесс транспорта РНК.

**Ключевые слова:** белок SIDT1, гем, РНК, транспорт РНК.

RNA is well known as a participant of the gene expression process. However, more and more data is rising for the signalling role of the non-coding RNAs. It is known, that they regulate the development of the complex organisms and set up the process of the RNA interference. It is obvious that the systems of its transport exist. It was shown that RNA may be transported across the membrane by the gap junctions, plasmatic nanotubes and SIDT1 protein [1].

SIDT1 is a human protein which mediates dsRNA transport across the membrane. It possibly plays a role in the RNA interference, however the physiological role remains unknown [2]. Bioinformatical and biochemical data predict SIDT1 to contain a large (300 aa) extracellular domain (ECD) and 11 transmembrane domains. ECD forms the main part of the protein outside the cell and is likely to play a role in the substrate recognition. It was found experimentally that ECD forms the stable tetrameric puck-shaped structure suggesting that SIDT1 may function as an oligomer and the process of oligomerization may control transport activity. The exact mechanism of dsRNA transport by SIDT1 is unclear [6].

Heme is well known as a prosthetic group of proteins taking part in oxygen transport, oxidative catalysis and respiratory electron transport. The new functions including the regulation of transcription, translation, protein degradation, miRNA processing and signalling have been recently revealed. In this case, heme reversibly is bound with proteins in heme sensor motifs, such as Cys-Pro-motif. A lot of heme functions are still unknown [4]. It was suggested that SIDT1 may play direct or indirect role in iron homeostasis [3]. The bioinformatic research has shown the homologous relationship between the SID-1 family and alkaline ceramidases, which are iron-dependent hydrolases [5]. No 3D structures for SIDT1 are available. Thus, the aim of this study is to analyse heme-binding abilities of the SIDT1 sequence. The novelty of our research can be explained by the fact that such type of investigation of this protein has never been carried out.

SIDT1 sequences of different species were obtained from NCBI Protein database. Multiple alignments were constructed using Clustal O (1.2.0) program. Sequence-based analysis for heme-binding activity was performed using HemeBind service. Recognition of disulphide-bonded cysteines was made by CYS\_REC program.

Two CP cysteine-based motives were revealed in SIDT1 sequence: two CP motives and PC motive in ECD and one CP in small extracellular region. The prediction

of disulphide bridges has shown that none of these Cys participate in formation of SS-bond. As SIDT1 is a transmembrane protein, we suggest that only extracellular and intracellular regions will have availability to free heme. So we examined only ECD without signal peptide (22-304). The sequence-based analysis of ECD by HemeBind has revealed potential heme-binding ability of Cys222 and Cys212 in CP and PC motives as well as of some hydrophobic amino acids (mostly Phe, Val, Leu, Ile) or Tyr. The hydrophobic interactions should be less specific and strong comparing with cysteine-based.

Multiple alignments had showed high identity of SIDT1 sequence among mammals and vertebrates. Potential heme-binding CP motives appeared to be highly conservative among vertebrates and it proves our idea. As for invertebrates, this protein is highly diverse; in some species it is even absent, for example, in *Drosophila melanogaster*. The ECD is less conservative than transmembrane part of the protein. The potential heme-binding sites are not very conservative and tend to vary in organisms with different oxygen-binding proteins.

As heme is supposed to be bound with ECD we predict that it may be the way to control SIDT1 oligomerisation. Heme is also known as a signal of stress or trauma. So, believe that heme to regulate the RNA transport. According to the fact that it is predominately expressed in cells of lymphatic system, it may play a role in the adjusting of the immune reaction. Heme as a signal of stress or trauma may play the regulatory role for siRNA transport.

Finally, possible CP-containing heme-binding sites were revealed. The exact mechanism of heme and SIDT1 interaction remains unknown. The perspective of our research is modelling and the analysis of the 3D structure of the SIDT1 protein and phylogenetic analysis of this protein.

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# HETEROCHROMIA IRIDIS

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**Summary:** The article is about heterochromia iridis. It covers the causes of the disease and specific eye color changes, also it describes the types of heterochromia iridis. The article also tells about the ways of treatment of the disease.

**Key words:** disease, heredity, heterochromia, iris, melanin.

**Анотація:** Стаття присвячена гетерохромії райдужної оболонки ока. Вона охоплює причини виникнення захворювання та особливості зміни кольору очей, також у ній описуються типи гетерохромії райдужної оболонки ока. Стаття також розповідає про шляхи лікування захворювання.

**Ключові слова:** гетерохромія, захворювання, меланін, райдужна оболонка ока, спадковість.

**Аннотация:** Статья посвящена гетерохромии радужной оболочки глаза. Она охватывает причины заболевания и особенности смены цвета глаз, а также в ней описываются типы гетерохромии радужной оболочки глаза. Статья также рассказывает о путях лечения заболевания.

**Ключевые слова:** гетерохромия, заболевание, меланин, наследственность, радужная оболочка глаза.

Heterochromia (Greek: heteros 'different' and chroma 'color') is a difference in coloration, usually of the iris but also of hair or skin. Heterochromia iridis is a condition in which the iris in one eye has a different color than the iris of the other eye. The iris is the tissue of the eye that surrounds the pupil and imparts a color, whether green, blue, brown, hazel, grey, or other, to the eye. In complete heterochromia, one iris is a different color from the other. In partial heterochromia or sectoral heterochromia, part of one iris is a different color from its remainder. Iris color is the result of the pigment that is present in the iris. Brown eyes have large amounts of melanin pigment deposits, and blue eyes have a lack of melanin.

Melanin is a broad term for a group of natural pigments found in most organisms (arachnids are one of the few groups in which it has not been detected). Melanin is a derivative of the amino acid tyrosine, however it is not itself made of amino acids and is not a protein. The pigment is produced in a specialized group of cells known as melanocytes. There are three basic types of melanin: eumelanin, pheomelanin, and neuromelanin. The most common type is eumelanin, and is produced in 'black' and 'brown' subtypes. Pheomelanin is a cysteine-containing red-brown polymer of benzothiazine units largely responsible for red hair and freckles. Neuromelanin is found in the brain, though its function remains obscure. In humans, melanin is the primary determinant of skin color. It is also found in hair, the pigmented tissue underlying the iris of the eye, and the stria vascularis of the inner ear. In the brain, tissues with melanin include the medulla and pigment-bearing neurons within areas of the brainstem, such as the locus coeruleus and the substantia nigra. It also occurs in the zona reticularis of the adrenal gland [3].

Although eye color is inherited, the inheritance pattern is complex, with interaction of more than one gene. These genes interact to provide the full constellation of colors. Other genes may determine the pattern and placement of pigment in the iris, thereby accounting for solid brown as opposed to rays of color. Normally, the two irises of an individual are of the same color. In heterochromia, the affected eye may be

hyperpigmented (darker or hyperchromic) or hypopigmented (lighter or hypochromic) [5]. Eye color is determined primarily by the concentration and distribution of melanin within the iris tissues. Although the processes determining eye color are not fully understood, it is known that inherited eye color is determined by multiple genes. Environmental or acquired factors can alter these inherited traits.

Central heterochromia is an eye condition where there are two colors in the same iris; the central (pupillary) zone of the iris is a different color than the mid-peripheral (ciliary) zone, with the true iris color being the outer color. Eyes displaying central heterochromia are often referred to as "cat eyes" because of their multi-colored iris. Central heterochromia appears to be prevalent in irises containing low amounts of melanin. A famous case of a person with central heterochromia was Baroness Rozsika Edle von Wertheimstein, whose daughter wrote: "She was a very beautiful woman... She had dark, dark brown eyes, but each eye had a purple ring to it, about a quarter of an inch of purple around these dark brown eyes" [3].

Heterochromia is classified primarily by its time of onset as either genetic (congenital, present at or shortly after birth) or acquired. Most cases of heterochromia are hereditary, and these may be associated with a congenital syndrome. Other cases are acquired and caused by a disease or due to an injury. Sometimes one eye may change color following certain diseases or injuries.

Specific causes of eye color changes include:

1. Blood in the anterior chamber (hyphema) of long duration from trauma can lead to iron deposition in the iris from the breakdown of blood products;
2. Familial heterochromia;
3. Foreign object in the eye;
4. Benign tumors of the iris, iris cysts, and iris abscesses can cause darkening or lightening of the iris;
5. Glaucoma, or some medications used to treat it;
6. Malignant melanoma of the iris or metastatic tumors of the iris;
7. Injury;
8. Mild inflammation affecting only one eye;
9. Neurofibromatosis;
10. Chediak-Higashi syndrome is a rare genetic disorder that may manifest in childhood with recurrent infections, peripheral neuropathy, and color changes in the skin and eye;
11. Congenital syndromes:

I. Waardenburg syndrome, a genetic condition that can cause hearing loss and changes in coloring of the hair, skin, and eyes;

II. Congenital "Horner's syndrome" is not a genetic syndrome, but a group of findings due to birth injury or intrauterine brain injury involving the sympathetic nervous system innervation to one eye. On the affected side, the pupil is small, the lid is drooping, and the iris is lighter. It is not associated with hearing loss or additional pigmentation anomalies;

III. Sturge-Weber syndrome, a syndrome characterized by a port-wine stain in the distribution of the trigeminal nerve on the face and tumors known as angiomas of the brain and choroid;

IV. Tuberous sclerosis, also known as Bourneville disease, causes

nonmalignant tumors in various organs including the eyes;

V. Hirschsprung disease, a bowel disorder, may be associated with iris heterochromia due to reduction in iris pigmentation;

VI. Incontinentia pigmenti, also known as Bloch–Sulzberger syndrome, affects the skin, hair, teeth, nails, and central nervous system. In this condition, the iris may be darker in the affected eye;

VII. Parry-Romberg syndrome, or progressive hemifacial atrophy, is a condition that causes the breakdown of the skin and soft tissues of half of the face [2].

Familial genetic abnormalities, ocular trauma, and inflammation are all risk factors for the development of heterochromia iridis. The use of prostaglandin analogue eyedrops is a modifiable risk factor.

If the heterochromia is secondary to an underlying cause such as inflammation, treatment should be directed at the underlying condition. In situations in which there is a major cosmetic impairment, a tinted contact lens may be used to darken the lighter appearing eye or lighten the darker appearing eye. Two different colored contact lenses may also be used to arrive at an average color.

The vast majority of people with heterochromia iridis have an excellent prognosis and have no visual complaints. Most cases are very mild, nonprogressive, and unassociated with any other illness or eye disease. In patients with associated ocular or systemic problems, treatment of the underlying abnormality is often successful in preventing visual loss [1].

Heterochromia iridis is a rare condition that causes the two eyes to be different in color. There are many potential underlying causes of heterochromia iridis including genetic and acquired conditions. Heterochromia iridis is often recognized by a parent (in the case of an affected infant) or by the patient or a family member (acquired heterochromia iridis). Treatment includes addressing the underlying condition or wearing tinted contact lenses to make the eyes look more uniform. The majority of people with heterochromia iridis have an excellent prognosis.

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# OZONE THERAPY: USE, PERSPECTIVES

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**Summary:** Ozone therapy, a revolutionary medical treatment producing far-reaching results in human health care is under consideration in the presented article. The nature, mechanisms of action and medical applications are regarded.

**Key words:** ozone therapy, antioxidants, ozone tube, free radicals, free radical scavenger, oxygenation, ozone administration, immune system, HIV.

**Анотація:** У поданій статті розглядається озонотерапія, революційний медичний засіб лікування, який має далекосяжні наслідки для охорони здоров'я суспільства. Досліджуюся характер, механізми дії та медичне застосування.

**Ключові слова:** озонотерапія, антиоксиданти, озонова трубка, вільні радикали, пастка вільних радикалів, насичення киснем, застосування озону, імунна система, вірус імунodefіциту.

**Аннотация:** В представленной статье рассматривается озонотерапия, революционный метод лечения в медицине, который имеет грандиозные результаты для будущего здравоохранения. Исследуются характер, механизмы воздействия и применение в медицине.

**Ключевые слова:** озонотерапия, антиоксиданты, озоновая трубка, свободные радикалы, ловушка свободных радикалов, насыщение кислородом, иммунная система, вирус иммунодефицита.

Ozone therapy, a revolutionary medical treatment producing far reaching results in human health care has now become a reality and is being practiced in the world today. With the noble intention of bringing up a healthy humanity such a privileged medical specialization is made available. This therapy is the first of its kind in the world [1, p. 27].

Ozone therapy is the most powerful cleansing modality. Medical ozone is produced by lightening in nature and by pulsing high currents of electricity through medical grade oxygen. Oxygen is O<sub>2</sub> and ozone is O<sub>3</sub>. Ozone is very powerful in that it increases the stability of normal good healthy cells and it destroys all those immature, sick and deformed cells, which are foreign to the body, like viruses, bacteria, fungi, etc. Ozone is an energized form of a supercharged molecule classified scientifically as O<sub>3</sub>, O<sub>4</sub>, O<sub>5</sub>, etc. chemically, ozone is oxygen with an extra molecule added. Electrically, Ozone is oxygen with a higher energy level. It is unstable and highly reactive. Singlet oxygen O<sub>1</sub> is a highly reactive free radical that acts as a scavenger of other free radicals. The oxygen reacts with them to render them harmless, thereby protecting cells from damage. Oxygen is the most vital element required for human life and it is the key to good health. The best way to optimize health is to oxygenate every cell in our body. The more oxygen we have in our system, the more energy we produce. The more efficiently we can eliminate wastes.

Oxidation is the process of passing electrons from one substance to another. An oxidant receives electrons. The substance that gives them up is oxidized. So ozone (and oxygen to a lesser extent) is an oxidant because it receives electrons, as it binds to the other substance, which gives up the electrons.

Oxygen has a negative electrical oxidation potential. To make ozone, oxygen is passed through a tube where billions of electrons are freely available. With the addition of these electrons, the oxygen becomes energized and super active, and its negative electrical oxidation potential becomes even more negative.



An oxygen molecule is spinning at a certain rate, and if it collides with objects of an opposite spin, some of its spin energy is imparted to the other object, altering it. If electricity is pumped into the oxygen, as happens in an ozone tube, the spin increases a great deal. Now, when the ozone molecule with its greater spin bumps into another object, it has enough energy to destroy the other object, such as a bacterium, by blowing a hole in the wall (called cell lysis). This model explains why ozone, created by adding energy, has more effect than plain oxygen [2, p. 6].

Vitamin C and other so-called antioxidants compete with ozone at the cell wall. Ozone is neutralized (short circuited) by these antioxidants. However, it has been shown that ozone does not deplete Vitamin C. If you do the ozone first, its effects are completed in 10 to 20 minutes. Then you can take the antioxidants without any interference.

The assumption in the promotional literature is that a 'free radical' equals to a 'bad guy'. It is not that simple. No chemical reaction can occur without the creation of free radicals (unpaired charges, positive or negative). Therefore, all life is dependent on them. Free radicals are being created in your body each second, by the billions. If they were not, you would be instantly dead.

The body is perfectly designed to handle free radicals, and the free radical scavenger enzymes (glutathione peroxidase, superoxide dismutase, reductase, and catalase) are easily able to handle any left-over free radicals from normal body processes. The trouble comes when toxins are allowed to build up in the system because we do not eat, exercise and cleanse our bodies properly. These toxins prevent the enzymes from physically contacting the free radicals, allowing the radicals to escape their birthplace and do damage elsewhere, where the enzymes cannot find them.

So the cause of the problem is not with the free radicals themselves, which are necessary, but rather with the buildup of toxins that allows the free radicals to hide and escape neutralization by the scavenger enzymes. The solution is not to take expensive artificial anti-oxidants. The solution is to take an oxidant – ozone – to clean out the toxins, and allow the free radical scavenger enzymes to do their work.

As a side benefit, it has been verified many times in tests that the levels of natural free radical scavengers in the body greatly increases under the beneficial oxidative free radical stress provided by ozone therapy.

Anything, including water and oxygen, is toxic if given in amounts that exceed the body's capacity to utilize it. Ozone is found naturally in the body. The white cells make it as part of the immune response. Pure medical grade ozone, when it is used according to the established medical guidelines, has a safety record that is unparalleled.

The use of hydrogen peroxide and ozone in medicine is based on the belief that the accumulation of toxins in the body is normally burnt up by the process of oxidation, wherein a substance is changed chemically because of the effect of oxygen upon it.

Oxidation breaks the toxins down into carbon dioxide and water and eliminates them from the body. However, if the oxygen system of the body is weak or deficient, whether through lack of exercise, environmental pollution, poor diet, smoking, or improper breathing, our bodies cannot eliminate them adequately and a toxic reaction can occur [3, p. 78].

In minor cases, a toxic buildup can lead to fatigue, while a wide range of diseases can result when poor oxygenation is chronic.

The major effects of ozone therapies are the following:

1. Ozone therapy stimulates production of white blood cells. These cells protect the body from viruses, bacteria, fungi and cancer. If, deprived of oxygen, these cells malfunction. They fail to eliminate invaders and even turn against normal, healthy cells (allergic reactions). Ozone significantly raises the oxygen levels in the blood for long periods after ozone administration; as a result, allergies have a tendency to become desensitized.

2. Interferon levels are significantly increased. Interferons are globular proteins. Interferons orchestrate every aspect of the immune system, inhibit viral replication.

3. Ozone therapy stimulates the production of Tumor Necrosis Factor. TNF is produced by the body when a tumor is growing. Ozone stimulates the secretion of IL-2. Interleukin-2 is one of the cornerstones of the immune system. It is secreted by T-helpers. T-helper causes it to produce more IL-2. Ozone's main duty is to induce lymphocytes to differentiate and proliferate, yielding more T-helpers, T-suppressors, cytotoxic T's, T-delayed's and T-memory cells.

4. Ozone therapy kills most bacteria at low concentrations. The metabolism of most bacteria is on average one-seventeenth as efficient as our own.

5. Ozone is effective against all types of fungi. This includes systemic candida albicans, athlete's foot, molds, mildews, yeasts, and even mushrooms.

6. Ozone fights viruses in a variety of ways. As discussed above, Medical ozone also goes after the viral particles directly.

7. Medical ozone is antineoplastic. This means that ozone inhibits the growth of new tissue because rapidly dividing cells shift their priorities away from producing the enzymes needed to protect themselves from the ozone. Cancer cells are rapidly-dividing cells and are inhibited by ozone.

8. Medical ozone oxidizes arterial plaque. It breaks down the plaque involved in both arteriosclerosis and atherosclerosis.

9. Medical ozone has a tendency to clear blockages of large and even smaller vessels. This allows for better tissue oxygenation in deficient organs.

10. Medical ozone increases the flexibility and elasticity of red blood cells.

11. Medical ozone accelerates the Citric Acid Cycle. Also known as the Krebs Cycle or TCA Cycle, this is a very important step in the glycolysis of carbohydrates for energy.

12. Medical ozone makes the antioxidant enzyme system more efficient.

13. Medical ozone degrades petrochemicals. These chemicals have a potential to place a great burden on the immune system [4, p. 46].

In-vitro studies to evaluate the ability of ozone to kill the HIV virus in the test tube were undertaken by scientists in the United States, Russia and Canada. It was proved that ozone can inactivate HIV. HIV could be 99 percent inactivated with only 0.5 micrograms of ozone per ml of serum, and completely inactivated by ozone concentrations of 4 micrograms per ml of serum. At the same time, these concentrations of ozone did not harm healthy cells. The data indicate that the antiviral effects of ozone include viral particle disruption, reverse transcriptase inactivation, and/or a perturbation of the ability of the virus to bind its receptor to target cells. The studies of ozonation of the blood supply determined the ability of ozone to kill HIV, hepatitis and herpes viruses in blood used for transfusion.

A virus is encapsulated in an envelope made of lipids which are fats or fat-like substances. Tiny bulbs on the virus spikes are known as 'receptors'. It is through these receptors that a virus can connect with, and eventually infect, other cells.

Through the application of ozone or hydrogen peroxide a number of events rapidly take place. The virus spikes are inactivated because the addition of ozone to the blood changes the structure of the receptor. Although still alive, the virus cannot join with the cell. At the same time, the ozone oxidates the virus's outer envelope. Without this envelope, it cannot survive.

In addition to the effects of hydrogen peroxide introduced from outside the body, the cell itself reacts to the virus. When a cell is threatened, it naturally defends itself by producing its own hydrogen peroxide. In some cases, especially when the cell is unhealthy to begin with, the hydrogen peroxide produced by the cell causes it to 'burst' before reproduction of the virus can take place.

In other cases, the peroxides introduced by added ozone or hydrogen peroxide act synergistically with the hydrogen peroxide inside of the cell, which destroy any virus that has penetrated it. Stated more simply, if the cell is unhealthy, it is destroyed by a hydrogen peroxide burst. If it is strong, it kills off the virus and becomes even stronger than before due to the increased oxygenation brought about by added ozone or hydrogen peroxide. As a result, the virus is either inhibited or destroyed.

As powerful immunomodulators, ozone and hydrogen peroxide can also strengthen a compromised immune system. They can help guard against opportunistic infections and enable persons suffering from the disease to lead longer, more active and productive lives.

While bio-oxidative therapies should not be considered a cure for AIDS, they may open the door to long-term remission, especially when used in synergistic combination with other immune-strengthening therapies. Investigations are now going on to delineate such combinations, including ozone and/or hydrogen peroxide and oral Alpha-Interferon, staph vaccine, lentinan (shiitake mushroom extract), and Chinese herbs [6, p. 24].

Using ozonated steam in cabinets is currently being used around the world for alternative health by aestheticians, chiropractors, massage therapists, and other practitioners because they recognize this natural way to detoxify and cleanse. Ozonated steam stimulates circulation and increases the oxygen supply.

Ozonated olive oil has many therapeutic uses and benefits. It is used as topical applications for dry skin and beauty aid for wrinkles, and for treatment of sunburn. It can be inhaled directly when bubbled through the olive oil. Ozonated olive oil works when applied for cuts, bruises and other conditions.

Another method of inhalation in low concentration is through room air purifiers. This method is the simplest for absorbing it into the lungs and circulatory system.

Lemon, orange and Aloe Vera juice can be ozonated for drinking or applications to the skin. Ozonated fresh lemon juice has been used on all skin conditions like skin cancer, dry skin, psoriasis and ulcers.

Other topical applications have been used on bruises, burns, fistula, decubitus, gangrene, infections, muscle pains, radiation damage, and used to promote the healing of wounds.

Some physicians are injecting ozone directly into cancer tumors or into the muscle (Intra-muscular) for treating infections. Injecting it into the blood through the portal vein (Intra-arterial) may cause some adverse effects in some people. Another method, which purifies the blood of bacteria and infectious disease causing mycoplasmas, is called autohemotherapy. About 50 to 100ml. is withdrawn and mixed with medical ozone and then reintroduced by intravenous drip back into the patient [6, p. 4].

Ozone is the only natural alternative to purify water. Research shows drinking ozonated water helps allergies, carcinoma, cold sores, headaches, gastritis, gum disease, mouth ulcers, thrush, ulcers, yeast infections, increases circulation, reduces infections after dental work, helps remove free radicals, helps colds, the flu and viruses, cleans wounds and minor bruises.

Drinking ozonated water also increases the oxygen level throughout and accelerates the healing process [7, p. 11].

It is essential to provide your bodies with the necessary supplements during any oxygen therapy. OXY-MEGA colon cleanser and liquid vitamin and mineral supplements like Tropical Sunrise will accelerate the efficiency of medical ozone therapy and stimulate the internal cleansing and healing process.

Hyperbaric oxygen therapy (HBO) involves putting the patient in a pressurized chamber in which he or she breathes pure oxygen for a period of 90 minutes to two hours. HBO may also be administered by using a tight-fitting mask, similar to the masks used for anesthesia. A nasal catheter may be used for small children.

Patients interested in oxygen/ozone therapies must consult with a physician before receiving treatment. Hyperbaric oxygen treatment should not be given to patients with untreated pneumothorax, a condition in which air or gas is present in the cavity surrounding the lungs. Patients with a history of pneumothorax, chest surgery, emphysema, middle ear surgery, uncontrolled high fevers, upper respiratory infections, seizures, or disorders of the red blood cells are not suitable candidates for oxygen/ozone therapy. In addition, patients should be aware that oxygen is highly flammable. If treatments are administered incorrectly or by an unskilled person, there is a risk of fire.

Much of the concern related to ozone therapy revolves around the safety of blood ozonation. It is well established that when inhaled by mammals, ozone reacts with compounds in tissues lining the lungs and triggers a cascade of pathological effects. Since ozone has the capacity to oxidize organic compounds in an atmospheric environment; it should also logically oxidize blood components and endogenous human tissues. When infused into human blood, ozone produces reactive oxygen species (ROS) or free radicals, an over-abundance of which is known to cause oxidative stress and cell damage, and is implicated in the progression of some degenerative diseases. High levels of inhaled ozone is known to be toxic, though single-dose inhalation of lower levels is not [5; 8].

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## STRESS

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**Summary:** Stress is inalienable part of human existence; the only thing we need is to learn how to distinguish the permissible degree of stress and too strong stress. Over the past years the problem of stress has become one of the most actual themes in the world's psychological science and practice.

**Key words:** health, organism, stress, psychological science,

**Аннотация:** Стресс является неотъемлемой частью человеческого существования, единственное, что нам нужно, знать, как отличить допустимую степень стресса и слишком большой стресс. За последние годы проблема стресса стала одной из самых актуальных тем в психологической науке и практике в мире.

**Ключевые слова:** здоровье, организм, стресс, психологическая наука.

**Анотация:** Стрес є невід'ємною частиною людського існування, єдине, що нам потрібно, дізнатися, як відрізнити допустиму ступінь стресу і занадто сильний стрес. За останні роки проблема стресу стала однією з найактуальніших тем у психологічній науці і практиці в світі.

**Ключові слова:** здоров'я, організм, стрес, психологічна наука.

These days stress is one of the most widespread effects. In the modern life stresses play a considerable role. They influence a man's behavior, his ability to work, health, relations with those around him and the family as well. Stress is a state of an excessively strong and prolonged psychological tension that arises up when the nervous system gets overloaded emotionally.

The most widely used definition is the following. Stress (derived from the Eng. word “stress”-tension) is a state of a psychical tension, arising up when a man is under the influence of dramatic effects. It can impact the vital functions both positively and negatively, up to their complete disorganization. Stress occurs in everyone's life because stress impulses are present in all spheres of a human life and activities, undoubtedly.

Any event, a fact or a piece of news which can cause stress, is to become a stressor. A great variety of factors can be stressors, for example, microbes and viruses, different poisons, high or low temperatures of the environment, traumas etc. Besides, it appears that any emotional factors, is factors influencing the emotional sphere of a man, can become the same stressors. It includes everything that can discompose us: a misfortune, a rude word, an undeserved offense, a sudden obstacle to our actions or aspirations.

Thus, which situation will actually become the reason of stress, one or another, depends not only on a situation itself but also on a man's personality, his experience,

expectations, self-confidence etc. What is especially vital is estimation of threat, expectation of hazard consequences involved.

So, the origin of stress and the way a person experiences it depends much more on human factors, the traits of a man's character (his ability to estimate situations, to compare the capabilities he has with those which are required etc.) than on the objective ones.

Stress situations happen at home and at work as well. From the management point of view, the organizational factors that cause stress on workplaces are of most interest. Knowledge of these factors and paying a special attention to them will help to prevent many stress situations and promote efficiency of administrative labour, and also to achieve the aims of organization with the minimum psychological and physiological losses among the personnel. In fact, stress is mainly to cause many of diseases and it does serious harm to the man's health, while health is one of the terms to achieve a success in any sphere.

In English 'stress' means pressure, tension, while 'distress' means grief, hoodoo, indisposition, need. According to Hans Selye, stress is a non-specific (i.e. the same on different influences) response of the body to any demand upon it that helps to adjust it to any new difficulty and cope with it. Every surprise that breaks the usual flow of life can cause a stress. Here Hans Selye claims that it does not matter whether a situation we meet is pleasant or unpleasant. The only thing that matters is what intensity of readjustment or adaptation is needed.

As an example a scientist gives a dramatic situation where a mother suffered the strongest nervous breakdown after she was told about her only son's death in the fight. If many years after it appears that the report is false and the son enters the room unexpectedly with no injuries, she will feel the strongest gladness.

Since stress as a phenomenon is so multifold it was required to set up the whole typology of its displays. Presently it is common to divide stress into two basic kinds: physiological and psychical. Since a man is a social creature and a psychical sphere plays a leading role in activity of his integral systems, it is a psychical stress that appears to be the most important for the process of adjustment.

Specific results of these two events, grief and gladness, are quite the opposite, but their stress action (a nonspecific demand of adaptation to a new situation) can be identical.

Presently scientists distinguish evstress (a positive stress that leads to a desirable effect and mobilizes an organism) and distress (when we feel that things are getting out of our control, stressors are accumulating constantly and we are no longer able to cope with a situation) .

Hans Selye identified three distinct phases of General Adaptation Syndrom (GAS):

1) the alarm reaction when the body is getting prepared to meet a new stressful situation;

2) the resistance stage when the body uses its own resources to overcome a stressor;

3) the exhaustion stage when the body's resources are drastically reducing [2].

During the alarm phase the level of adrenalin released into the bloodstream is increasing, the heart starts beating faster. Blood glucose level is increasing, muscles are

warming up. The body's reserve capacity is mobilizing and productivity is increasing significantly, thyroid gland is contracting.

The body is getting prepared for effective actions. It takes place when the stress is caused by a hazardous situation, such as cold, abstinence from food. In these cases stress "awakes" hidden body potential calling to "the fight" increasing strength, speed and flexibility of the movements. After the relief of stress caused by overloading of nervous system these effects return back to normal level.

The resistance phase is inherent. These forms of reaction, however, are often slowing down during the human evolution and the body cannot use the energy released during the stress effectively. It leads to exhausting the nervous system, overwhelming, exhaustion, chronic pathology. Along with the nervous system the musculoskeletal system suffers too, muscles are getting tensed and the blood circulation is increasing. The back muscles, for example, are contracting in order to prepare the body for the quick reaction. However, if there is no action and situation is continuing to be stressful, the metabolism products are increasing in the blood and a human starts feeling pain. In this example the pain appears in the loins.

Modern society often places a human into a condition where he can reject the "fight" and choose to be passive which is harmful to the health. The heart, blood vessels, stomach, thyroid gland and other organs are suffering from that. However, in this case we can state the presence of a distressful emotion rather than a stressful one. If danger, too much information or, on the contrary, absence of any information cause the negative reaction making person demobilize and disorganize, he is affected by the influence of distress.

However, if a human does not give up and instead of getting deeper into negative emotions fights actively trying to find the way to cope with challenging situations, the negative emotion is not harmful. Energetic resistance to challenges and active behavior are good from the social and medical points of view.

Finally, the third phase of stress is exhaustion. Endured arousal, mobilization and activation of all the man's resources for a short term, a high-flow of vitality require further recovery. Due to acute or repeated stress, the body is unable for a while to restore the energy required for a normal life and as a result, the chronic stress may occur causing a wide range of diseases.

First of all, you need to pay attention to the early signals - the earlier you recognize them, the easier it will be to cope with the reasons and consequences of the upcoming breakdown. No doubt, by trying to look into yourself you will be able to improve the quality of life. Also, by taking the early signals of hazards seriously you will be able to choose the right way how to keep you healthy and increase your longevity.

There are physical signals: a headache, back pain, heartburn, chest pain, feeling sick, jerky and short breathing, dizziness, allergic reactions, high blood pressure, muscles spasms. Those are the signals, which clearly demonstrate that you are overstressed.

There are such psychological signals: depression (usually starts with irritability), lack of organization (stress preoccupies and reduces to minimum the ability to focus). These signals can result in untidiness, absent-mindedness or wrong decision-making, and a defensive pose (a signal that reflects an inadequate self-demand "to be strong"). A person should not be weak and affected by stress; many people are trying not to fall

under the upcoming stress. They become despotic in very simple situations, any disagreement is taken as an intention to humiliate their dignity and undermine their authority. Dependency (some people lose their ability to perform their duties under stress). The process of degradation begins: they would prefer to stay the same - self-confident and capable - and therefore they are afraid of realizing those signals, and become even more worried that their indecisiveness will be noticed by the people around them. The feeling of guilty makes the stress even worse. Losing business qualities (difficulties in decision making and getting planned things done) [2].

#### Symptoms of stress tension

The following list of stress signs is likely to be incomplete here. Every person has to analyze his own well-being and identify the reasons of stress tension that are likely to be specific to a particular person (based on man's self-observations).

Inability to concentrate; making too many mistakes at work; memory is getting worse; sense of tiredness is arising too often; rapid speech; flight of thoughts; frequent headache, back pain and stomach ache; irritability; the work does not bring happiness as it used to; losing a sense of humor; smoking of cigarettes is rapidly increasing; alcohol addiction; loss of appetite; inability to complete work on time.

If you notice any signs of stress tension in your body you have to study the triggers carefully.

Factors that cause stress: more often you have to do things that you don't want to do but you must due to your commitments; you lack for time - you are not able to finish things on time; you are chased by somebody or something, you are always in a rush; you start feeling that people around you are bound in the vice of the internal pressure; you are always sleepy - you are not able to get enough sleep; you see too many dreams especially when exhausted during the day; you smoke too much; you consume more alcohol more than usual; you conflict at home and at work all the time; you are unsatisfied with life permanently; you get into debts without knowing how to pay those back; you have an inferiority complex; you have no one to share your problems with, and even no desire to do that; you have no feeling of being respected - neither at home nor at work. Influence of stress and nervous tension on your health and your family's life [1].

Strong health and welfare of a man are the key to the quality of his life. If any of us is under plenty of stresses, nervous tension, we undermine our health, happiness and prosperity. How do stresses and nervous tension influence our health and life?

Stress and nervous tension can affect you and your health in different ways. Do you feel tired, uneasy or does it seem to you that you are standing at the edge of the abyss feeling that you don't have any future ahead but hopelessness and apathy? Does your body hurt or do you feel a stomach ache? And if you really feel so, it means you have all signs of nervous tension and stress.

And as you feel all these symptoms, tension and stress are doing exactly that work they can do most properly - they are destroying you from inside and taking away all your health and energy.

As stress and nervous tension develop, these symptoms can outgrow in a chronic form or become more frequent. In this case they will show up much more often and more intensively and then influence the immune and the hormonal systems and can even change it. Nervous tension and stress influence the state of the whole body, and if



you have felt stress and nervous tension at least once, it will affect your health slowly and weaken it.

You become more receptive to other illnesses, viruses; you collapse and you also lose self-confidence and you are always in low spirits. And, obviously, nervous tension and stress can not pass without leaving a trace, without affecting your family that, in its turn, affects them, you and those around you.

Nervous tension and stress also influence your brain activities, physical activities, and now those tasks that have been easy for you seem difficult, and at times even impracticable. You can feel as if you are already a million years old, generally speaking, you do not exist at all, you do not have forces for anything. And if only one man in a house undergoes stress or nervous tension, all family life will go head over heels, and it can result in terrible consequences.

Here are some of the side effects of stress and nervous tension which people can show up: loss of energy, insomnia, feeling of awkwardness, loss of mood, spite, estrangement, apathy and this list cannot be stopped. There are other plenty of symptoms that a man can experience during a stress. Nervous tension and stress are a disease that can hide in your body for a long time and outgrow in a much heavier form, if stress and tension are not eradicated at once.

You not only feel bad, you also look very bad. Thus, you must fight against this evil and no ways yield to it.

Nervous tension and stress are diseases that cause serious health problems. For example, such as blood pressure, heart trouble, diabetes, stomach diseases etc. Stress can also result in gaining weight, miscarriage and cause just more and more pain.

Nothing of the mentioned above can be ignored as all these symptoms prove how stress and nervous tension influence a man's body, his health and prosperity in general. Literally, nervous tension and stress can be fatal for you. Protect yourself and your family from such a tragedy. Nervous tension and stress can not be cured in itself. It is a part of you, your personality and stress does not give you a chance for development.

People are strong in some degree, but when unexpected negative events occur, our forces seem to vanish. We can cope with a daily stress at home, at work etc. if we concentrate a little more, but what to do when the question concerns life itself, fatal disasters? Can we cope with them? Tension and stress can completely destroy our health and welfare. Stress can completely change a man, both the inner man and his appearance, if we allow it.

Fighting against daily stresses can cause illnesses while fighting against tragic situations can cause death. This is vital and it is necessary to take off nervous tension and stress in any way. It must become a daily habit for you, the same as to clean teeth, for example.

You will be never able to get rid of stress and nervous tension completely, but, surely, you can lessen this load. Precautions can lessen the negative effect of stress and nervous tension on your body, your health and prosperity.

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## **CLUSTERS: BETWEEN MOLECULES AND SOLIDS**

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**Summary:** The main conceptions of cluster physics are discussed. The techniques of generating metal clusters and sources of their production are considered. The fields of engineering and technology in which clusters and materials based on them are used have been given.

**Key words:** cluster, evaporation, inert gas condensation, magic numbers, supersonic expansion.

**Аннотация:** Обсуждаются основные понятия физики кластеров. Рассматриваются методы образования металлических кластеров и источники их генерации. Приведены отрасли техники и технологии, в которых применяются кластеры и материалы на их основе.

**Ключевые слова:** кластер, магические числа, сверхзвуковое расширение, конденсация инертного газа, испарение.

**Анотація:** Обговорюються основні поняття фізики кластерів. Розглядаються методи утворення металічних кластерів та джерела їх генерації. Наведено галузі техніки та технології, в котрих застосовуються кластери та матеріали на їх основі.

**Ключові слова:** кластер, магичні числа, надзвукове розширення, конденсація інертного газу, випаровування.

The concept of a cluster was introduced in 1964 by the American chemist Frank Albert Cotton and meant compounds in which metal atoms are formed between each other by a chemical bond. However, it was not the first discovery of compounds of such type, because the big clusters formed in solutions, also called colloids, were studied by Faraday in 18th century.

At present the number of experimentally studied clusters is more than 1000. However, there is no clear definition of the concept of clusters, but clusters are often defined as finite aggregates of atoms or molecules containing various numbers of particles. They have a wide range of properties intermediate between those of the isolated monomer and the bulk or solid-state material and thus they are a new type of material, which is located between the molecular and condensed state. So the study of clusters can provide an explanation of the transition from a single molecule to a solid and how properties of matter evolve as the cluster size changes. Some of the phenomena, for example, superconductivity, phase transitions and superfluidity, which are observed for solids and absent for single atoms, take place, when the cluster size increases [1].

There are various types of clusters depending on their different characteristics. According to their size clusters can be: microclusters which have from 3 to 10-13 atoms, small clusters have from 10-13 to about 100 atoms, large clusters which have from 100 to 1000 atoms and small particles or nanocrystals which have at least 1000 atoms. According to the structure of the clusters are: chains, rings and polyhedron, which can be body-centered cubic, face-centered cubic and hexagonal close packing, and the combination of these types. And, finally, clusters can be divided according to the different nature of the forces between the atoms: van der Waals clusters, metallic clusters, fullerenes, molecular, semiconductor, mixed clusters. So clusters can be very

different and they can exist in all forms of matter too: solid-state, liquid, gases and plasmas.

The information about cluster electronic and ionic structure is essential and we need something that can give it for us. Such a role is performed by a magic number. Understanding the magic numbers of a cluster is similar to understanding its electronic and ionic structure. Mass distribution of a cluster is never stable – it always has peaks corresponding to the increased stability of the clusters of specific sizes. And these peaks meet to the certain number of atoms or molecules in the cluster, which is called a magic number. Clusters with atoms not arbitrary corresponding to the magic numbers are often referred to as magic clusters. They are more stable and can be used as building blocks or basis to form a cluster assembled solid. The structure of stable clusters is similar to the dense packing of identical spheres related to each other. For example, the magic numbers for sodium arise from the formation of closed shells of delocalized electrons and clusters containing 2, 8, 20, 40... valence electrons become very stable [2].

The most studied and having a fairly widespread type of clusters is metal clusters. They are similar to van der Waals clusters with an additional weak covalent contribution. The study of metal cluster electronic structure started in the late 1960s and early 1970s with pioneering experiments and the theory of alkali metal clusters [3]. Then, some of the most important experiments were provided in 1984 by Knight W. D. for sodium and potassium and by I. Katakusa with co-workers for copper, silver, gold and zinc. In these experiments it was shown that metal clusters have the same magic numbers as in atomic nuclei and atoms [4].

Molecules in metal clusters contain a core surrounded by ligands (individual atoms or groups of atom molecules) of the metal atoms at small distances, allowing direct metal-metal interaction. In metal bonding electrons responsible for the cohesion of the metal are not bound to any specific atom-core, they move between the positive atomic cores and form an electron cloud. And the attractions between the positive cores and the negative charges hold the cloud metals together. The most ideal metallicity bound substances are monovalent alkali-metals while for other metal-elements the delocalization of the valence electrons is not as simple [5]. In general, metal clusters can be described by the formula  $M_m L_n$ , where  $M$  - metallic core,  $n$  - nuclear,  $L_m$  – ligands. Depending on the ratio between  $n$  and  $m$  clusters are classified into small ( $m/n < 1$ ), medium ( $m/n \sim 1$ ), large ( $m/n > 1$ ) and very big ( $m > n$ ). Clusters can be homometallic, where the core is composed of atoms of one metal and heterometallic clusters containing the atoms in the backbone of two or more metals. The metal core is stabilized by ligands and monoatomic ligands can be disposed within the metallic core.

The study of clusters is an active research field and there are several different techniques for the production of clusters. Their form and function depend on the size and type of generated clusters. The most commonly used sources for producing clusters are: supersonic expansion, inert gas condensation, laser vaporization, electrical arc discharge, ion bombardment, liquid metal ion source. Some of them are discussed in this paper.

*The technique of supersonic expansion* means that gas is cooling adiabatically during its expansion from a pressurized stagnation through a nozzle into a vacuum (Fig. 1). Pressure difference between the gas line feeding the nozzle and the chamber generates an adiabatic expansion of gas where the gas temperature decreases rapidly and

the gas enters a supercooled state and rare gas clusters are formed. Evaporated metal atoms in the warmed furnace attach to inert clusters; the metal atoms can form bonds with each other. In this process chaotic thermal energy of gas molecules is transformed to the directed kinetic energy of a supersonic stream and clusters are formed in the vicinity of the exit of the nozzle if sufficient collisions occur before the beam becomes too rarefied and cooling is stopped [6]. Obtained clusters can contain from two to hundreds of thousands atoms and have low translational temperature and high vibrational temperature, which may lead to rapid destruction of the cluster.

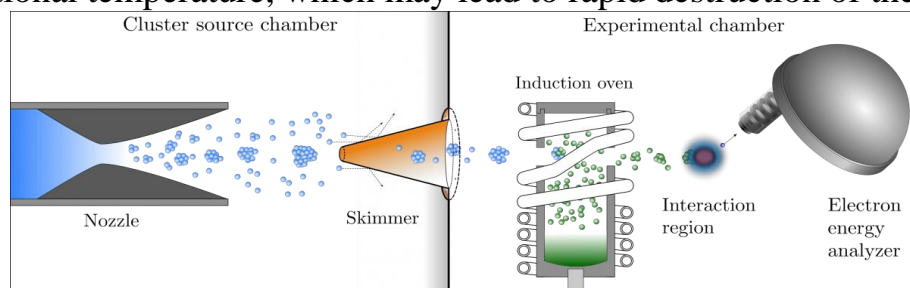


Fig. 1. The scheme of technique of supersonic expansion [5].

*The technique of inert gas condensation* is based on the process when hot metal is evaporated into a flowing stream of the cold inert gas and then the metal vapor is condensed on the cold surfaces, producing clusters with a broad distribution of sizes. As well as in the supersonic expansion method, clusters extracted in the inert gas flow out into a high vacuum, but the clusters are formed before the expansion into the high vacuum region.

*The laser vaporization source* is a pulsed source which can be used to produce ionized, neutral metallic clusters and semiconductor materials. The metal vapor is generated by intense laser radiation acting on the target. Then vapor is entrained by flow of cold gas like in the inert gas condensation source and that leads to the metal atom cooling followed by condensation and cluster growth. The geometry of the growth channel strongly influences the size of clusters produced.

Clusters are a part of our ordinary life and used for the development of technology. Due to detailed knowledge of a single molecule and the cluster structure new materials and nano-structures may be created for using of them in biology, medicine, pharmaceuticals, astrophysics, modern physics, microelectronics and others branches of science. In medicine, the clusters can be used for diagnostics and treatment of cancers without surgery, only using laser radiation. Gold-silicon clusters, introduced into a cancerous tumor – when exposed to a laser or microwave radiation can find and destroy cancer cells. Clusters are also used in photography, production of new materials, coatings and perfumes. In the energy sector the development of nanotechnology will lead to less energy-intensive and more environmentally friendly production.

Clusters are often called the fifth state of matter, after solid, liquid, gas and plasma. The unique properties of clusters fall between those of single atoms and molecules and those of bulk solids. The rapid development within the fields of cluster and nanoparticle physics clearly indicates the vital role that will be played by these systems in the future.

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# CLIMATE DYNAMICS IN TEN MOST POPULOUS CITIES OF THE USA (1973-2012)

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**Summary:** This article presents characteristics of climate variability on indicators of changes in temperature, wind speed, number of rainy and snowy days in ten largest U.S. cities by population for the period of 40 years (1973-2012).

**Keywords:** microclimate, climate change, temperature mode, atmosphere.

**Анотація:** У публікації подано характеристику коливання клімату за показниками зміни температури, швидкості вітру, кількості днів з дощем та снігом в десяти найбільших за населенням містах США в період за 40 років (1973-2012 рр.).

**Ключові слова:** мікроклімат, зміни клімату, тепловий режим атмосфери.

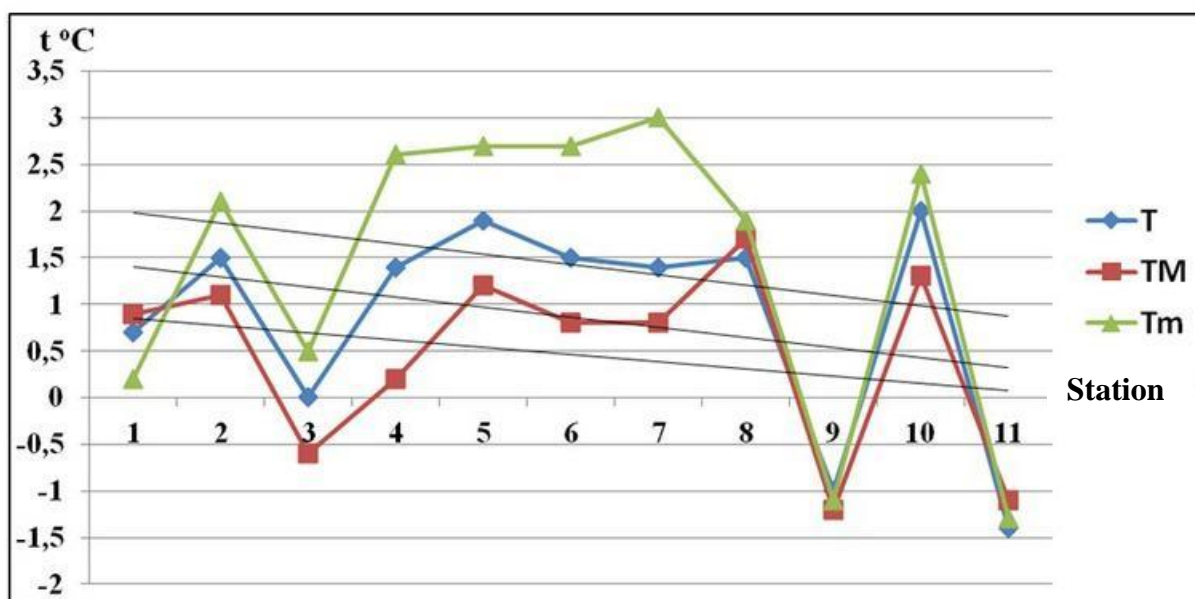
**Аннотация:** В статье рассматривается характеристика колебаний климата по показателям изменения температуры, скорости ветра, количества дней с дождем и снегом в десяти самых больших по населению городах США за период 40 лет (1973-2012).

**Ключевые слова:** микроклимат, изменения климата, тепловой режим атмосферы.

The period from 1973 to 2012 is characterized by a significant contribution of an anthropogenic component to the impact of global and regional climate. This is an intensive industrial development, population growth and transport, landscape change due to urbanization processes. The purpose of the study is to trace the dynamics of climate in U.S. cities with the population over one million people (San Jose about 960 thousands). In New York, it was decided to study the two control points - Kennedy International Airport and Newark Liberty Airport due to discrepancies between the data despite the close location of the two stations.

According to indicators of average (T), maximum (TM) and minimum (Tm) temperatures, average wind speed, the number of days with rain and snow on the 11 stations of the United States we have constructed graphs, trends and defined the change in the parameters for the specified period of time (see Fig.1).

## 1. Change in thermal conditions of the surface air



**Figure 1.** Dynamics of minimum, average and maximum temperatures on the 11 stations of the USA (1973-2012)

### Stations:

1. New York, Kennedy International Airport
2. New York, La Guardia Airport
3. Los Angeles International Airport
4. Chicago Midway Airport
5. Houston Intercontinental Airport
6. Philadelphia International Airport
7. Phoenix Sky Harbor International Airport
8. San Antonio International Airport
9. San Diego International-Lindbergh Field
10. Dallas, Fort Worth International Airport
11. San Jose International Airport

From the graph we see the trend of rising temperatures for most cities: New York City (Airport LaGuardia), Chicago, Houston, Philadelphia, Phoenix, San Antonio and Dallas.

The decrease in average, maximum and minimum temperatures is typical for San Diego: 1; 1.2; 1.1 °C and 1.4; 1.1; 1.3 °C in San Jose. In Los Angeles maximum temperature decreased only by (-0.6 °C), the average temperature remained unchanged and the minimum temperature increased, but compared to other cities only slightly (+0.5 °C).

The data from New York are somewhat different. At the station Kennedy International Airport the minimum, average and maximum temperatures increased by 0.7, 0.9 and 0.2 °C accordingly, while at the station La Guardia Airport - by 1.5, 1.1 and 2.1 °C. The first station was located near the natural reserve of Jamaica Bay Wildlife Refuge, Gulf Jamaica Bay and the national recreation area Gateway. Temperature in these areas is traditionally lower than in general background of the city due to preservation of natural environment in the completely urbanized territory. This phenomenon is called microclimate.

All three cities having a tendency to decreasing temperatures, are located in California (32 - 37° North Latitude) on the Pacific coast where the climate is affected by the cold California current [2].

However, if changes in the temperature mode are explained only by natural causes, the question arises why there is a clear trend to increase in all specified meteorological variables at 1.4, 0.8 and 3 °C for the city Phoenix which is located next to Los Angeles (about 526 km) and San Diego (about 571 km)? Although it should be noted that Phoenix is located to the east and has no outlet to the ocean, in contrast to the other three cities. Therefore, there is a factor of special climatic conditions in coastal areas.

Nevertheless, in Los Angeles with a population of 2.5 times as large as the population of San Diego and almost four times as large as the population of San Jose, an increase was observed only in one meteorological variable (average maximum temperature) 0.5 °C for the indicated period, given that all three cities have a similar geographical location and are coastal.

The other three cities that have a similar geographical location are: Dallas, San Antonio and Houston. In these areas there is a clear tendency to increase the temperature of the surface layer.

Chicago, Philadelphia and New York have also similar values of the increase in temperature, except Kennedy International Airport station in New York which is characterized relatively to the previous cities by small indicators of climate fluctuation (0.7; 0.9; 0.2 °C vs 1.5; 0.8; 2.7 °C in Philadelphia, 1.4; 0.2; 2.6 °C; in Chicago and 1.5; 1.1; 2.1 °C at La Guardia Airport station in New York) [1]. But we have already mentioned placement features of Kennedy International Airport station. The data from this station cannot give the truthful characteristic of a temperature change mode of the city because they are lower against the general urban infrastructure and industrial centers of New York because of the arrangement near natural parks and the gulf which form a special microclimate in the middle of the city. Therefore it is reasonable to use the data for La Guardia Airport station for comparison.

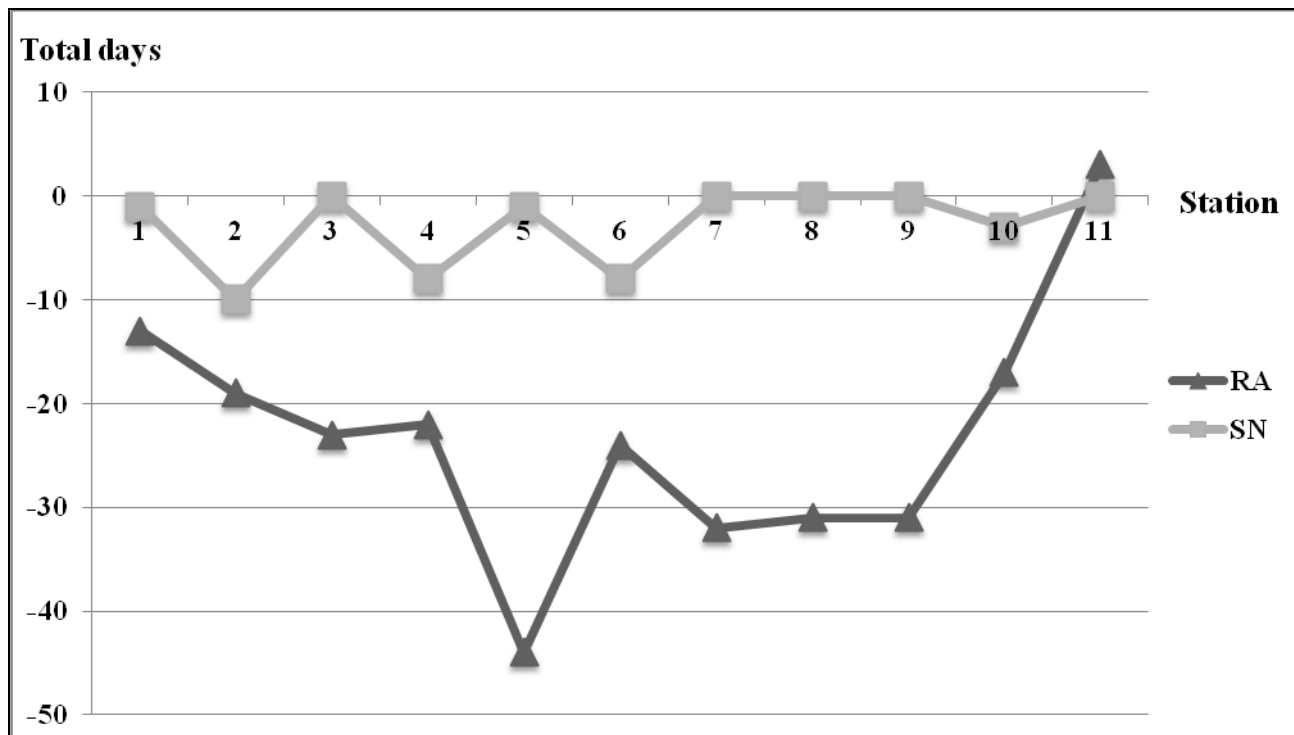
## **2. Change in the number of rainy and snowy days**

According to a IPCC report on changes in precipitation substantial spatial variability is characteristic. During XX century rainfall that fell on the land surface mainly increased in the high northern latitudes. The frequency of heavy precipitation (or part of the fallout from the heavy rains of the total precipitation) increased in most areas (likely) [3, p. 3]. The rains that fell on the land surface in the XX century increased on the territory between 30 °C and 85 °C north latitude as a whole [3].

There is speculation that the global climate change will lead to increased rainfall in some places (most of the northern hemisphere) and increased drought on other territories (arid areas, most of Africa). An increase in the amount of precipitation in the Americas, Europe and Russia could face flooding of large areas. In particular, in many climate models New York can be underwater.

The study conversely showed a decrease in the number of rainy days (RA) and snow (SN). The largest decrease in the number of days of rain is typical for the following cities: Houston (-44 days), Phoenix (-32), San Antonio and San Diego (-31 days). A significant decrease also occurred in cities: Los Angeles (-23), Chicago (-22), Philadelphia (-24). In New York the number of rainy days fell by 13 at the station Kennedy International Airport and by 19 days at the station La Guardia Airport, in Dallas by 17 days. The only city where the number of days with rain grew was San Jose (+ 3 days). However, the change is minor and normal for annual fluctuations. Therefore, we can assert that there wasn't any change in this indicator in San Jose.





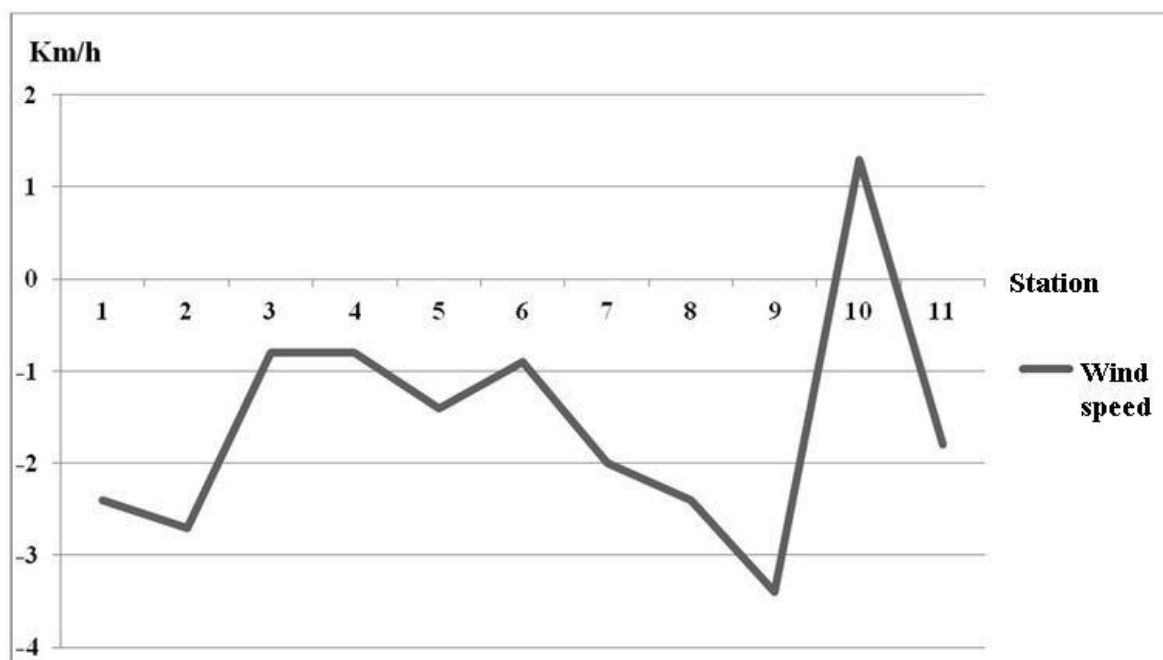
**Figure 2.** Change in the number of days of rain and snow a year at the 11 stations of the United States during 1973-2012.

### 3. Change in mean annual wind speed

As you know, the city violates the natural air circulation, wind speed in the city is slower than in the suburbs by 20-25%, but calm days are very rare. Heat island causes convection circulation in the atmospheric boundary layer directed toward the center of the city, in this case the wind speed reaches 2-3 m/s [2].

The overall movement of air masses is transformed by conditions of placement of buildings. The wind is directed along the streets and often does not coincide with the general direction of air masses over the city. In the areas of intersection of streets airflow becomes turbulent, gives rise to vortices. Wind speed increases sharply in the narrow passages.

However, despite the scientifically proven fact that an increase in wind speed in the big cities is due to human influence (placements of buildings), the study has shown a decrease of the average annual wind speed at 10 out of 11 stations. Therefore, we can assume that in the suburbs indicators of the reduced wind speed were higher. Thus, the wind speed reduction is not a local phenomenon but a result of global climatic changes.



**Figure 3.** Dynamics of average annual wind speed (km/h) at the 11 stations of the United States (1973-2012)

### CONCLUSIONS

This study suggests that it is impossible to draw conclusions about the predominant anthropogenic factor in the climate change with increasing temperatures on all territories, as there are local variations including the decrease in temperature even in the cities-millionaires, which are traditionally the most contaminated areas due to industrial, transport, etc. emissions. An important condition is characteristic features of buildings location as one of the reasons for creating a "heat island" which was supposed to give a positive growth in the temperature of the surface layer of the atmosphere primarily in the urbanized areas.

A similar trend was observed for the change in the average wind speed and the number of days with rain and snow. However, for these parameters, unlike temperature, a decrease was recorded almost on all the territory, other than Dallas - here average annual wind speed increased by 1.3 km/h, and the city of San Jose recorded slight increase in the number of days with rain (+3 days).

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## ENVIRONMENTAL PROBLEMS CONNECTED WITH THE PRODUCTION OF POLYMERS

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**Анотація:** ця стаття розглядає екологічні проблеми, пов'язані з виробництвом полімерів. Виробництво полімерів приносить багато екологічних проблем для навколишнього середовища. Це використання різних токсичних мономерів і каталізаторів, утворення стічних вод і газових викидів, утилізація яких пов'язана з високими енергетичними, сировинними витратами, а також витратами на оплату праці, і це не завжди вірно, виконується виробниками.

**Ключові слова:** полімери, виробництво полімерів, екологічні проблеми, пов'язані з виробництвом полімерів.

**Аннотация:** эта статья об экологических проблемах, связанных с производством полимеров. Производство полимеров приносит немалые экологические проблемы для окружающей природной среды. Это использование различных токсичных мономеров и катализаторов, образование сточных вод и газовых выбросов, обезвреживание которых сопряжено с большими энергетическими, сырьевыми и трудовыми затратами и не всегда добросовестно выполняется производителями.

**Ключевые слова:** полимеры, производство полимеров, экологические проблемы связанные с производством полимеров.

**Summary:** this article is about the environmental problems connected with the production of polymers. Polymer production brings a lot of environmental problems for the environment. It is the use of different toxic monomers and catalysts, formation of wastewater and gas emissions, disposal connected with high energy, raw material and labor costs and it is not always faithfully executed by producers.

**Key words:** polymers, polymer production, environmental problems associated with the production of polymers.

Polymer production is one of the fastest growing industries. Polymer producers primarily connected such an interest with the possibility of obtaining a variety of technically-based materials.

Due to the unique physical – chemical, structural and technological properties polymeric materials based on various plastics and elastomers are widely used in various fields of national economy and medicine [1].

The functioning of society is inextricably linked with the formation of waste at all stages of production and processing of polymeric materials. Hence the relevance of the problem of their disposal, as well as the harm brought by human health and the environment, is still acute. Polymeric materials are generally multicomponent system themes, as to create them using various components except polymer (ingredients). Preparation of polymeric materials that will meet the various branches of industry, agriculture, is the task of the production technology of polymeric materials.

Creation and application of polymers directly or indirectly are due to the impact on the human body, environmental production environment and habitat rights, and the environment in general. The latter is especially important after using polymers and products made of them when waste materials are disposed to the soil, and harmful substances are released during the decomposition of the polymer material, contaminate soil, waste water, thereby worsening state of the environment [2].

What consequences of the pollution can be? Primarily it will lead to reduction of the natural habitat of living creatures. Secondly, some pollution endangers neighboring

areas due to migration of contaminants, for example, through subterranean aquifers. Third, air pollution, noxious gases, including methane and carbon dioxide, the greenhouse effect, may lead to global environmental change.

According to sources of formation all polymer wastes are divided into three groups:

- technological waste production;
- waste industrial consumption;
- waste of public consumption.

Waste plastics arise during their synthesis and their processing. They are divided into unavoidable and avoidable technological wastes. Unavoidable wastes include edge trimming, sprues, debris, burrs, etc. Such waste is generated from 5 to 35 %. Fatal wastes are high quality raw materials, their properties do not differ from the original primary polymer. Processing it into products requires no special equipment and is produced in the same facility. Removable technological waste products are formed by non-observance of technological regimes during synthesis and processing, i.e. it is the technological union which can be minimized or completely eliminated. Wastes of different products are used as an additive to the feed, etc.

Waste of industrial consumption accumulates from polymeric materials not used in various industries. These wastes are the most homogeneous and therefore represent the greatest interest from the point of view of their recycling [3].

Public consumption waste accumulates in our homes, factories and power, etc., and then fall on the city dumps. These wastes constitute more than 50% of the waste of public consumption. The greatest difficulties are associated with processing and use of mixed waste. The reason for this is the incompatibility of thermoplastics that are part of household waste, which requires the stepwise selection of materials.

These wastes are specific occupying land area, polluting settlements, water, forests. When burning they emit toxic gases, landfills are favorable environment for the life of rodents and insects [3, p.22].

Thus, industrial and municipal plastic products waste represents an environmental hazard.

What approaches are used to combat pollution of nature associated with production of polymers?

1. Thermal methods of recycling and disposal of waste polymeric materials. It would seem that the most natural thing would be the oxidation of organic compounds at high temperatures or simply burning them. However, in principle, valuable substances and materials are eliminated. Combustion products in the best case are water and CO<sub>2</sub> and it means that you cannot even return the initial monomers by polymerization of which decimated polymers are received. Furthermore, as it was mentioned above, emission of large quantities of carbon dioxide into the atmosphere leads to the CO<sub>2</sub> global undesirable effects, in particular to the greenhouse effect. But what is worse, when burning harmful volatile substances are formed, they pollute the air and, respectively, water and land. Not mentioning numerous additives, including dyes and pigments, which allocate various compounds to the environment, including heavy metals used as catalysts in the synthesis of polyethylene that is very harmful to people's health [3].

2. Creating a polymeric material with an adjustable period of operation. In recent years, new ideas of synthesis "green" polymers and products of them emerged and began to be

implemented practically. We are talking about polymers and materials capable of more or less rapid decomposition under natural conditions. There are three types of biodegradable polymeric materials, namely:

- photodegradable ;
- biodegradable ;
- soluble .

They all have a sufficient stability under normal conditions and readily undergo decomposition. To impart the ability to degrade polymeric materials under the action of light, specific additives are used into the composition of the photosensitive group [4, p.55].

### 3. Compositions containing waste plastics.

Waste plastics are widely used in building. Most asphalt pavements the main binder is bitumen of different nature. They are distinguished by the lack of water resistance. All this greatly deteriorates the properties of asphalt pavements and shortens their operation. Use of polyolefin in the composition of bitumen is one of the traditional directions, allowing to modify the properties of coatings.

4. Use of waste plastics by repeated processing. Much more promising and reasonable way to reduce pollution is recycling polymers overage polymers and products of them. This problem, however, is not as simple as it may seem at first glance, if only because we are dealing with usually dirty waste which include, for example, particles of sand. This eliminates the possibility of using high-performance and high-tech equipment used in primary processing of raw polymers [4].

The present generation of people had suddenly become convinced that our environment – land, water and air cannot have an infinite immunity against chemical use, though today people have begun to understand and re- evaluate the catastrophic consequences.

The importance of addressing environmental problems led to stringent requirements on the polymers and their production technologies: polymers production should be environmentally friendly or, at least, have a minimal impact on the environment; polymers must be technically recyclable after their operation.

Polymeric materials in processing occupy the same place as secondary raw material now occupies in industry.

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**DMSO EFFECT ON HUMAN RED CELLS: THE STUDY WITH  
FLUORESCENT PROBE (2 - (2' -OH-PHENYL)-5- PHENYL -1,3-OXAZOLE)**

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**Summary:** Using a fluorescent probe (ortho-hydroxy-oxazole), we have investigated the influence of penetrating cryoprotectant dimethyl sulfoxide (DMSO) on the membrane of human erythrocyte. It has been shown that in erythrocyte membranes DMSO locates in the area of glycerol residues of phospholipids and in the region of the carbonyl groups of phospholipids. It has been found that increase in DMSO concentration increases perturbation in the packing of the membrane phospholipids and, thus, leads to an increase in hydration of the membranes.

**Key words:** biomembrane, cryoprotectant, DMSO, erythrocytes, fluorescent probe.

**Анотація:** За допомогою флуоресцентного зонда (орто-гідроксипохідне оксазолу), досліджувався вплив проникаючого кріопротектора диметилсульфоксиду (ДМСО) в мембрані еритроцитів людини. Було показано, що ДМСО локалізується в мембранах еритроцитів в області гліцеринових залишків фосфоліпідів, в області карбонільних груп фосфоліпідів. Встановлено, що збільшення концентрації ДМСО призводить до порушення упаковки фосфоліпідів і, отже, призводить до збільшення гідратації мембран.

**Ключові слова:** біомембрана, ДМСО, еритроцити, кріопротектор, флуоресцентний зонд.

**Аннотация:** С помощью флуоресцентного зонда (орто-гидроксипроизводного оксазола), исследовалось влияние проникающего криопротектора диметилсульфоксида (ДМСО) в мембране эритроцитов человека. Было показано, что ДМСО локализуется в мембранах эритроцитов в области глицериновых остатков фосфолипидов, в области карбонильных групп фосфолипидов. Установлено, что увеличение концентрации ДМСО приводит к нарушению упаковки фосфолипидов и, следовательно, приводит к увеличению гидратации мембран.

**Ключевые слова:** биомембрана, ДМСО, эритроциты, криопротектор, флуоресцентный зонд.

Dimethyl sulfoxide (DMSO) is one of the penetrating cryoprotectants which is widely used during the last 50 years in cryopreservation of biological objects of different levels of organization (Kovalenko et al, 2009). Various methods based on the usage of DMSO have been developed to cryopreserve human erythrocytes, however, all of the methods have certain disadvantages. Among the main disadvantages is the cytotoxicity of DMSO. Cryoprotectants can modify the lipid-lipid and lipid-protein interactions, modify the surface potential (Linnik et al, 2010). Despite the large number of publications on the effects of DMSO on lipid membranes (Kovalenko et al, 2009; Linnik et al, 2010; Dyubko et al., 2006), the information about the localization of DMSO in the erythrocyte membrane is absent. This resulted in conducting this study of the localization embedding DMSO in the erythrocyte membrane. One of the approaches that allows us to evaluate the degree of the DMSO influence on the condition of the lipid bilayer and to determine the topology of DMSO distribution therein is the use of fluorescent probes, which molecules are non-covalently bound to the membranes, and fast enough to respond to the microenvironment [7].

The purpose of this study was to investigate the localization of DMSO in the lipid bilayer of the erythrocyte membrane and finding possible structural changes in erythrocyte membranes under the influence of DMSO with the use of fluorescent probe [1-2]. As a fluorescent probe we used ortho-hydroxy derivative of oxazole.

## Materials and Methods

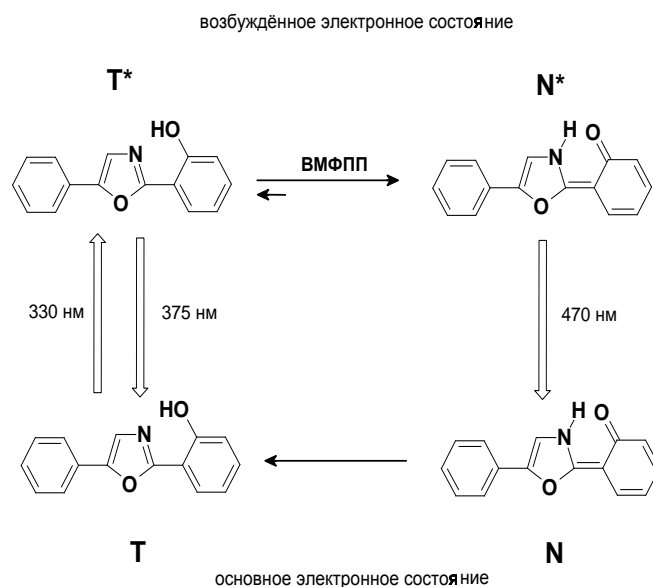
The material was analyzed in erythrocytes II Men - group Rh (+) derived from red cell taken on glyugitsirovom safeguarding Kharkiv regional blood station. Before the experiment erythrocytes were washed by centrifugation fourfold 3 min at 3000 rev / min. Buffy coat, and the supernatant was removed by aspiration. Modification of erythrocytes was performed during 40 min exposure to DMSO (0%, 2.5%, 5%, 7.5%) by mixing 1:1 (40-45% hematocrit). Control sample cells were not exposed by DMSO.

Fluorescent probe was dissolved in acetonitrile. One hour after the adding the probe to the cell suspension the measurements of the fluorescence spectra were conducted with the use of spectrofluorimeter «Hitachi 850».

## Research results

To study the effect of DMSO on the erythrocyte membrane, we used a fluorescent probe, previously successfully used for the studies of biological membranes [4-6]: 2-(2'-OH-phenyl)-5-phenyl-1,3-oxazole (probe O1O).

The choice of fluorescent probe O<sub>1</sub>O (ortho-hydroxy 2,5-diaryl-1,3-oxazole) to study the effect of DMSO on the physicochemical properties of biomembranes is due to the fact that the fluorescence characteristics of the probe depend on the physicochemical properties of the microenvironment: on hydrogen binding ability (i.e. ability to form hydrogen bonds), on the polarity and viscosity of the microenvironment [4-7]. In the excited state the ortho-hydroxy 2,5-diaryl-1,3-oxazole is characterized by the reaction of excited state intramolecular proton transfer (ESIPT) (Fig. 1): the hydroxyl group at the ortho position of the benzene ring acts as a proton donor, and nitrogen atom of oxazole cycle - as proton acceptor [5-7]. This results in the formation of the phototautomer form (T\*), fluorescent in significantly more long-wavelength region in comparison with the fluorescence maximum of the original form (N\*) [5-7].

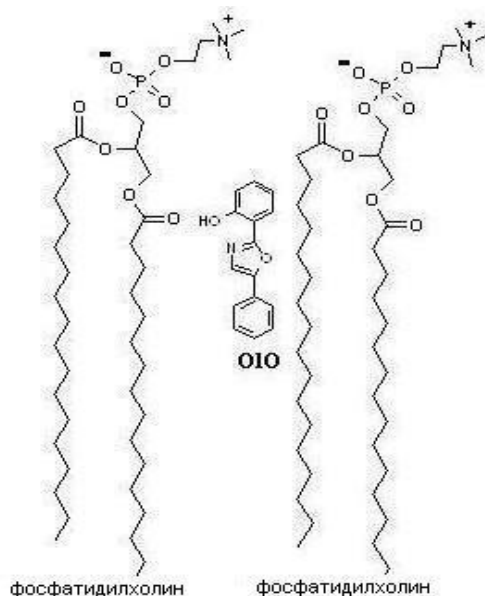


**Fig. 1.** The scheme shows excited state intramolecular proton transfer (ESIPT) in 2-(2-OH-phenyl)-5-phenyl-1,3-oxazole (probe O1O). The arrow, which points up, is the electronic excitation and the arrows, pointing down, represent light emission (fluorescence). Corresponding fluorescence maxima are presented in nanometers.

The presence of dual fluorescence allows ratiometric measurement, the usage of the ratio of fluorescence intensities of phototautomer form ( $I_{T^*}$ ) and of the original form

( $I_{N*}$ ) as a parameter to evaluate the physicochemical properties of the microenvironment. Using ratiometric fluorescent probes one can eliminate measurement errors associated with the deviation of the concentration of fluorescent probe (for example, uneven content of fluorescent probe in various membranes), and a measurement error associated with the deviation of the settings of fluorescence equipment (deviation of excitation source intensity, a change in focus, changes in the sensitivity of the photodetector, etc.) [6].

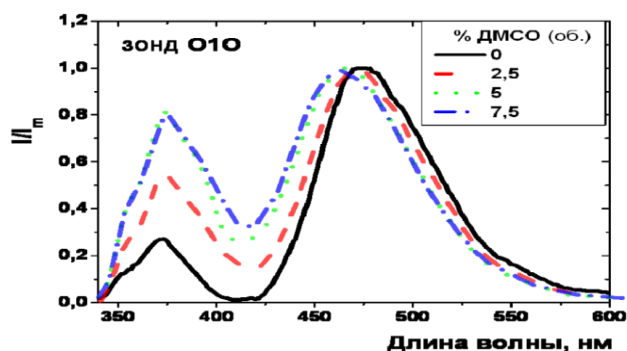
For our study lipophilic compound was selected [6]. It is expected that the selected region of localization of the probe in the membrane corresponds to its lipophilicity (Fig. 2) [6-9]. Sensor O1O is located in the region of the carbonyl groups of the phospholipids and in the region of the glycerol residues near the carbonyl groups of the phospholipids (Fig. 2).



**Fig.2.** Expected location and orientation of fluorescent probe O1O on the basis of its fluorescent properties in lipid membranes [3-5], and on the basis of its structural similarity to fluorescent probes with known localization in lipid membranes [6]. To indicate the localization of probes two molecules of phosphatidylcholine from the outer monolayer are shown.

Fluorescent Probe O1O practically do not fluoresce in an aqueous medium, but it has considerable fluorescence when embedded in the membrane (the fluorescence intensity of the probe O1O increases hundreds of times on passing from aqueous to hydrophobic environment [7]). Thus, the probe O1O can monitor the changes caused by the action of DMSO in erythrocyte membranes.





**Fig. 3.** Fluorescence spectra of probes O1O in solutions containing red blood cells: control (black line), exposed to 2.5% DMSO (red line), exposed to 5% DMSO (green line), exposed to 7.5% DMSO (blue line).

As a result of DMSO action on the erythrocytes the fluorescent probe showed a marked increase in the intensity of the shortwavelength fluorescence band of normal form ( $I_N^*$ ) and hypsochromic shift of the longwavelength fluorescence band of phototautomer ( $T^*$ ) of the probe O1O. Increasing the intensity of the shortwavelength fluorescence band of the normal form ( $I_N^*$ ) and hypsochromic shift of the longwavelength fluorescence band of phototautomer ( $T^*$ ) of the probe O1O indicates the increase in polarity and in hydrogen-bonding the ability of the microenvironment of the probe in erythrocyte membranes after the action of DMSO. Discussed increase of polarity and of hydrogen-bonding ability of O1O probe microenvironment may be caused by the accumulation of the solvent DMSO in the areas of localization of this probe and by the increase of hydration of the microenvironment of probe O1O due to the breach in packaging of erythrocyte membranes under the influence of DMSO.

Thus, it was found that the initial concentration of DMSO which causes the changes in human erythrocyte membranes is about 2.5 % vol. It is shown that the changes in erythrocyte membranes exposed to DMSO occur in areas of localization probe O1O, i.e. in the polar regions of the membrane, in area of glycerol residues phospholipids and carbonyl groups of phospholipids. It has been found that the increase in the concentration of DMSO leads to the disruption of the packing of phospholipids, and, consequently, to the increase in the hydration of the membrane.

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## **THE FORMATION OF NEW TOURIST ROUTES IN THE CRIMEA (ON THE EXAMPLE OF GASTRONOMIC TOURISM)**

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**Summary:** This paper is devoted to the development of tourism in the Crimea on the example of gastronomic routes. It analyzes the plan of the route, which goes through the main gastronomic centers of the Crimea peninsula.

**Key words:** tourism, gastronomic routes, national cuisine, tourism in Crimea.

**Анотація:** Стаття присвячена розгляду розвитку туризму в Криму на прикладі створення гастрономічних маршрутів. Вона аналізує план маршруту, який пролягає через основні гастрономічні центри півострова Крим.

**Ключові слова:** гастрономічні маршрути, національна кухня, туризм в Криму,

**Аннотация:** Статья посвящена рассмотрению развития туризма в Крыму на примере создания гастрономических маршрутов. Она анализирует план маршрута, который пролегает через основные гастрономические центры полуострова Крым.

**Ключевые слова:** гастрономические маршруты, национальная кухня, туризм в Крыму.

Modern trends in the world economy characterized by growth in the share of non-production sector and the transition economies of the developed countries to the post-industrial type of development. In these processes, a certain role plays the tourism industry, which is part of the non-production sphere.

At this stage, there is a dynamic development of the tourism industry, which accounts for 7% of the investment and its share is more than 30% of world trade in the world. [3] According to the World Tourism Organization, the number of international tourist arrivals each year, is growing by 5% [2]. So the steady growth of interest in the world's population to tourist travel demonstrates the significant development prospects of the industry.

Ukraine can not remain aside of these processes, which, as shown by holding the "Euro-2012" is attractive to foreign tourists. Many citizens of our country have an interest in new internal tourist routes. So, the domestic tourism industry has to offer to consumers of tourism services interesting place to rest and learning, and new types of tourism destinations.

In recent years, one of perspective directions of the tourism industry becomes a gastronomic tourism. This is one of the most dynamically developing segments like tourism and restaurant business in the world. However, in Ukraine only is its formation. So the question of gastronomic tourism in our country is quite relevant.

There is still no single concept on this type of tourism in the Ukrainian science. The scientific literature uses the following terminology: gastronomic tourism, culinary tourism, gourmet tours.

The term "culinary tourism" emerged in the 90 years of the twentieth century. It was suggested by Lucia Longo, Professor Ohayo University (USA) [1]. Since then started active research this subject in the world. In Ukraine, the development of gastronomic tourism is most relevant in the last 5 years thanks to the work and research of such scholars as T. Bozhuk, A. Busygina, I. Komaritsky, T. Kuklina, L.Prokopchuk, V. Fedorchenko and others. However, issues relating to the organization of gastronomic tours explored insufficiently at regional level.

The purpose of the research study about the formation of new tourist routes in Crimea on the example of gastronomic tourism.

Analysis of various opinion polls showed that Ukraine associated in neighboring states with the holiday destination, fruits, with a unique culture and delicious cuisine. Thus, we can assume Ukrainian national cuisine as one of the segments of the tourism industry in the country and actively promote gastronomic tourism, which is acquaintance and tasting national cooking tradition of the region. From the organizational point of view it provides familiarity with technology features cooking local food, history and traditions of consumption and the possible participation of tourists in the preparation of national dishes, visiting festivals and cooking competitions. Gastronomic tourism can be considered as an auxiliary tool in understanding the cultural heritage of countries and regions, as the national cuisine is one of the elements of displaying life style, philosophy, traditions, ethnicities. One of the attractive tourists in respect of regions of Ukraine are the Crimea (ARC). She attends most of the entry of foreign and Ukrainian tourists. Therefore, we will focus on issues of gastronomic tourism in the Crimea.

The Crimean peninsula is not only the most attractive for the development of different types of tourism over the country, but also - a unique place combining many distinct cultures. Ukrainian cuisine perfectly complements in the Crimea homemade Crimean cuisine and catering facilities that offer dishes of various cultures. The cuisine of indigenous population of the Crimea - Crimean Tatars had features Mediterranean. After the deportation of the Crimean Tatars to their Motherland, their national dishes are also absorbed the traditions of Uzbek cuisine, which has a high calorie content, the availability of special spices and additives specific local green and cotton oil.

Armenians also have a long history residence in the territory of the Crimea because their national traditions have brought certain features of the general principles of cooking in the Crimea in Armenian catering.

Karaites - another small ethnic group of Crimea, which has kept its own traditions of cooking, which is a great number of meat dishes. The Greeks, who established city-states in the Crimea in ancient times, were also reflected in the national dishes of the Crimea.

It should also be noted that a significant share of the Crimean population are Russians, so local catering meet dishes of Russian cuisine, familiar to many tourists from CIS countries - shchi, solyanka, okroshka, syrnyky, pancakes, chicken coop and others.

Thus, the cultural traditions of the Crimea combine the features of national cuisines of many nations. However, each of the above ethnic groups together with their cuisine traditions has its residence in the center of the ARC. Therefore, it is necessary to offer tourists a gastronomic route with the purpose of knowing the cultural heritage of the ARC that will a certain stage their acquaintance with the local traditions of the region.

The gastronomic route, in our opinion, we should start from the city of Yevpatoria, situated in the west of the peninsula. This ancient city was recognized the center of gastronomic tourism in the Crimea on the Second International Exhibition of tourist routes. That Yevpatoria will generally introduce to tourists the national cuisine of the Crimea. In the program route it's offered to include visiting of catering such as restaurant of Ukrainian cuisine "Budmo", restaurant of jewish cuisine "Yoskyn kit", karaite cafe "Karaman", restaurant of tatar cuisine "Dzheval" and so on.

The second point of our route stops can be in village Pozharsky of Simferopol district. In the cultural and ethnographic center "Jawor" where you can see the Ukrainian national traditions and try typical Ukrainian dishes.

Familiarity with Greek cuisine can occur in the Greek cultural and ethnographic center "Karachel", which is located in the village Chornopillya of Bilohirsk district. Here, in a private Greek mansion, visitors can immerse themselves in eating of Greek national cuisine and acquainted with the customs and traditions of the ethnic group.

Then we offer to visit the village Morskoe near Sudak. "Kapsihor - Ai Serez", the Tatar center, is situated there. The purpose of this visit is to introduce ethnic and cultural center of the traditions and life of the Crimean Tatars. After a walking through the old village, visitors are usually offered a variety of dishes of tatar cuisine and interesting folk program. Visiting this center should include as a necessary stage of the gastronomic route, as the Crimean Tatars are the ethnic group that is formed in the Crimea because familiarity with their culture and cuisine can help visitors to feel the original atmosphere of the Crimean peninsula.

To conclude this region of Ukraine has great prospects for the development of new tourism destinations. However, cultural and historical features of the region the creation of new tourist should comprise underutilized. Perspective direction for the development of new attractive tourist routes is gastronomic tours which allow not only to get acquainted with features of the local national cuisines, but also to know the cultural and historical traditions of the region.

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# PHASE SEPARATION IN OXYGEN DEFICIENT $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$ SINGLE CRYSTALS: EFFECT OF HIGH PRESSURE AND TWIN BOUNDARIES

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**Summary:** We investigate the influence of high hydrostatic pressure on the electrical resistance in the ab-plane in  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single crystals with oxygen deficiency. It is determined that the high-pressure induced redistribution of the labile oxygen enhances the phase separation, which is accompanied by structural relaxation and ascending diffusion within the volume of the sample. It is determined that the formation of the low-temperature phase can occur at the twin boundaries.

**Key words:**  $\text{HoBaCuO}$  single crystals, hydrostatic pressure, labile oxygen, metal-to-dielectric transition, pseudo-gap anomaly, twin boundaries.

**Анотація:** У роботі досліджено вплив високого гідростатичного тиску на електроопір в аб-площині монокристалів  $\text{Ho}_1\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}$  з нестачею кисню. Встановлено, що індукований високим тиском перерозподіл лабільного кисню приводить до посилення фазового розшарування, що супроводжується процесами структурної релаксації і висхідної дифузії в об'ємі експериментального зразка. Висловлено припущення про те, що зародження низькотемпературної фази може відбуватися на межах двійників.

**Ключові слова:** гідростатичний тиск, лабільний кисень, межі двійникування, монокристали  $\text{HoBaCuO}$ , псевдощільна аномалія, перехід метал-діелектрик.

**Аннотация:** В работе исследовано влияние высокого гидростатического давления на электросопротивление в аб-плоскости монокристаллов  $\text{Ho}_1\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}$  с недостатком кислорода. Установлено, что индуцируемое высоким давлением перераспределение лабильного кислорода приводит к усилению фазового расслоения, которое сопровождается процессами структурной релаксации и восходящей диффузии в объеме экспериментального образца. Высказано предположение о том, что зарождение низкотемпературной фазы может происходить на границах двойников.

**Ключевые слова:** гидростатическое давление, границы двойникования, лабильный кислород, монокристаллы  $\text{HoBaCuO}$ , псевдощелевая аномалия, переход металл-диэлектрик.

An important characteristic of high temperature superconducting compounds (HTSC) of the system  $\text{ReBa}_2\text{Cu}_3\text{O}_{7-\delta}$  ( $\text{Re} = \text{Y}$  or rare earth ion) is the ability to realize a non-equilibrium state under a specific oxygen non-stoichiometry [1,2]. This can be initiated by external means, such as temperature [1] or high pressure [2]. A characteristic peculiarity of the oxygen deficit samples (with  $\delta \geq 0.3$ ) is the broadening of the resistivity transfers under pressure [2]. The reason of such behavior has not been completely determined. In spite of a number of studies on the relaxation processes in the 1-2-3 system under high pressure, many aspects such as the charge transfer and the nature of the redistribution of the vacancy subsystem are still undetermined [3]. In the case of single crystals the existence of twin boundaries (TB) influences the transport properties in the normal state. This aspect is not yet sufficiently studied, due to experimental difficulties in determining the contribution of these defects. In the present study we investigate the effect of hydrostatic pressure up to 5 kbar on the electro-transport characteristics and the structural relaxation in the ab-plane of oxygen deficient  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single crystals. Two different kinds of transport current geometry were

investigated: (a) parallel ( $I \parallel TB$ ) when the impact of the TB in the carriers scattering processes is minimized and (b) at an angle of  $\alpha = 45^\circ$  between  $I$  and TB.

#### Experimental techniques

$\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single crystals were grown from the flux in a gold crucible using similar technology as for the growth of  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single [2]. The experimental geometry was selected so that the transport current vector in the  $ab$ -plane, was either parallel,  $I \parallel TB$ , (sample S1), or at an angle of  $\alpha = 45^\circ$  (sample S2) to the twin boundaries, as it is shown in the insets of Fig.1. To reduce the oxygen concentration, the crystals were annealed in an oxygen flow at higher temperature range for three to five days. The resistance in the  $a$ - $b$  plane under hydrostatic pressure was measured using the standard method for two opposite directions of a direct current up to 10 mA as it was described in detail previously [2].

#### Results and discussion

Fig. 1 (a) and (b) shows the temperature dependence of the resistivity in the  $ab$  plane,  $\rho_{ab}(T)$ , for the S1 and S2 single crystals measured after the high hydrostatic pressure application-removal procedure. Part of the curves in this and the following

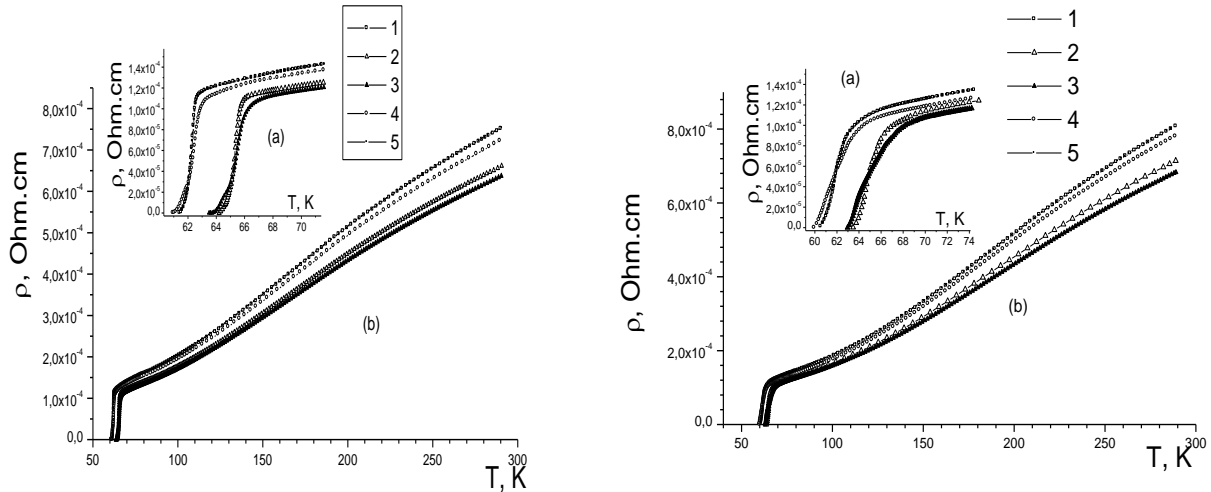


Fig. 1 Temperature dependence of the resistivity  $\rho_{ab}(T)$  for samples at different pressures. The insets of Fig. 1 show the geometry of the experiment and the resistivity transitions to the superconducting phase figures is not coerced for clarity. The insets (a) of Fig. 1 show the resistivity transitions to the superconducting state in  $\rho_{ab}(T)$  and  $d\rho_{ab}(T)/dT$  coordinates, respectively.

Curve 1 was obtained prior the application of pressure; curve 2 – was obtained immediately after the application of pressure 4.8 kbar; curve 3 – was measured after keeping the sample in room temperature under pressure 4.8 kbar within a week; curve 4 – was obtained immediately after the removal of pressure and curve 5 – was measured immediately after keeping the sample for three days under zero pressure. The insets (b) of Fig. 1 show the geometry of the experiment and the resistivity transitions to the superconducting phase.

The application of pressure, leads to a decrease of resistance and to an increase of  $T_c$ , with a rate  $dT_c/dP \approx 0.7 \text{ K.kbar}^{-1}$ . This value is in consistent with previous studies

[2,3], concerning oxygen deficient  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  samples. Interestingly, the electrical resistivity is decreasing not only as a consequence of the high pressure application, but also in the isobar process of keeping the sample at room temperature just after the application of high pressure. From Fig.2 (transition to the superconducting phase in  $\rho_{ab}/dT$ -T coordinates), it is determined that the retention of the sample at room temperature in the application-removal of high pressure process has a significant influence on the width and shape of the superconducting transition. A characteristic feature of the influence of retaining the samples at room temperature for 3-5 days, is the significant peak displacement, up to  $\Delta T_c \approx 0.5\text{-}1.5\text{K}$ , in the  $\rho_{ab}(T)/dT$  dependence (according to [2] the temperature corresponding to this maximum is  $T_c$ ), upwards and downwards in temperature, which indicates the change of the transport current flow paths. This in turn can occur in the case of strengthening the phase separation of the non-stoichiometric oxygen samples. The latter requires oxygen transport between phases with different  $T_c$ .

Comparing curves 2 and 3 shows, that after holding the sample under pressure for a week, the absolute value  $\rho_{ab}(T)/dT$  is reduced by about 1.5 times and the transfer itself significantly spreads. The dependence measured directly after the pressure removal (curve 4) there is change only in the absolute value of  $T_c$ , while the transfer width and value  $\rho_{ab}(T)/dT$  both remain practically unaltered. The comparison between curves 4 and 5, demonstrates that after the sample experienced atmospheric pressure for 3 days at room temperature, the width and the transfer regained their initial values. Therefore, when the pressure increases a part of the oxygen of the lower  $T_c$  phase, migrates to a higher critical temperature phase and when the pressure is reduced, the reverse process takes place.

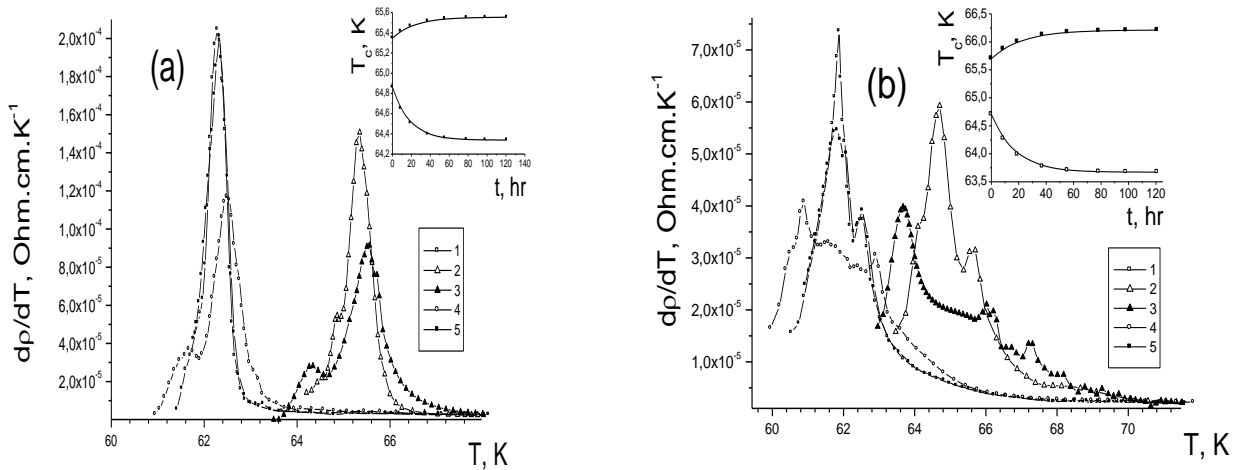


Fig. 2. The temperature dependence  $\rho_{ab}(T)/dT$  in the interval of the transition to the superconducting phase. The numbering of the curves corresponds to the numbers in Fig. 1. The insets (a) and (b) in Fig.2 show the temporary dependence of the isobar relaxation  $T_c(t)$  of the critical temperature for high  $T_c$  and low  $T_c$  phases (dark and light symbols respectively)

This effect can be possible in the case of the realisation of an ascending diffusion process [2], in which there is an inhomogeneous field of mechanical stresses (eg. due to external compression). The reversibility of this effect is also an important feature. For

example, when removing the external stress the reverse ordering of the concentration of the point defects in the sample will occur.

The insets to Fig. 2 (a) and (b) show the temporary dependence of the isobar relaxation  $T_c(t)$  of the critical temperature for high  $T_c$  and low  $T_c$  phases (dark and light symbols respectively) for both samples, obtained during the step by step annealing at room temperature after the application of pressure of 4.8 kbar. The solid lines are presented the results by the expression proposed by Jorgensen et al. [4]:

$$T_c(t) = T_c(\infty) + [T_c(0) - T_c(\infty)] \exp[-(t/\tau)^{1/2}], \quad (1)$$

where  $T_c(\infty)$  and  $T_c(0)$  are the equilibrium and the initial value of the critical temperature, respectively, and  $\tau$  is a characteristic time for the relaxation process. Calculations with Eq. (1) show that the equilibrium value  $T_c(\infty)$  in the step by step annealing is accelerated for the low temperature phases in comparison to the high temperature phases:  $\tau(T_{c1})/\tau(T_{c2}) \approx 1.32$ . Apparently, this phenomenon is due to a difference of the diffusion path during the high-pressure-induced redistribution of labile components. It appears that, for the same reason, the reverse process (alignment of the labile oxygen's concentrations) is occurring, after the pressure removal. In the second case, the oxygen atoms have to overcome smaller distances to leave the high-temperature (oxygen richer) phase than in the first case when the atoms of the labile oxygen have to overcome greater distances in order to find a vacancy in the low-temperature (oxygen depleted) phase.

Using the values of  $\tau$ , obtained by Eq. (1) using our experimental data, we can determine the activation energy of the relaxation process in our samples [5] using the Arrhenius law:

$$\tau = \tau_0 \exp\left(\frac{E_A}{k_B T}\right), \quad (2)$$

where  $\tau_0 = 1.4 \cdot 10^{-12}$  s is the characteristic period [1], which, according to [5], is independent the pressure. The activation energy value obtained from our data  $E_A \approx 0.94$  eV is slightly lower than the typical values for the  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  compounds with reduced oxygen concentration [2]. It should also be noted that all the characteristic shape changes in the temperature dependence and absolute values of the resistivity parameters that were observed in the isobaric annealing process at room temperatures, in  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  were more pronounced compared to  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$ . In  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  the Ho ion (which has larger ionic radius than Y) plays an important role to the structural order of the system affecting the oxygen ions interactions in the CuO planes [6].

In previous works [7], the value of critical temperature in  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  was correlated with the number of holes in the  $\text{CuO}_2$  layers via:

$$T_c = T_c^{\max} \left[1 - 82.6(n - n_{\text{opt}})^2\right], \quad (3)$$

where  $T_c^{\max}$  is the maximum critical temperature and  $n_{\text{opt}} = 0.25$  is the optimal number of holes in the surface (layer) for this compound. According to Eq. 3 when we increase the pressure at room temperature, the number of carriers for the low-temperature phase is reduced by about 2-3%, whereas at the same time in the high-temperature phase the reverse process is taking place as the number of holes increases. This is consistent with the concept that the application of high hydrostatic pressure leads to a diffusion



redistribution of the labile components from the phase of lower critical temperature to the high-temperature superconducting phase. In our case, one of the possible reasons of the phase separation could be the origination of the low  $T_c$  in the TB boundaries. This assumption can be justified by the different forms of superconducting transitions obtained with the different experimental geometries (here  $I \parallel TB$  and an angle between  $I$  and the TB of  $45^\circ$ ). Figure 2 shows that for  $I \parallel TB$  the height of the peak of the  $\rho_{ab}(T)/dT$  dependency of the low-temperature phase is almost 3 times lower than the height of the peak corresponding to the high-temperature phase. Together with this, the more pronounced maximum, corresponding to high-temperature phase. In the second experiment geometry (angle between  $I$  and the TB of  $45^\circ$ ) we observed an inverse  $\rho_{ab}(T)/dT$  dependence with a more pronounced maximum, corresponding to low-temperature phase. Since in the first case, the TB is parallel to the transport current there is a high probability of percolation paths mediating the current flow in the high-temperature phase. When the TB is oriented at an angle of  $45^\circ$  relative to the transport current vector (measurement of electrical resistance of the single crystal K2), the percolation paths of current flow in the high-temperature superconducting phase are missing. Therefore, the intensity of current carriers scattering should be minimal when the experiment geometry is  $I \parallel TB$ , which is reflected in the transformation of the shape in the corresponding  $\rho_{ab}(T)/dT$  dependence. The latter preposition is indirectly confirmed by the difference of the absolute value of resistivity at room temperature, which is less than 7% in the case of the experiment geometry  $I \parallel TB$ , in comparison with the case of the experiment geometry when the angle between  $I$  and TB is  $45^\circ$ .

To conclude, twin boundaries are effective scattering centres of normal carriers in  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  compounds. Reducing the oxygen stoichiometry of  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single crystals, results to an uneven distribution of oxygen in the volume of the crystal and the formation of phases with different critical temperatures. Herewith, the substitution of yttrium with holmium significantly affects the charge distribution and the effective interaction in the CuO-planes, thereby stimulating the disordering in the oxygen subsystem. Induced by high pressure the redistribution of labile oxygen is enhances the phase separation in the volume of oxygen deficient  $\text{HoBa}_2\text{Cu}_3\text{O}_{7-\delta}$  single crystals. Additionally, it stimulates ascending diffusion processes between the superconducting phases with different oxygen stoichiometry.

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УДК 620.97

## GEOTHERMAL HEATING

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**Summary:** This article deals with one of the most promising and renewable sources of heating and cooling based on low-grade heat transfer fluids, being an effective substitute to common schemes of receipt and transmission of thermal energy for heating.

**Key words:** geothermal heating and air conditioning, heat pump, geothermal outline.

**Анотація:** У даній статті розглядається один з перспективних та відновлюваних джерел опалення та кондиціонування на основі низькопотенційних теплоносіїв, що є ефективною заміною поширеним схемами отримання та передачі теплової енергії на потреби опалення.

**Ключові слова:** геотермальні системи опалення та кондиціонування, тепловий насос, геотермальний контур.

**Аннотация:** В данной статье рассматривается один из перспективных и возобновляемых источников отопления и кондиционирования на основе низкопотенциальных теплоносителей, являющийся эффективной заменой распространенным схемам получения и передачи тепловой энергии на нужды отопления.

**Ключевые слова:** геотермальные системы отопления и кондиционирования, тепловой насос, геотермальний контур.

Currently for heating traditional sources of energy: gas, coal, electricity, peat, wood, diesel fuel are used. However, prices for these fuels are extremely unstable. Parallel to this, every year environmental situation in the world gets worse. For example, about 40% of carbon dioxide (CO<sub>2</sub>) comes into atmosphere from burning fuel to generate heat. These figures are comparable to the loss inflicted to environment by car exhaust.

Today the most profitable source of energy, of course, is natural gas. Nevertheless, gas heating has many negative sides. If the house is not connected to the gas pipeline, its installation is very expensive and requires a lot of work and in some situations is simply impossible. Gas equipment is insecure, therefore, requires the installation of the mass of the special permits, strict adherence to safety standards and ongoing maintenance. Moreover, discovered gas deposits remained at 40...60 years of intensive use, what means that the rates for this kind of fuel will continue to grow.

In connection with this problem, modern innovation has become urgent, i.e. geothermal heating and air conditioning. The use of geothermal energy is the way to reduce the harmful effects on the environment, reducing the consumption of coal, gas and oil, because in the work of geothermal systems exclusively non-conventional energy sources are used. About 80% of all thermal energy comes from geothermal

system - environmental energy: solar energy accumulated during the warmer months and then “pumped” from the soil, bedrock or lake [1]. Today this is the most efficient and economical alternative to traditional systems.

In the core of the geothermal heat pump is the physical process of heat transfer from the environment to the refrigerant, similar to what happens in the domestic refrigerator or a standard air conditioner of reversible type (can be heated and cooled). But, unlike the air-conditioning installations, heat pump has extended functions and adapted to work in all weather conditions and, in particular, in sub-zero temperatures. Cars do not fully reflect the principle of operation of geothermal heat pump. Circulating in the vertical heat exchangers (soil probes), antifreeze falls under the ground, where it is heated, taking away the heat from the soil. After which it goes up and enters the evaporator. In the evaporator contains refrigerant (freon), which absorbs the heat from the cooling water, heated up to +6...+8 degrees and turning to steam. After that, refrigerated antifreeze again acts on the heat exchangers into the ground, where again accumulates heat energy and hot freon in a vaporous condition is sent to the compressor. In the compressor steam is compressed, so that it falls in the form of hot condensate (+65 C), highlighting the large amount of heat. In the heat exchanger of the condenser heat from refrigerant is transmitted to the working fluid and the refrigerant passing through the relief valve quickly cooled to -15 and returns back to the evaporator, closing the cycle. Next, the heated fluid comes from the condenser into the thermal battery which is used as storage for thermal energy and stabilizing the heat pump. Then working fluid goes from battery directly into the heating network. Coefficient of heat output reaches 5,01, i.e. the essence of geothermal heat pump is that for each 1 kW consumed power, he is providing up to 5 kW of heat energy, while the complementary kilowatts of «taken» out of the ground, the body of water or air.

Such a system can regenerate itself, not damaging energy and environmental balance of the planet, and this allows to judge about geothermal systems as absolutely safe for the environment. It does not pollute the atmosphere with harmful emissions and creates the optimal conditions of comfort (heating/air-conditioning) [2].

Because of the heat pump there is no combustion of any fuel, geothermal systems are safe, not subject to the risk of fire or explosion and does not form harmful oxides type of CO, CO<sub>2</sub>, NO<sub>x</sub>, SO<sub>2</sub>, PbO<sub>2</sub> in the process of work. The heat pump installation does not require special equipment like chimneys and hoods, takes up a little space, is silent and does not emit unpleasant smells and harmful emissions. Unlike cumbersome liquid- and solid-fuel heating systems, geothermal equipment does not destroy the infrastructure of the city, and the integrity of the interior and facades of buildings, its operation is completely invisible to the inhabitants of the house or business enterprises. Also consumers must not think about the purchase, delivery and storage of fuel, thermal energy of the earth virtually inexhaustible. Management of the heat pump geothermal systems of some manufacturers is via the Internet. In addition, by installing a heat pump, it is possible to heat the building in winter and cool it in the summer, using the same equipment. In the summer period geothermal heating can cool the premises, almost without consuming electricity: the heat pump at this time is switched off and the heat from the house passed in geothermal circuit (passive air-conditioning).

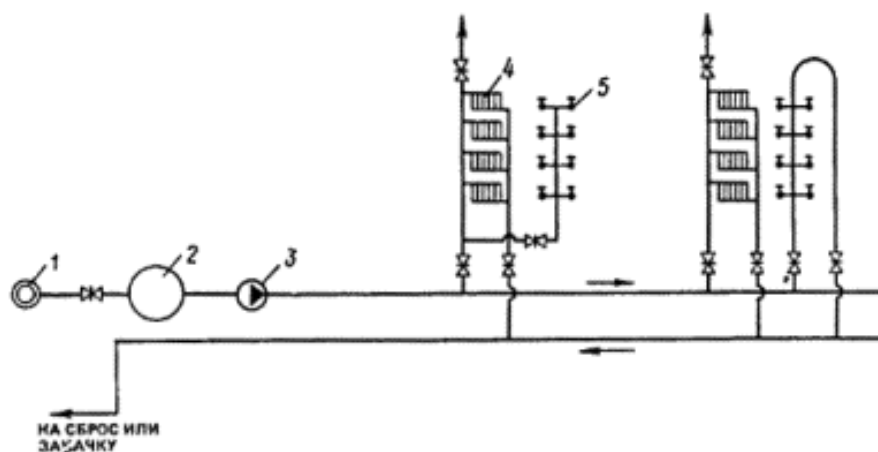
The heat pump can also be used for heating or cooling pools, ground heating and air greenhouses in the early spring, heating tracks of homestead gardens and Parking (melting system), cooling summer ice rink and other.

Besides heat pump, geothermal heating system includes placed in the soil pipe called geothermal path. There are three methods through which the heat pump can be installed with minimum space. First – it is with the use of underground probes. Path filled with anti-freeze, is lowered into a borehole to a depth of 30 to 100 meters. Naturally, this leads to a higher cost of such a geothermal system. The second method is based on the use of heat groundwater. In this case, the ground water pump is being pumped from the well and is run through a heat exchanger and then return in another well, located downstream groundwater. The third way is the lining of horizontal probes on the bottom, below the level of the winter glaciation. Transformation ratio of such water systems is higher than that of systems with a closed primary circuit [3].

According to departmental building norms VSN 56-87 of 1989 there are the following concepts of geothermal heat supply systems:

1. Opened heat supply systems, providing only hot water;
2. Closed systems of geothermal heat supply;
3. Drainage-free geothermal heat supply system;
4. Geothermal heat supply and cooling system with heat pumps;
5. Opened geothermal system with a combination of water and air heating;
6. Complex geothermal heating system.

The approximate calculation of the open two-pipe geothermal heat supply system with the accession of hot water supply to the supply pipe, i.e. with parallel feeding of geothermal heat carrier for heating and hot water (see Fig.1) for the Belgorod region was held.



*Figure 1. Outdoor geothermal two-pipe heat supply system:*

*1 - geothermal wells; 2 - tank battery; 3 - network pump; 4 - heaters; 5 - hydrant*

When the duration of the heating season is 181 days and rated temperature of external air for heating is  $-11\text{ }^{\circ}\text{C}$ , coefficient of utilization of the wells for heating and hot water respectively  $\tau_{w.h.}=0.193$  and  $\tau_{w.h.w.}=0.902$ , and the average value of the coefficient of use of the well  $\tau_w=0,31$  [4, p.70].

In the scheme of geothermal loop small-sized portable drilling rigs can be used, which do not violate the landscape. If necessary, the trenchless technology is used too.

Today's modern methods of implementation of all options of geothermal heating, taking into account climatic zones and features of the location of heated objects, are used in commercially efficient projects, which prove their prevalence on different geographical latitudes of the European States. Confirmation of this is the fact that in some European countries the implementation of such methods of heating is about thirty years of age, and the systems of heating suffered three generations of modernization, reaching more efficiency per unit of foreign consumed energy. To date, these systems as industrial technology has long been out of the discharge experiment on the territory of Russia, thereby proving its efficiency and commercial relevance.

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УДК 616-006

## **INNOVATIONS IN CANCER TREATMENT**

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**Summary:** New approaches to cancer treatment and innovational methods and devices are considered in the article. The medical statistics are presented.

**Key words:** cancer, gene, inhibit, malignant tumors, nanobots, nanoparticles, radiofrequency techniques, receptor proteins, RNA, thermoablation.

**Анотація:** У статті розглядаються нові підходи до лікування раку та інноваційні методи та пристрої. Показані медичні статистичні дані.

**Ключові слова:** ген, злоякісні пухлини, інгібувати, нанороботи, наночастки, радіочастотні методи, рак, рецепторні протеїни, РНК, термовидалення.

**Аннотация:** В статье рассматриваются новые подходы к лечению рака и инновационные методы и аппараты. Представлены медицинские статистические данные.

**Ключевые слова:** ген, злокачественные опухоли, ингибировать, нанороботы, наночастицы, рак, радиочастотные методы, рецепторные протеины, РНК, термоудаление.

According to medical statistics in most industrial counties cancer takes the second place on the death rate, after cardiovascular diseases. Cancer affects everyone: young or old, rich or poor. Over a tenth of global deaths in the year of 2000 were caused by malignant tumors. Even if you never get cancer, no doubt you know someone who has or will. A couple of years ago the World Health Organization estimated that by 2020 cancer rates will have doubled affecting 15 million people worldwide. Physicians constantly improve old and try to find new methods for cancer treatment. Nevertheless we cannot predict the complete victory from this disease.

Cancer incidence and mortality statistics reported by the American Cancer Society and other resources were used to create the list. To qualify as a common cancer for the list, the estimated annual incidence for 2013 had to be 40,000 cases or more.

The most common type of cancer is prostate cancer, with more than 238,000 new cases expected in the USA in 2013-2014. Then breast cancer and lung cancer follow [6].

Because colon and rectal cancers are often referred to as ‘colorectal cancers’, these two cancer types are combined. For 2013, the estimated number of new cases of colon cancer and rectal cancer are 102,480 and 40,340, respectively, adding to a total of 142,820 new cases of colorectal cancer.

Kidney cancers can be divided into two major groups, renal parenchyma cancers and renal pelvis cancers. Approximately 92 percent of kidney cancers develop in the renal parenchyma, and nearly all of these cancers are renal cell cancers. The estimated number of new cases for 2013 is 59,938.

Statistics for the estimated numbers of new cases and deaths for each common cancer type are presented in the table:

<b>Cancer Type</b>	<b>Estimated New Cases</b>	<b>Estimated Deaths</b>
Bladder	72,570	15,210
Breast (Female – Male)	232,340 – 2,240	39,620 – 410
Colon and Rectal (Combined)	142,820	50,830
Endometrial	49,560	8,190
Kidney (Renal Cell) Cancer	59,938	12,586
Leukemia (All Types)	48,610	23,720
Lung (Including Bronchus)	228,190	159,480
Melanoma	76,690	9,480
Non-Hodgkin Lymphoma	69,740	19,020
Pancreatic	45,220	38,460
Prostate	238,590	29,720

Thyroid	60,220	1,850[2].
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In March 2010 the journal “Nature” published an article that described the quite an unusual method. Scientists of the California Institute of Technology have created so-called “nanobots” based on nanoparticles that can “navigate” through the blood of patient and turn off certain genes which are involved in the development of cancer.

The method proposed by the American researchers, is based on RNA interference – special mechanism that allows to inhibit certain genes. The “nanobots” are covered above by a particular protein transferrine, which is able to “seek out” the cancer cells by interacting with receptor proteins on their surface. Getting inside the cancer cell, the particles release the so-called small interfering RNA, which can block the gene that produces a ribonucleotide reductase protein that participates in the formation of malignant tumors.

Clinical trials of the method have shown really good results. Thus, patients with various types of cancer were administered nanoparticles four times a day with an interval of 30 minutes for 21 days. As a result, the target gene was really managed to block. However, experts say, that yet, it is too early, to make some global conclusions.

Radiofrequency techniques are one of the main hopes of millions physicians worldwide. And the opportunities and capabilities of radiofrequency techniques are not limited. In fact, the radio frequency thermoablation is a “heat treatment”. A special probe is introduced in the tumor tissue, and then the affected area is simply burnt.

This method of destruction is possible for the treatment on the early stage of cancer of the liver, kidneys, lungs, breast, and bones. In contrast to radiation therapy or chemotherapy, this procedure has the advantage – it can be repeated if necessary and systemic side effects are absent.

One more sensational data were obtained in August 2010. It turned out that salmonella bacteria mobilize the immune system and that is why they help in the fighting with cancer. Such useful “bacterial” effect was discovered by scientists from Italy and the USA. It is interesting that in the norm, these microorganisms do not cause any disease, but lead to the activation of immune cells.

In the early stages of cancer immune cells often detect the affected cells as anomalous and destroy them. The whole process of “identification” is based on the fact that the specific protein molecules, allocated by tumor cells enter through integral membrane protein connexin-43 in immune cells and act on it as a kind of “red flag”, causing a specific immune response.

The main problem is that with the development of the disease cancer cells become invisible to the immune system, because the organism allocated insufficient amount of protein connexin-43. Thus, the tumor grows and the organism gradually stops reacting to it.

With the introduction of salmonella bacteria in infected tissues of mouse and human melanoma cells, the level of connexin-43 has abruptly increased, which leads to activation of the immune system and to destruction of most of the affected cells. Moreover, this method also has been effective in protecting the body from spread of the disease to other organs.

Another method that is widely used in cancer treatment is the insulin therapy. However, here insulin acts rather as an activator of the other drugs. In particular, the hormone is a kind of a “conductor” of the drug and is responsible for optimizing its “delivery” to the tumor cells. Thus, the dosage of the drug and side effects can be reduced. However, this method is effective only in the early stages of the disease.

In 2008 the Austrian doctors also reported about the benefits of hormone therapy. They showed that one of the drugs from osteopathy renders antitumor effects. It has been shown that using of this drug reduces the risk of recurrence by half, and the frequency of metastases is reduced by 35%.

Experts from France admit that the future is still for “therapy a la carte”: identifying the signs of a sub-type of cancer, their diagnosis and treatment. The technology that uses biomarkers for early detection of the disease is at foreground [1].

Biopharmaceutical researchers are now working at 981 medicines and vaccines for cancer, according to a new report by the Pharmaceutical Research and Manufacturers of America (PhRMA). Many are high-tech weapons to fight the disease, while some involve innovative research into using existing medicines in new ways.

The selected medicines that are in development for cancer treatment include the following:

1. *Interfering with Cancer Cell Metabolism.* Glucose plays an important role in the growth of cancer cells and has been used for detection purposes in PET imaging scans. Now, researchers are studying ways to disrupt the way cancer cells metabolize glucose in an effort to deprive them of energy for growth. One medicine in development for pancreatic cancer – which affects more than 40,000 Americans each year – disrupts the biochemical alterations in the conversion of glucose to energy that occurs in many, if not all, types of cancer cells. The altered cancer cell is considered to be a hallmark in the transformation of normal cells to cancer cells. The medicine is designed to disrupt the alteration and its link to a pathway controlling cancer cell growth, development and death.

2. *Two Ways of Inhibiting Tumor Growth.* Non-small cell lung cancer (NSCLC) is the most common form of lung cancer, accounting for about 85 percent of lung cancer cases. It is difficult to treat, especially when it has spread to other parts of the body. About 75 percent of NSCLC patients are diagnosed late with metastatic or advanced disease, where the five-year survival rate is 6 percent. One first-in-class medicine in development targets two different cancer pathways. It inhibits the insulin receptor of anaplastic lymphoma kinase (ALK), which is found at high levels in cancer cells where it is believed to play a key role in tumor cell growth and survival. The medicine also inhibits the growth factor c-MET, which has been associated with cell proliferation, motility, invasion and metastasis.

3. *Using Immunotherapy to Kill Cancer Cells* – Cancer of the head and neck include cancers of the oral cavity, salivary glands, sinuses and nasal cavity, pharynx, larynx and lymph nodes in the upper neck area. According to the National Cancer Institute, these cancers account for approximately 3 to 5 percent of all cancers in the United States and are more common in men and in people over age 50. One potential medicine in development for head and neck cancer is a first-in-class combination immunotherapy (combining both passive and active immune activity). Passive immunotherapy refers to the use of antibodies created outside the body to destroy



cancer cells in a targeted way, while active immunotherapy stimulates the body's own immune system to fight the cancer.

4. *Alerting the Immune System to Cancer.* Melanoma is the most serious form of skin cancer. More than 68,000 Americans will be diagnosed with the disease each year, and nearly 9,000 will die. A potential new DNA-based immunotherapy targets late-stage metastatic melanoma. The therapy is designed to stimulate both innate and adaptive immune responses in primary and metastatic tumors. It alerts the immune system to recognize and destroy tumor cells, inducing a powerful immune response.

5. *Inhibiting Mutated Cancer Cells.* Leukemia is a form of cancer in which abnormal white blood cells take over the body's bone marrow and prevent it from making enough normal blood cells (white, red and platelets), leaving the patient highly susceptible to serious infections, anemia and bleeding episodes. Each year, more than 43,000 Americans are diagnosed with some form of leukemia and more than 21,000 will die. A medicine in development potentially inhibits the FLT-3 cell receptor that is mutated in about one-third of all patients with acute myeloid leukemia (AML) as well as other targets thought to play a role in AML. Activation of the receptor by different types of mutations may play an important role for tumor cell proliferation, resistance to apoptosis (cell death), and prevention of abnormal cell development.

6. *Regulating Cancer Cells.* Sarcomas are a group of aggressive cancers of the body's connective tissue. They are divided into two forms bone sarcoma and soft tissue sarcoma. There are more than 10,000 new cases of soft tissue sarcomas diagnosed each year in the United States and nearly 9,000 will die from the disease. Bone sarcomas are rare, with 2,600 new cases and 1,500 deaths each year. A potential medicine in development for both types of sarcoma is an inhibitor of the protein mTOR (mammalian target of rapamycin) that controls cell growth by regulating cellular processes, including protein synthesis, cell proliferation, cell cycle progression and cell survival.

7. *Increasing Efficacy with Nanoparticles.* A potential treatment in development is a nanoparticle containing the anti-cancer medicine docetaxel that is targeted to prostate-specific membrane antigen, a cell surface antigen expressed on the surface of cancer cells and on new blood vessels that feed a wide array of solid tumors. Nanoparticles concentrate the delivery of the anti-cancer agent at the specific disease site, reducing systemic exposure, increasing efficacy and reducing side effects.

8. *Selectively Blocking a Cancer Cell's Make-up.* Ovarian cancer causes more deaths than any other cancer of the female reproductive system, with nearly 14,000 deaths each year. A potential first-in-class medicine in development works by selectively inhibiting the polo-like kinase-1 (PLK-1), which is an enzyme crucial for cell division. PLK-1 is expressed in proliferating cells and most tumors. Its inhibiting activity disrupts cell division, which induces cell death and reduces cancer growth [4; 5; 7].

Screening tests can find diseases and conditions on early stages when they are easier to treat.

1. Colorectal Cancer Tests;
2. Breast Cancer (Women);
3. Cervical Cancer (Women);
4. Prostate Cancer Screening (Men): a prostate-specific antigen (PSA) test or digital rectal examination (DRE);

## 5. Skin Cancer Screening [3]

Many authorities recommend that after the age of 50 tests should include regular colonoscopy for cancer of the colon, serum prostatic-specific antigen (PSA) for prostate cancer, mammography for breast cancer, and enhanced lung CT imaging for lung cancer.

In the conclusion it can be said that the new technologies and methods for the diagnosis and treatment of cancer are very important for all mankind. Maybe some day scientists will invent a vaccine that can be injected at birth and it will protect us from all diseases.

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## FLUORESCENT SENSORS FOR DETECTION OF HEAVY METAL IONS IN WATER BASED ON SOME 2,6-DISTYRYLPYRIDINE DERIVATIVES

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**Summary:** The article deals with problem of heavy metal ions pollution of water. The results of the study are as follows: 2,6-distirilpyridine derivatives are efficient luminophores, fluorescent properties of which strongly depend on the medium acidity and the concentration of metal ions. The possibility of using sensor materials based on these compounds for the detection of heavy metals ions in natural and technological water has been determined.

**Key words:** 2,6-distyrylpyridine derivatives, complexation, fluorescent sensors, heavy metal ions, intensometric probes, ratiometric probes .

**Анотація:** Стаття присвячена дослідженню можливості створення флуоресцентних сенсорів на основі похідних 2,6-дистирилпіридину. В результаті дослідження було визначено, що похідні 2,6-дистирилпіридину є ефективними люмінофорами, флуоресцентні властивості яких суттєво залежать від кислотності середовища і концентрації йонів важких металів. Була досліджена можливість використання сенсорних матеріалів на основі цих сполук для виявлення йонів важких металів в природній та технологічній воді.

**Ключові слова:** інтенсометричні зонди, йони важких металів, комплексоутворення, похідні 2,6-дистирилпіридину, радіометричні зонди, флуоресцентні сенсори.

**Аннотация:** Статья посвящена исследованию возможности создания флуоресцентных сенсоров основанных на производных 2,6-дистирилпиридина. В результате исследования было определено, что производные 2,6-дистирилпиридина являются эффективными люминофорами, флуоресцентные характеристики которых существенно зависят от кислотности среды и наличия ионов тяжелых металлов. Была исследована возможность использования сенсорных материалов

основанных на этих соединениях для определения ионов тяжелых металлов в природной и технологической воде.

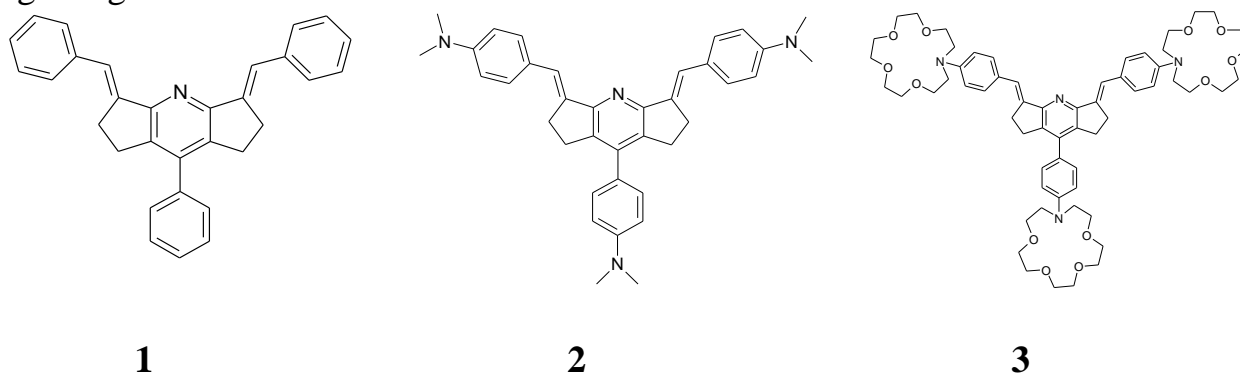
**Ключевые слова:** интенсометрические зонды, ионы тяжелых металлов, комплексообразование, производные 2,6-дистирилпиридина, ратиометрические зонды, флуоресцентные сенсоры.

With the development of analytical, environmental and biological chemistry now the problem of multiple testing of the natural and biological objects arises to determine different metal ions, various organic and inorganic compounds. Particular attention is given to the possibility of express analysis. To resolve these problems in recent years an interesting method of fluorescent analysis has been used, because modern technology allows constructing cheap and portable fluorescent analyzers, which could be used even in the field.

However, the application of the fluorescent method requires fluorescent probes and markers, fluorescent properties of which can vary significantly depending on various factors: the presence of metal ions, acidity medium, proton-donor ability and the polarity of the microenvironment etc. Besides both the synthesis and design of ratiometric probes are still important for it [1].

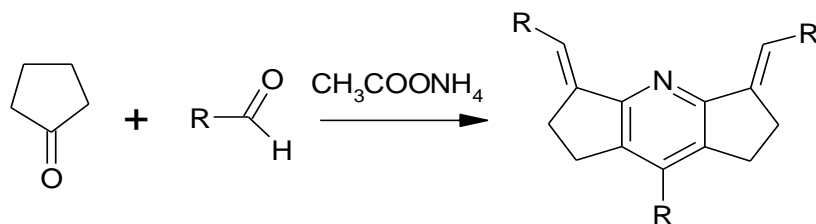
Unlike required intensometric probes that can only be used in conjunction with a set of standard samples and the preliminary calibration, this kind of fluorescent probes exhibits irradiation in two different spectral regions. This allows using an analytical signal fluorescence intensity at one wavelength, which depends on many factors. Application of ratiometric probes allows using the ratio of intensity at two wavelengths, which is constant and depends only on one factor.

The derivatives of 2,6-distyrylpyridine are efficient luminophores, fluorescent properties of which strongly depend on the medium acidity and the concentration of metal ions [2]. In the presence of metal ions, they exhibit two-band fluorescence, allowing using them as ratiometric sensors.



The structural rigid bis-methylene analogue 1 of pyridine was first obtained under the Chichibabin reaction, by reacting an aromatic aldehyde with ammonium acetate and cyclopentanone in a boiling ethanol. Synthesis of compounds 2-3 was performed under similar conditions but in the presence of an oxidant, needed for effectively carrying out the dehydrogenation in the formation of the pyridine fragment. After isolation and purification by repeated recrystallization from acetone, yellow crystalline substance was obtained, the individual by TLC, readily soluble in chloroform, DMSO, acetic acid, and alcohols. Their structure was confirmed by  $^1\text{H}$  - and  $^{13}\text{C}$  - NMR spectroscopy,

elemental analysis and mass spectrometry. Synthesis was carried out according to the scheme:



The complexation of 2,6-distyrylpyridine derivatives 1 - 3 [3] with the ions of Hg(II), Cd(II), Pb(II), in model water-ethanol solution and immobilized on silica gel [4] was studied in this work.

For spectrophotometric measurements specially prepared and purified according to [5] ethanol was used. To study the complexation applied mercury (II) acetate, cadmium (II) Acetate and Lead (II) acetate were prepared in accordance with [6]. Quality of salts dehydration was controlled by gravimetric values. Complexation constants were determined in ethanol-water (50% by volume).

Carrying out the titration solution containing the original form of matter with spectrophotometric concentration (about  $2 \cdot 10^{-5}$  mol / L) and the solution of the same concentration of the organic ligand, but containing salt in an amount necessary to create a certain concentration metal ion were prepared.

Titration was carried out in spektrofluorymetric cuvette. 2 ml of the solution of a test compound was placed there, thereafter the addition of salt solution was made by dosimeter and absorption and fluorescence were filmed.

Absorption spectra were obtained on a spectrophotometer Hitachi U3210, fluorescent spectra on a Spektrofluorimeter Hitachi F4010. Substances concentration were  $10^{-5}$  -  $10^{-4}$  mol / L. The thickness of the absorbing layer was 10 mm. Measurements performed in the isothermal chamber at  $t = 20 \pm 0,1$  ° C.

For analysis 20-25 analytical wavelengths within the wavelength absorption (fluorescence) band were taken. Constant values obtained were averaged using the weighted average formula [7].

We carried out 18 spectrophotometric titrations. After processing the results we have obtained the conclusions that: 2,6-distyrylperidine derivatives are efficient luminophores and can coordinate metal ions by nitrogen atoms in pyridine moieties of molecules. At coordinating metal ions in the absorption and fluorescent spectra a significant bathochromic shift of band is observed. The value of shift depends on the metal ion radius.

Complexation constant of the investigated compounds is determined by the follow ions: Cadmium (II), Mercury (II) and Lead (II). 2,6-distyrylpyridine derivatives coordinate metal ions by the nitrogen atom of central pyridine moieties.

Molecules of azacrown derivative of 2,6-distyrylpyridine has four centers of complexation, but in spectral investigations only coordination of three metal ions is observed: one of them is coordinated by the nitrogen atom of central pyridine moieties and other two ions by two azacrown moieties. Considerable sensitivity of azacrown-derivative of 2,6-distyrylperidine from concentration of metal ions used as an metalochromic indicator proved to be possible. Thus the given compounds can be

proposed as a background for the design of the new sensing materials for detecting heavy metal ions in solutions, including natural and technological water.

Within the present researches the ability to complex formation of some 2,6-distyrylpyridine derivatives with Hg(II), Cd(II) and Pb(II) ions in model water-ethanol solutions has been investigated. Fluorescent characteristics of formed complexes and their stability constants have been determined. The possibility of using sensor materials based on these compounds for the detection of heavy metals ions in natural and technological water has been determined.

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