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WHAT ARE THE EFFECTS OF TITANIUM DIOXIDE AND ALUMINUM ON THE BRAIN?

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Abstract. *Synthetic food colorants are organic compounds that do not occur naturally, meaning they are artificially produced. Most of them have been used in the global food industry for decades. Many of these colorants form insoluble complexes (lakes) with metal ions and, in this form, serve as pigments for coloring powdered products, dragees, tablets, and chewing gum. Unlike natural food colorants, synthetic ones do not exhibit biological activity and do not contain flavoring compounds or vitamins. However, they offer significant technological advantages over natural colorants, as they are less sensitive to processing and storage conditions while providing bright, easily reproducible colors [7], [8], [9].*

Key words: *E 171, titanium dioxide, nanomaterials, E173, aluminum, natural brain barrier, cumulation.*

Inrtoduction. Like other fine-particle food additives, titanium dioxide is mainly found in food products. It is found in large quantities in carbonated drinks, various colored sweets, packaged salty and fatty crackers, potato chips, paper candies, pastries, dairy and cheese products, and sausage products.[1]

Titanium dioxide is actively used not only in the food industry, but also in the pharmaceutical industry, in the production of personal hygiene products, and cosmetics as a bleaching agent. Titanium dioxide is a water-insoluble substance with low toxicity. [2]

In the body, titanium accumulates in the form of proteins. Enterally administered titanium dioxide interacts with the aggressive environment of the stomach significantly affecting the properties of proteins and enzymes changes.

In a laboratory study, chronic (90 days) enteral administration of titanium dioxide to rats resulted in spleen damage, thrombocytopenia, lymphopenia, decreased hemoglobin levels, and decreased immunoglobulin levels. [4]

In another laboratory study, administration of titanium dioxide at a dose of 10 mg/kg resulted in severe liver damage, nephron apoptosis, and impaired immunoregulation.

When titanium dioxide was administered enterally at a dose of 100 mg/kg for 10 days, it was found that CD4 lymphocytes increased in all areas of the intestine, and the secretion of cytokines IL-4, IL-12, IL-23, and TNF increased mainly in the colon wall. [5]

Many studies have been devoted to the effects of titanium dioxide on the body, especially on the lungs, and the changes that occur in it. In this, solutions were sought to the questions related to the entry of small-sized titanium dioxide through the respiratory tract in the workplace and the development of pathological processes. Experiments conducted on rats with high doses of titanium dioxide for two years showed that tumors developed in the lungs of the rats, which indicated the carcinogenic properties of titanium dioxide. [6]

Fine-particle titanium dioxide, which enters the body through the intratracheal route, damages the cellular structure of alveolar macrophages and leads to impaired function. In addition, it reduces the chemotoxic properties of alveolar macrophages. Small amounts of titanium dioxide increase the phagocytic properties of macrophages, while large amounts reduce this property. With an increase in the amount of fine-particle titanium dioxide, the production of NO and TNF increased, since more

pro-inflammatory mediators were synthesized under the influence of fine-particle titanium dioxide than with conventional titanium dioxide. [7] Small amounts of titanium dioxide increased the sensitivity of the upper respiratory tract by twofold, and the number of cells responsible for inflammation increased by up to threefold. Histological examination revealed edema, epithelial destruction, and inflammation [8].

Free titanium dioxide causes denaturation of cytoplasmic proteins [9].

E 173 Aluminum is one of the most common elements on Earth, ranking third after oxygen and silicon. Aluminum compounds occur in nature in a variety of forms. Aluminum compounds are part of more than 280 minerals and are actively used in various fields of human activity. Despite the widespread use of aluminum compounds, their negative consequences remain one of the most important and necessary problems of modern medicine. In particular, its complications related to the brain are the cause of much discussion. There is still much debate about whether Alzheimer's disease, autism, Parkinson's disease, multiple sclerosis, and similar profound changes in the brain are caused by aluminum and its compounds. (11) Aluminum in drinking water, inhalation and food products despite entering in large quantities through mucous membranes in small quantities reabsorption occurs. luminum is not essential for the human body and metabolic processes (13). This element has a strong toxic effect on the body and the brain. The many ways in which aluminum enters the body and its widespread use further emphasize its toxic properties. [11,12,13].

This toxic effect is especially pronounced in Alzheimer's disease, autism, progressive sclerosis, and other brain dysfunctions. The attention of international scientific journals has been focused on aluminum and the above-mentioned neurological diseases. [12]

The main part of aluminum enters the body through water, food dyes and used in packaging, preparation, and storage of food products enters through the details. Unprocessed food products the amount of aluminum in its composition is less than 5-7 mg/g. Aluminum entering the body with water is 0.3%, and with food - 0.1%. The daily intake of aluminum is 15 mg / day [14].

E 171 and E 173 are used as food dyes and give the product a white color. The fact that these dyes can change the analeptic properties of the product is very useful for entrepreneurs. But there is another side to the matter. All food additives, including food dyes that give color, can cause various pathological reactions in the body. processes are developing[6].

This article aims to demonstrate the effects and accumulation of the bleaching dyes E 171 and E 173 (when taken in large quantities) on the brain. The active substances of these dyes are: titanium dioxide (171) and aluminum (E 173). The effects of titanium dioxide and aluminum substances on the nervous system, including the brain, have been proven in numerous experiments. For example, titanium dioxide powder was given to experimental rats for a long time and changes in the brain were observed. When the EEG of the rat brain was performed, it was observed that active epileptic foci appeared in the brain and the rats became very aggressive. [1], [2], [3]. Aluminum is believed to be one of the main causes of neurodegenerative diseases: Alzheimer's disease, Parkinson's disease, autism [4], [5].

The purpose of the study: To determine the accumulation of titanium and aluminum elements in the brain.

Material and methods of research. We will study the extent to which titanium and aluminum accumulate in the brain, and how this accumulation is related to changes in the brain. White, inbred rats selected (the number of rats 40) for the experiment will be divided into 4 groups:

1. Control group-10
2. Group that received E171-10
3. Group that received E173-10
4. The group that received E171 and E173-10

The above group of rats was given enteral titanium dioxide and aluminum in the form of powder.

The standard for determining the mass amounts of macro- and microelements in the researched samples is carried out in relation to samples with known amounts of elements.

Instrumental neutron activation analysis It was shown that for 90 days, laboratory white rats were fed with food dyes E171 (TiO_2- titanium dioxide) and E173 (Al, aluminum) and the following results were obtained. The rats that received food dyes as an experiment were divided into 3 groups:

Group I E171 (titanium dioxide) was given 500 mg/kg orally per day for 90 days as an experiment. Our instrumental neutron activation analysis revealed that the test sample contained an average of 3.63 mg of titanium dioxide in the dry mass of the brain trace amount of titanium (Ti) was detected. In the brains of rats selected for control, this amount was 0.28 mg.

Group II was also given 500 mg/kg of food dye E173 (Al – aluminum) to laboratory white rats for 90 days as an experiment. In our instrumental neutron activation analysis, the test sample contained an average of 4.21 mg of aluminum in the dry mass of the brain. Element aluminum (Al) was detected in the amount of 0.53 mg/kg in the control group rats.

Group III E171 (titanium dioxide) 500 mg/kg and 500 mg/kg of E173 (Al – aluminum) food dyes orally for 90 days as an experiment. Our instrumental neutron activation analysis showed that the study sample contained an average of 3.7 μg / g of titanium (Ti) and 4.5 μg/g of titanium (Ti) in the dry mass of the brain traces of aluminum (Al) elements were detected.

Groups	Used substance	Average amount of substance in dry mass of brain after 90 days feeding	How much increased
E171 intaked	TiO_2	3.63 mg	13 fold
E173 intaked	Al	4.21mg	8 fold
E171+E173 intaked	TiO_2+ Al	TiO_2-3.7mg Al-4.5 mg	13.2 fold 8.5fold

Group	TiO_2	Al
Control	0.27mg	0.56mg

Results and discussion. The result obtained in the above experimental groups, compared with the control group, revealed differences in titanium: an average of 3.63/0.27 μg/g, 13 times more, and aluminum: an average of 4.21/0.56 μg/g, 8 times more. In addition, in the group given aluminum and titanium at the same time, compared with the control group, it was found that: titanium increased by 3.7/0.27 μg/g, 13.2 times, and aluminum increased by 4.5/0.56 μg/g, 8.5 times.

Conclusion. Around the worldl it is known that the brain has a natural blood-brain barrier, and the peculiarity of this barrier is its selective permeability. Accordingly, various toxic substances, poisonous products and many types of drugs circulating in the blood cannot pass through this barrier. However, there are exceptions, and there are 3 types of entry mechanisms for substances that have the property of crossing the barrier: 1) slow diffusion 2) active transport mechanism 3) endocytosis. The ability of the two food dyes titanium dioxide and aluminum shown in the experiment to cross the brain barrier has been proven in many experiments. If aluminum crosses the barrier by binding to proteins through the active transport pathway, then the physical properties of titanium dioxide help it in this way. Small particles (nanoparticles) of size 5-100 nm can easily pass through the brain barrier and show the property of accumulation. However, the question of how titanium enters the brain is a matter of much debate among scientists. During the 90 days of possible entry, it is shown that the active substances in the enterally administered dyes (E 171 and E 173): aluminum and titanium, accumulate in the brain to a high degree, and changes in the brain may be associated with the degree of this accumulation.

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