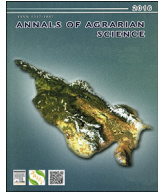




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## Metabolic effects of alimentary estrogen in different age animals

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## ABSTRACT

The article presents the results of studying the effect of alimentary exogenous estrogen that can be presented in agricultural products on state of lipid peroxidation, antioxidant system components and cholinergic neurotransmitter system in the organs of experimental different ages animals. It was established that the severity of the effects had been higher in females in puberty compared to sexually mature animals, which indicates the existence of specific age-related physiological conditions defined high sensitivity to exogenous estrogen-like compounds. Presents results on the effects of nutritional estrogens on metabolic processes in animals of different ages testify to the potential health risks of consumer products that may be contaminated with endogenous hormones. Despite the steady growth of agricultural production, development of agro-industrial pollution drugs like compounds of food is very likely. This phenomenon is of concern and requires increased control of both the responsible organizations and public associations that will enable to avoid the negative effects of dietary factors on the population health. Particular attention should be paid to the safety and quality of children's food, because this population is extremely sensitive to the influence of previously alimentary factors.

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## 1. Introduction

The human health affects a lot of factors, one of which is food. Food is considered to be safe, which does not create harmful effects on health, directly or indirectly, under the conditions of its production and turnover in compliance with sanitation and consumption (use) by appointment [1].

In modern agriculture (agriculture, livestock, poultry and fish farming) under intensive technologies of products cultivation for a significant increase in productivity technological regulations can disrupt and dangerous agronomic and veterinary drugs (hormonal growth promoters, antibiotics etc.) and pesticides are used illegally. Many of these compounds by the action are similar to steroid hormones, particularly estrogen. Products containing such substances are extremely dangerous to human health because of steroid activity manifestation with the following carcinogenic effects, causes a disruption of puberty and reproductive capacity. Food is one of the main routes of estrogens exposure on the human from the environment. Hormones aren't completely destroyed at cooked

products. Therefore, similar compounds naturally presenting in meat, milk, eggs, fruits and vegetables, and there are, at least sometimes, and in smaller doses. Steroid hormones are destroyed by heat processing less [2]. Male and female hormones are contained in meat (beef, pork, chicken), only female ones are in milk and eggs, fruits and vegetables include phytohormones, for example soy. All the hormones used in the agricultural sector, can affect the human body. Animal sex hormones are identical to human hormones. Getting into the human body with food, hormones are perceived by them as their own [3].

Estrogens are female sex hormones produced follicles of the ovaries, placenta partially adrenal cortex and testes and regulate specific sexual functions. On the chemical nature they are steroids. Estrogens spread through the bloodstream to various tissues, including the cardiovascular, immune and central nervous systems, and because of their lipophilic character can easily diffuse through cell membranes and hematoencephalic barrier, exerting effects [4]. They are inactivated in the liver and excreted in the urine. The mechanism of action of estrogen is probably based on the stimulation of RNA synthesis in cells and tissues of the reproductive organs leading to changes in the speed and scope of protein biosynthesis. Estrogens may lead to structural changes in the body, including the modulation of mitochondrial ATP synthesis [5].

Estrogen similar active are many compounds such as growth

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promoters animals, pesticides, antibacterial agents, veterinary drugs, industry chemicals (for example, DDT, bisphenol A) and foods containing phytoestrogens.

Estrogens were determined at concentrations in ng/kg in 10–100 range in the analyzed beef muscle tissues and milk samples. The same composition is detected about 10 times higher concentration (100–1000 ng/kg range) in eggs and kidney samples [6].

The theoretical maximum daily dose of estradiol-17 $\beta$ era (as growth promoter) for the consumption of cattle meat is calculated as 4,3 ng. After use of the products containing growth factors estradiol-17 $\beta$ era level increases from 4,6–20 ng, suggesting that a single dose and “good animal husbandry” aren’t observed. Pork and poultry probably include the same amount of estrogen as untreated cattle. In whole milk estradiol-17 $\beta$ era average concentration is estimated as 6,4 pg/ml the Few data report about 200 pg/g of estradiol-17 $\beta$ era in eggs [7,8].

The use of synthetic promoters of growth (for example, zeranol) as growth hormones in beef production in many countries, including Canada, Australia, New Zealand, South Africa, Mexico, Chile, Japan and the USA (trade name Ralgro) and an anabolic agent for more efficient conversion of feed into meat is debatable because of their ability to mimic the action of endogenous hormones of animals potentially leading to abnormal results [9]. At present zeranol officially is banned in Europe for safety reasons because of its potential carcinogenic and endocrine biological activity. Despite the prohibition by the European Union, the use of anabolic steroids and derivatives agents for cattle are still there. Mixtures consisting of several steroids are often used illegally, thereby impeding detection by lower levels of certain compounds [6].

Zearalenone (ZEA) is a mycotoxin produced by some *Fusarium* species in food and feed. Residual antimicrobials in food is established to be a risk to human health. ZEA and its metabolites related to the chemical structure of the mycotoxins toxicity is proved to be similar to natural estrogens. ZEA is the cause of reproductive disorders, genotoxicity and testicular toxicity in animals. As an endocrine “disruptor” zearalenone and its metabolites are involved in carcinogenic mutations [10].

Pesticides are widely used in various stages of plant cultivation and during storage for production protect against pests and/or quality safeguard. Through international trade of fruit and vegetables, as well as the lack of worldwide harmonized rules of pesticides application, including those with estrogenic properties, the risk of contaminated products consumption is quite high. Because of the international trade of fruit and vegetables, and lack of globally agreed rules for the application of pesticides, including the estrogenic properties, the risk of consumption of contaminated products is quite high. Despite the strict legislation of the European Union (EU) on ensure of pesticide low levels in baby food there is a threat of pesticide residues in this products [11].

Bisphenol A (BPA) is 4,4 - (propane-2,2-diol) phenol used in food packaging and coatings. BPA exposures carry out through the food and drinking water consumption and the right way through products containing this compound. It isn’t a mutagen, but can have genotoxic activity and cause oxidative stress. Effect of BPA can be harmful for humans, especially for behavioral and other effects in children [12].

Parabens are 4-hydroxy acid esters used as a preservative and antibacterial agent in many foods, cosmetics and pharmaceuticals are considered to be safe, but exhibits estrogenic activity through *p*-hydroxybenzoic acid as its main metabolite [13].

Such nutritional factors as phytoestrogens are contained in food. Legumes are particularly rich on them. At ingestion of phytoestrogens interact with many enzymes like endogenous estrogen and interfere with the process of them metabolism The most powerful

biological effects of phytoestrogens is their ability to inhibit sulfotransferase sulfating estrogenic steroids and various chemical substances from the environment, including dietary carcinogens [14].

Depleted endocrine system substances are a compound changing the hormonal and homeostatic systems and acting through different mechanism. Although most environmental estrogen activity was recognized as “weak” for many years because of their inability to cause transcriptional effects, at present it is proved that they are quite powerful initiators of signal cascades out of membranes [15].

In 1988, the FAO/WHO experts Committee on food additives declared that the steroid hormones remnants, usually presented in agricultural products were safe for human consumption. However, the risks associated with nutritional influence of exogenous hormones aren’t yet fully characterized, and publications give conflicting reports about long-term consequences of such products using [16].

Consumers are exposed to low levels of these substances throughout their lives. The effect of these compounds is being evaluated with a focus on mutagenicity and genotoxicity. However, this approach ignores the recent integration of new toxicological studies, for example, endocrine disorders, mixture toxicity and toxicity to development.

The most important period of postnatal ontogenesis is puberty characterized by a significant increase synthesis of estrogen. Elevated levels of estrogen circulating in the blood influence on many systems of the girl organism leading to a variety of physiological changes. Thus, at the different ages of life hormones carry out different effects on the body, and this is due not only to age hormonal homeostasis, but as hormone-dependent organs state [17]. Given the threat of contamination by chemicals with endocrine properties of diet of pubertant age children as a particularly sensitive populations analysis of risk regarding the occurrence of health problems in the future is required.

The aim of the presented work was the study of lipid peroxidation, antioxidant system components and cholinergic neurotransmitter system in the organs of experimental animals of different ages for exposure of alimentary synthetic estrogen.

## 2. Objectives and methods

The experiments were conducted on Wistar rats exposed to exogenous estrogen for 45 days. At the beginning of the experiment 3-month-old pubertant animals (group II) and 6-month-old sexually mature rats (group IV) were involved. The control group consisted of intact appropriate age animals (groups I and III).

For modeling exogenous estrogen impact rat’ meal is treated with the drug “Sinestrol” as stilbene derivative differing from steroid hormones estrogen on chemical structure, but by biological and medicinal properties similar to them in the rate of 2 mg per kg.

The research materials were brain, liver, kidney and blood serum of rats. The objects were indexes of TBA-active products, the total antioxidant activity, the activity of superoxide dismutase, glutathione peroxidase, glutathione transferase, glutathione reductase, glutathione content of the recovery, AchE activity.

The data were treated with standard methods of variation series estimation. The difference between the comparative values was considered probable at  $p < 0.05$ .

## 3. Results and analysis

Lipid peroxidation (LPO) is a universal biological mechanism occurring in cellular membranes constantly. Its pathological amplification leads to disruption of the structure and,

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