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"EFFECTS OF DRUGS ON ANIMAL ORGANISMS"

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Abstract. Phytoestrogens are biologically active compounds naturally produced in plants that are chemically similar in structure to endogenous estrogens of mammals. They are particularly found in legumes, soybeans, alfalfa, clover, and other forage crops. The main groups of phytoestrogens include isoflavones, coumestans, and lignans. Genistein, daidzein, formononetin, biochanin A, and coumestrol are among the most common representatives of these compounds found in animal feed.

This article analyzes, based on scientific literature, the mechanisms of action of phytoestrogens on the animal organism, their sources in feed, their metabolism in ruminant and monogastric animals, their effects on the reproductive system, as well as the potential positive and negative consequences that may arise in livestock production.

Keywords: phytoestrogen, genistein, daidzein, formononetin, coumestrol, isoflavone, estrogen receptor, reproduction, spermatogenesis, livestock production, animal nutrition, endocrine system.

Introduction. In livestock production, the high productivity of animals depends not only on the energy and protein value of feed, but also on the biologically active substances contained in it. In addition to proteins, carbohydrates, fats, vitamins, and minerals, plants contain numerous biologically active compounds known as secondary metabolites. Phytoestrogens are among these substances.

Phytoestrogens are secondary metabolites involved in the defense mechanisms of plants, and their molecular structure is to some extent similar to that of 17β-estradiol. Therefore, after entering the animal organism, they can interact with estrogen receptors. However, the effects of phytoestrogens are not limited to a simple "estrogenic effect": some compounds can activate estrogen receptors, while others, under certain conditions, can suppress estrogen signaling.

The importance of phytoestrogens for animals is particularly significant when leguminous forages are used. Soybeans and their products, alfalfa, clover, and other leguminous plants are important sources of protein in animal diets. At the same time, some varieties of these plants may contain high levels of biologically active phytoestrogens.

Scientific studies indicate that the effects of phytoestrogens on the animal organism are complex and dose-dependent. For example, in some cases, isoflavones such as genistein and daidzein may exhibit antioxidant and immunological effects and may have positive effects on growth and nutrient metabolism. On the other hand, excessive or prolonged exposure may potentially lead to disturbances in reproductive system function.

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Therefore, it is scientifically incorrect to evaluate phytoestrogens as either exclusively harmful or exclusively beneficial substances. Their effects should be assessed comprehensively, taking into account the animal species, dose, and physiological status.

Isoflavones — genistein, daidzein, formononetin, and biochanin A;

Coumestans — the main representative is coumestrol;

Lignans — compounds found in plants that can be converted into biologically active metabolites in the animal organism;

Other polyphenolic estrogen-like compounds.

Isoflavones, particularly, play an important role in soybeans and leguminous plants. Genistein and daidzein are considered the main phytoestrogens in soybean products. Formononetin is found in certain clover species and other leguminous forages. Coumestrol is associated with certain leguminous plants, particularly alfalfa, and may have strong estrogen-like biological activity.

The biological activity of phytoestrogens is generally much lower than that of endogenous estradiol; however, when their levels are high or animals are fed phytoestrogen-rich feed for a prolonged period, their overall physiological effects may become significant.

Entry and Metabolism of Phytoestrogens into the Animal Organism. To understand the effects of phytoestrogens in the organism, it is important to consider how they are transformed in the digestive system.

In ruminant animals — cattle, sheep, and goats — a significant portion of phytoestrogens undergoes metabolism under the influence of rumen microorganisms. For example, daidzein can be converted by rumen microorganisms into other metabolites, including equol.

As a result of these metabolic changes, the biological activity of the substance may differ from that of the original compound.

Studies have also reported adaptation of rumen microorganisms to the degradation of phytoestrogens. According to some data, after phytoestrogen-containing feed is provided, the ability of the rumen microbiota to metabolize these compounds may change over a period of approximately 6–10 days.

In the next stage, phytoestrogen metabolites are absorbed from the intestine and enter the bloodstream. In the liver, they undergo phase II metabolic reactions such as glucuronidation and sulfation. Some metabolites may return to the intestine through bile and participate in enterohepatic circulation.

Because of these processes, the same amount of phytoestrogens may not produce the same biological outcome in different animals. For example, there are differences between the metabolic characteristics of sheep and cattle. Therefore, in addition to assessing the amount of phytoestrogens in feed, it is also necessary to consider the metabolites produced in the animal organism.

Mechanism of Action through Estrogen Receptors. One of the most important biological properties of phytoestrogens is their interaction with estrogen receptors. In mammals, the main estrogen receptors are ERα and ERβ.

Genistein, for example, can bind to both estrogen receptors, although its affinity for these receptors is lower than that of endogenous estradiol.

After binding to the receptor, phytoestrogens can affect intracellular signaling systems. As a result, gene expression, cell proliferation and differentiation, metabolic processes, and reproductive system functions may change in hormone-responsive tissues.

The effects of phytoestrogens may manifest in two ways. First, they may mimic the effects of estrogen and produce an estrogen-like effect. Second, by binding to the receptor, they may

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partially limit the action of stronger endogenous estrogens. Therefore, phytoestrogens are often considered substances with selective or modulatory estrogen-like effects.

The final outcome of the effect also depends on the dose. The biological response observed at low concentrations may differ from that observed at high concentrations.

Effects of Phytoestrogens on the Reproductive System of Female Animals. One of the most extensively studied effects of phytoestrogens is their influence on the reproductive system of female animals.

Estrogen hormones play an important role in regulating ovarian activity, follicular development, changes in the uterine mucosa, and the sexual cycle. Therefore, estrogen-like substances may interfere with these processes.

In some animals that have consumed high-phytoestrogen forage for a prolonged period, disturbances of the sexual cycle, reduced fertilization rates, embryonic loss, and other reproductive problems have been reported. Sheep, in particular, are among the animals widely studied for their sensitivity to the reproductive effects of phytoestrogens.

In sheep, prolonged consumption of phytoestrogen-rich pastures has historically been associated with “clover disease,” that is, reproductive disorders associated with clover. In this condition, high levels of isoflavones such as formononetin have been an important factor. Effects of phytoestrogens on the reproductive system have also been observed in cattle, although cattle are generally considered less sensitive than sheep to the effects of certain isoflavones. In cows and heifers, phytoestrogens may alter signs of the sexual cycle, affect reproductive tract tissues, and under certain conditions may be associated with temporary infertility.

In addition, reproductive tract changes characteristic of estrogen-like effects have been reported in heifers fed diets high in phytoestrogens. Some studies have associated consumption of feed containing high levels of coumestrol with vaginal prolapse.

Effects on Pregnancy and Embryonic Development. Another important aspect of phytoestrogens is their potential effect on the early stages of pregnancy.

The balance between progesterone, estrogen, and other reproductive hormones is important for maintaining pregnancy. Interference of phytoestrogens with these hormonal systems may affect embryo implantation and the continuation of pregnancy.

Studies conducted in cattle have shown that increased levels of phytoestrogen metabolites — particularly equol and p-ethylphenol — in the context of high-soy diets were associated with early embryonic loss. In some heifers receiving high-soy diets, reduced fertilization rates and the need for more artificial inseminations to achieve pregnancy have been reported.

Effects on the Reproductive System of Male Animals. The effects of phytoestrogens on male animals are also of considerable scientific interest. In the male reproductive system, testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and other hormones regulate spermatogenesis.

Estrogen-like substances may interact with these hormonal systems. In particular, during embryonic and neonatal development, the endocrine system may be highly sensitive to external estrogens.

Effects of Phytoestrogens on Cattle. In cattle production, phytoestrogens enter the animal organism mainly through leguminous forage and soybean-based feeds.

The effects of phytoestrogens in cattle may be relatively lower than in sheep; however, reproductive changes may occur under conditions of high intake and prolonged consumption.

Studies have shown that certain phytoestrogens may affect the sexual cycle, ovarian function, and embryo survival in cows and heifers. At the same time, phytoestrogens may also affect metabolism, the immune system, and productivity.

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An interesting aspect is that some experiments have shown that isoflavones such as genistein and daidzein may have positive effects on growth performance. For example, in some phytoestrogen-rich diets, the average daily weight gain of sheep and lambs was higher than in the control group. In one study, after an eight-week feeding period, the average daily weight gain of sheep was 26.3% higher, while that of lambs was 31.7% higher.

This result indicates that the biological effects of phytoestrogens are not limited to the reproductive system.

Transfer into Milk and Animal Products. After being metabolized in the animal organism, some phytoestrogen metabolites may be transferred into milk and other biological products.

In ruminants, the transfer of phytoestrogen metabolites into milk may depend on the amount of estrogen-like feed consumed by the animal. Studies have identified a relationship between dietary phytoestrogen intake and certain metabolites in milk.

This issue is important from the perspectives of veterinary medicine and food safety. However, when assessing phytoestrogen levels in animal products, not only the initial composition of the feed but also metabolism in the animal organism, the lactation period, and other factors should be taken into account.

Main Factors Determining the Effects of Phytoestrogens. The effects of phytoestrogens on the animal organism depend on several factors.

The first factor is dose. A low amount of phytoestrogens and a high amount of phytoestrogens may not produce the same biological response.

The second factor is animal species. Sheep, cattle, pigs, poultry, and laboratory animals metabolize phytoestrogens differently.

The third factor is age and developmental stage. The sensitivity of the endocrine system in fetuses, newborn animals, and adult animals is not the same.

The fourth factor is duration of exposure. There may be a significant difference between single or short-term exposure and exposure lasting for months.

The fifth factor is the overall composition of the diet. Protein, energy, minerals, and other biologically active components may alter the effects of phytoestrogens in the organism.

The sixth factor is the intestinal or rumen microbiota. Particularly in ruminants, microorganisms play an important role in the formation of biologically active metabolites of phytoestrogens.

Conclusion. Phytoestrogens are complex biologically active compounds of plant origin that may exhibit estrogen-like biological activity in the animal organism. Their main representatives include genistein, daidzein, formononetin, biochanin A, and coumestrol.

The effects of phytoestrogens on the animal organism are multifactorial, and it is not appropriate to classify them simply as “beneficial” or “harmful.” Their effects depend on the chemical properties of the compound, dose, animal species, sex, age, reproductive status, duration of exposure, and the activity of microorganisms in the digestive tract.

From a practical livestock-production perspective, the main task is not to completely avoid phytoestrogen-containing forages, but to use them in a scientifically justified and balanced manner. In particular, in farms where breeding animals, pregnant animals, and high reproductive efficiency are important, it is advisable to control feed sources rich in phytoestrogens.

Thus, phytoestrogens are important plant compounds that can influence endocrine, reproductive, metabolic, and immunological processes in the animal organism. A deeper understanding of their biological effects is of significant scientific and practical importance for veterinary medicine, animal science, animal nutrition, and improving the efficiency of livestock production.

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