

Estrogens

Subjects: Biology

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Estrogens are a group of steroid hormones that recently have gained even more attention in the eyes of scientists. There is an ongoing discussion in the scientific community about their relevance as environmental contaminants and the danger they pose to animal health and welfare. In available literature we can find many examples of their negative effects and mechanisms that are involved with such phenomena.

Keywords: hormones ; welfare ; animals ; estrogens

1. Introduction

Currently we can observe a growing interest in the state of the environment, methods of its protection, and the impact that the pollutants present in it have on the health of living organisms. Our knowledge of already present and emerging types of pollution is still expanding, but at an insufficient pace. Sex hormones are one of the groups of pollutants that have recently attracted the attention of scientists. The available literature indicates that the most important of them in terms of environmental impact are hormones belonging to the group of estrogens. Estrogens are a group of sex hormones that include estrone (E1), estradiol (E2), estriol (E3), estetrol (E4)—produced only during pregnancy, and often synthetic ethinylloestradiol (EE2). Estrogens are also called female hormones and they play crucial a role in female organisms, but it should be taken into consideration that they are also necessary for proper functioning of male organisms ^[1].

Estrogens mainly imply their effects by interaction with isoforms of the estrogen receptor (ER)—ER α and ER β which then bind these hormones in the cytoplasm of cells and transport this complex to the cell nucleus. As a result, the activation of response elements in gene promoters begins the transcription process. Aforementioned receptors can be divided into nuclear estrogen receptors (nERs) and membrane estrogen receptors (mERs). Beside the “traditional” estrogen action, additional ways have been described—influence through cell signal transduction tied with mERs rather than genomic activity process. The available literature discusses the differences in the affinity and mechanism of action of these receptors, however, as shown by the latest studies, there is a high degree of functional and structural similarity between mERs and nERs ^[2]. Recently, additional receptors, namely, ER-X and Erx were described in the literature but additional research on them and mechanisms involved with their action are highly advised.

There are many potential sources of contamination of the environment with estrogens, such as animal farms, slaughterhouses, or large urban agglomerations (**Figure 1**) ^{[3][4]}. Estrogens present in excreta, due to natural or artificial processes (like hormone therapy or contraception) contaminate, by wastewater or fertilization, water and soil. An additional factors determining the degree of risk resulting from the presence of sex hormones in the environment are their half-life, which varies depending on the physico-chemical conditions, the microbiological richness of contaminated waters and soil, from 12 h to even 180 days in the case of water reservoirs without a stabilized population of microorganisms ^[5]. Removal of estrogen from the aquatic environment is important, however, it is difficult to achieve even with the use of modern filtration methods ^{[6][7][8]}. As evidenced by recent research, microbial degradation of estrogens can be led by many bacteria strains i.e., *Rhodococcus*, *Novosphingobium*, *Acinetobacter*, *Agromyces*, and *Sphingomonas*, thus showing possible safe and inexpensive ways for the reduction of threat involved with such pollution ^{[9][10][11][12][13]}. It is worth noting that some fungi, mainly species belonging to *Aspergillus* genus are also reported to perform aerobic degradation of estrogens ^[9]. Another threat related to the presence of hormones in the aquatic environment may be the processes of their accumulation in bottom sediments, from which they can be released again under appropriate physical and chemical conditions ^{[9][10][11]}. Another factor of risk can be their bioaccumulation in living organisms ^{[9][11][14][15]}.

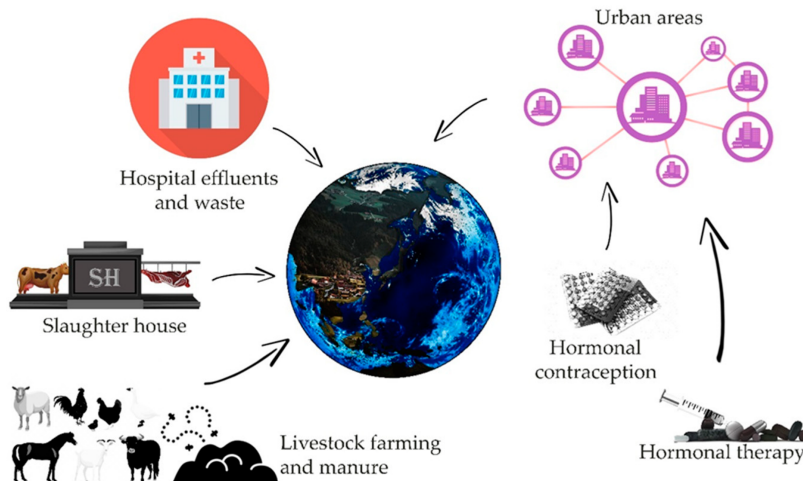


Figure 1. Sources of estrogens present in

the environment and their simplified pathways leading to the environment (based on ^{[4][5][6][7][8]}).

Occurring in the environment, they can lead to many negative consequences for health or the functioning of organisms directly or indirectly related to it. Those effect include feminization, dysregulation of natural processes related to reproduction, deterioration of the general condition of organisms, disturbances in the regulation of apoptotic processes ^[16], or even promoting processes leading to cancerogenesis ^{[17][18]}.

2. Impact of Estrogens Present in Environment on Health and Welfare of Animals

2.1. Invertebrates

Invertebrates are one of the groups most vulnerable to environmental estrogens contamination; it is related to the periodic exposure of their juvenile forms, often related to the aquatic environment, or the constant exposure of these organisms to the effects of these compounds. In the case of invertebrates, attention should be paid to a slightly different functioning of the endocrine system, both in terms of biochemistry and the mechanisms of regulation themselves ^{[19][20]}, however, it does not change the fact that the presence of both natural and synthetic estrogens can affect many aspects of their lives. There are a lot of evidence in the available literature confirming the negative influence of the presence of sex hormones in invertebrates. Bovier et al. showed that the addition of EE2 solutions to the medium administered to individuals belonging to the model invertebrate species *Drosophila melanogaster* statistically significantly reduced the survival and fertility parameters of the studied insects ^[21].

2.2. Fish

Fish, which are the most numerous and diverse group of vertebrates, due to the degree of similarity of endocrine systems functioning within this subtype to analogous systems in mammals, are significantly exposed to contamination of the environment with estrogens. In the case of fish, as in mammals, estrogens regulate behavior not only related to reproduction, but also to territorialism ^[22] or regulation of the immune response ^{[23][24]}. An additional risk for fish may be the process of accumulation and periodic release of estrogens to the waters from bottom sediments ^{[14][25]}, as well as the phenomenon described in the literature as a mechanism “something out of nothing” resulting from the mutually reinforcing effect of estrogens and other chemical compounds present in the aquatic environment, often other chemical compounds, on the organisms of animals living in it ^[26].

2.3. Amphibians

Among the terrestrial vertebrates, amphibians are the group most closely associated with the aquatic environment. Hence, potential exposure to estrogen contamination appears to pose a relatively greater threat to them. Most estrogens get into the environment with surface runoff or in sewage leachate, where their concentrations may be at levels that are hazardous to the health of amphibians ^{[27][28]}. In recent years, researchers have increasingly suggested that the current global decline in the amphibian population is related to the increase in pollutants, especially those of the nature of steroid hormones ^{[29][30][31]}. This phenomenon is increasingly dangerous because of the wide range of estrogenic effects on various development stages. The observed effects of pollution may lead to behavioral or sensory changes, as well as physiological changes, disrupting ontogenesis at its various stages and even being lethal ^[32]. In the research, the most commonly used amphibians are Anura, with the clawed frog *Xenopus laevis* adopted as the model species; also, numerous representatives of the genus *Rana* and *Bufo*.

2.4. Reptiles

A significant part of the publications related to estrogenic effects in reptiles concerns communal pollutants and endocrine-active compounds. Of all vertebrate groups, reptiles are least frequently tested for toxicological environmental hazards [33]. However, there are a few reports detailing the effects of estrogens at different levels of the organization.

One of the few fully sequenced estrogen-binding domains in reptiles is the green anole estrogen receptor (*Anolis carolinensis*). The studies conducted by Matthews et al. [34] were aimed at comparing the affinity of receptors of various vertebrate species to selected estrogenic compounds. A total of 34 substances, both natural and synthetic, were tested. The comparison showed that the estrogen receptors had a much stronger affinity for dihydrotestosterone and numerous phytoestrogens than the mammalian, avian, or fish receptors. For natural estrogens, the degree of affinity is similar, regardless of the species.

2.5. Birds

In birds, as in mammals, estrogens are biosynthesized, inter alia, in the sex glands and in tissues other than the sex glands, such as skin, heart, muscles, liver, brain, adipose tissue, brain, pancreas, and adrenal glands. Estrogen plays a key role in the control of reproductive behavior and the regulation of the neuroendocrine system, and is also essential in regulating the growth and differentiation of axons and dendrites in the brain [35][36]. Chemical pollutants, including reproductive hormones, may adversely affect bird reproduction and viability, as well as the development and functions of the hypothalamic-pituitary axis [37][38].

Increasing the level of estrogens in birds reduces fertility, slows down sexual maturity of females, impairs male mating behaviors, and also accumulates in the tissues of an adult individual, as well as in eggs, which can negatively affect the development of embryos (including increasing their mortality) [38][39]. In addition, in the case of farmed birds, increasing the level of estrogen in the body may have adverse effects on the animal, but also resulted in the hypothesis that the use of their feces in farmland has recently been recognized as the main source of estrogen in the environment [4]. Poultry feces, causing contamination of surface waters with estrogens [5][40][41], negatively affect the reproductive behavior of wild birds (i.e., the perception of male sounds by females), including the development of their offspring, due to accumulation in the body (Figure 2) [42][43][44][45].

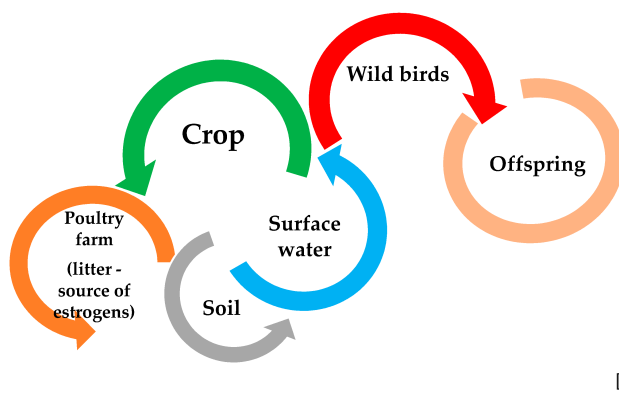


Figure 2. Estrogen contamination route (based on [5][40][41][43]

[44]).

2.6. Mammals

Estrogens can enter mammals in many ways, not only by ingesting water contaminated with them or through the skin during contact with it [46], but also through the food they eat, an example of which may be the accumulation of estrogens along with trophic levels in consumed foods, e.g., in plants [47][48], fish [49] or even as indicated in the literature in milk, however, in this case the literature reports are contradictory [50]. A very important phenomenon in the context of the threat posed by estrogens is the fact that very often mixtures of these are found in the environment, which in addition to the additive effect of these compounds may also show the synergistic effect mentioned previously [26][51]. There are a number of potential negative consequences of their action on mammals such as reproductive disorders and lowering the general condition of the body associated with their negative impact at their excessively normal concentrations [52]. There are many reports in the literature indicating an increased risk of carcinogenesis under the influence of estrogens [5][17][50][53]. Słowikowski et al. [54] describe two mechanisms that can lead to this, i.e., by destroying the structure of proteins or the structure of the genetic code. The effect of estrogens has been associated with cancers of the prostate, lung, endometrium, and breast [5][17][50][53].

3. Conclusions

The available literature clearly indicates the problem posed by estrogens in the environment. Contact with them can expose animals to many sicknesses and welfare disruptions. There is also a need for more research to help fill the gaps in our knowledge. Unfortunately, the amount of research conducted on the negative consequences of their impact on animal organisms is many times smaller than that of humans, despite the great richness and diversity of the fauna. Undoubtedly, the concentrations of estrogens present in the environment are alarming and can have far-reaching consequences for the health of animals. Particular attention should be paid here to the mechanisms of estrogen accumulation both in the environment and in animal organisms, along with the levels of the trophic chain, and potential interactions with other compounds present in the environment.

Equally alarming as the lack of complete knowledge on the negative effects of estrogens on animal health is the significant difficulty in removing estrogens present in the environment and the fact that the relevant technologies are still largely under development.

All these factors only confirm the strong need of defining estrogens as emerging contaminants and the need to focus science on the threat they currently pose.

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