NEGATIVE CONSEQUENCES OF USING NANOPARTICLES IN MEDICINE.

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The main problems of pharmacotherapy are no targency, high toxicity, rapid biodegradation of drugs, as well as the inability to penetrate vital medicines histohematogenous barriers. To solve them pharmacologists are working on the creation of new and improvement of existing drugs. The future pharmacology is the use of selective drugs and one of the most effective approaches for their preparation of nanosized drug use. In the past, the attention of the scientific community is focused on the field of nanomedicine. It develops very rapidly and affects the scale and social contribution of their achievements. The use of nanotechnology in the diagnosis, treatment and monitoring of diseases is becoming the norm of modern medical science and practice. However, the lack of knowledge about how nanoparticles are "embedded" in the biochemical processes of a living organism, gives particular concern. Given the novelty and variety of products, high mobility and reactivity of nanoparticles are necessarily unique risk assessment of nanopreparations application for security of the body conducted therapy.

Key words: nanotechnology, nanomedicine, drug design, negative effects.

Nanomedicine last years has developed extremely rapidly and attracted worldwide attention not only quite real achievements, but also their social contribution. This term now understands as the using of nanotechnology in the diagnosis, monitoring and treatment of disease**.**

For many decades was conducted (and do not stop till now) the searching for the ideal drug delivery systems, which is quite understandable and objective factor. The duration of the treatment and its success directly depends on the implementation of the action of drugs directly to the outbreak of the disease. This is particularly important in those cases where the treatment is necessary to use highly toxic drugs that are effective against the disease, but have toxic effects on other body systems. Often it makes stop using this kind of substances, and to resort to less effective drugs.

The industry of directional design of new drugs or drug design has a direct relation to subject of nanotechnologybecause interacting objects - drug and target - are molecular objects.

According to the experts researchers have not developed the tools such necessary for a 100% risk assessment of nanotechnology in healthcare yet. Such development for 3-5 years (and according to some estimates – more) lags behind in terms of the actual creation the most important medical nanomaterials. Nanomaterials are a completely new class of product, and the characteristics of their potential danger to human health and the environment in all cases is mandatory. Nanoparticles and nanomaterials have complex physical and chemical properties and biological activity (including toxic), which are often radically different from the properties of the same substance in the form of continuous or macroscopic phases dispersions (Table 1).

Table 1. Physico-chemical characteristics of the substances in the nanosized state. and changes in physico-chemical properties and biological action.

Physico-chemical properties of behavior substances at the nanoscale condition	Changes in physical and chemical properties and biological (including toxic) action

Increasing the chemical potential of substances on interphase border of the greater curvature	Changing of the atomic topology on the surface leads to a change in their chemical potentials, changing solubility, reactivity and catalytic ability of nanoparticles and their components.
The high specific surface of nano-materials (per unit mass)	Increased adsorption capacity, chemical reactivity and catalytic properties may lead to increased production of free radicals and reactive oxygen species and further damage to biological structures (lipids, proteins, nucleic acids, particularly DNA).
Small size and the variety of forms nanoparticles	Possible binding to nucleic acids (causing the formation of DNA adducts), proteins, incorporation into the membranes, penetration into cellular organelles and as a result, changes the function of biological structures. The processes of nanoparticle transport in an environment with air and water streams, their accumulation in the soil, sediment may also differ significantly from the behavior of particles of substances of larger size.
The high adsorption activity	Possible adsorption on nanoparticles of various contaminants and facilitating their transport into the cell, which dramatically increases the toxicity of the latter. Many nanomaterials have hydrophobic properties or are electrically charged, which enhances the adsorption processes in these various toxins and the ability of the latter to penetrate the barrier of the body.
High ability to accumulate	It is possible that due to the small size of the nanoparticles can not be recognized by the defense system, not be subjected to biotransformation and not excreted from the body, what leads to an accumulation of nanomaterials in plant, animal organisms but also in microorganisms, to transmission through the food chain, and as a result - to increase their revenues into the human body

In the advanced Western countries, activities related to the definition of nanotechnologies and nanomaterials safety for animals, humans and the environment, developing intensively. So, in 2000, formed the National Nanotechnology Initiative in the United States, which coordinates the work of 26 federal agencies. This is an interdepartmental program for evaluation the hazards to human health of chemical agents as a result of modern toxicology tests.

In the area of responsibility of the Food and Drug Administration US (FDA) is to ensure safety, efficiency and reliability of drugs, medical devices, biotechnology products, tissue products, vaccines, cosmetics and pharmaceuticals, created for humans and animals with the use of nanotechnology.

Nanomedicine, and nanotechnology in general, is new, and there is little experimental data about unintended and adverse effects. Lack of knowledge about how nanoparticles are "embedded" in the biochemical processes in the human body, gives particular concern. In a recent article in Medical Journal of Australia, said that the security rule for nanopreparations may require a unique risk assessment, given the novelty and variety of products, high mobility and reactivity of engineered nanoparticles.

It was found that nanoparticles poliamidoamindendrimers (PAMAMs), useful as drug delivery agents, cause cell damage in the tissues of the lungs, the results were published in Journal of Molecular Cell Biology. In a series of experiments conducted at the Chinese Academy of Medical Sciences on mice, found that nanoparticles PAMAMs run program "cell death". Project leaders immediately called

on the scientific community to pay special attention to the safety of the use of nanotechnology in medicine.

The most widely used, both in pure form and as part of nanomaterials, a titanium oxide (TiO2). Toxicological studies ultrathin (20 nm) TiO2 particles administered to rats by inhalation have shown that particles can accumulate in the lymphoid tissues, have a damaging effect on the DNA of brain cells and lymphocytes. The main mechanism of the toxic effect of TiO2 nanoparticles was the induction of reactive oxygen species. Severe toxic properties are aluminum nanoparticles, which are able to inhibit the synthesis of mRNA, induce cell proliferation, induce pro-atherogenic inflammation, mitochondrial dysfunction, and so on.

Fullerenes were intravenously administered to rats at doses of 15 and 25 mg / kg. Injection of 25 mg / kg for 5 minutes resulted in the death of two out of twenty rats. Fullerenes are almost entirely bound to plasma proteins and inactivated hepatic glutathione-S-transferase, glutathione peroxidase and glutathione reductase, inducing oxidative damage of rat hepatocytes. Like fullerenes, carbon nanotubes have a high affinity for DNA molecule, making them potentially dangerous mutagens. So, the main reason for the damaging action of carbon nanostructures is the induction of reactive oxygen oxidation of biological molecules.

Based on polystyrene nanoparticles (30 nm) in oral administration are able to penetrate the liver and spleen. Injections polymer nanoparticles (izobutiltsianoakrilat) of 200 nm at a dose of 40 ml / kg, led to death 50 percent of the mice.

Nanoparticles on the basis of organic polymers and dendrimers actively captured by macrophages and poliamidoamin dendrimer at concentrations 10-100 nmol increased pores in the membrane cells.

The data on the toxic properties of some nanomaterials is not exhaustive. It has been shown that the toxicity depends not only on the physical nature, production method, size, nanoclusters structure and nanoparticles, but also from the biological model in which tests are conducted. Target organs and mechanisms of toxic effects varied. Some nanomaterials because of their physical nature are able to induce reactive oxygen species, others - are able to penetrate tissue barriers and into cells to interact with intracellular components. The third - generation dendrimers of varying degree, some other types of nanomaterials, can disrupt the membrane structure, making them permeable. Considering the accumulated experimental material can be detected, which is not always and not all nanomaterials are toxic or otherwise damaging effect. For example, some researchers have uniquely discovered cytotoxic effect of magnetic particles based on iron oxide; others on the contrary, have shown that they are harmless. And these examples are enough. It shows how unique and varied in its properties of nanomaterials, even if they consist of the same chemical.

Experts point out that the area of nanotechnology may deem risky, dangerous and dubious investment, if the research will not be considered important security problems and human health. Nanomaterials are generally easier to enter into chemical transformations than larger objects of the same composition, so they are able to form complexes with properties not previously known. The nanoparticles, due to their small size, easy to penetrate into the human and animal body through the protective barriers (epithelia, mucous membranes, and so on), Respiratory system and gastrointestinal tract. Nanoelements absorbent properties are significantly higher than those of other molecules.

One of the leading experts in the health and environment professor E. Seaton (University of Edinburgh, UK) said that nanoparticles can cause human respiratory problems, heart, immune system and so on, but tests of such goods have not been conducted. Professor G. Oberderster (University of

Rochester, USA) showed that 35 nm diameter carbon nanoparticles are able to penetrate into the brain directly on sensitive nerve fibers. Specialists of the National Aerospace Agency of the USA report that the nanotubes, when inhaled in large quantities, lead to pneumonia. It was found that the nanotube is a compound of ultrafine needles, has a structure similar to asbestos, and this material by inhalation causes lung damage. Inhalation polystyrene nanoparticles also causes inflammation of lung tissue and, besides provoking thrombosis of blood vessels. There is evidence that the carbon nanoparticles can cause disorders of cardiac activity and inhibit the activity of the immune system.

In addition, scientists are paying attention to a very important fact of possible modification of nanoparticles properties after their penetration into the body, for example, coating in contact proteins in body fluids (blood, plasma). Depending on the concentration and properties of the used nanoparticles during their penetration into the body, we can get a wide range of intracellular changes.

In conclusion, we note that the need for a detailed study of all aspects of action nanodrugs on living systems is not dramatic and is in no way reduces the huge interest in the future drugs. Recall that such a step had to go and pharmaceutical industries "classic" drugs at the time of its creation and development, and this way was worth to mankind considerable losses. Gradually developed rules of developing new drugs to market, including strictly observe safety production standards, durable and comprehensive clinical trials, and so on.

Similarly, the study of nanoprocesses and mechanisms, development of standards, requirements, methodologies, standards, and then, based on them, the study of the chemical, pharmaceutical properties nanodrugs candidates, their toxicology, ecology and other characteristics will create new rules, the totality of which we have today conditionally call GNP (good nanotechnological practice). From this point on, no doubt, and the countdown will begin a new era in global health.

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