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Review article

Environmental impact of estrogens on human, animal and plant life: A critical review

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ABSTRACT

Background: Since the inception of global industrialization, steroidal estrogens have become an emerging and serious concern. Worldwide, steroid estrogens including estrone, estradiol and estriol, pose serious threats to soil, plants, water resources and humans. Indeed, estrogens have gained notable attention in recent years, due to their rapidly increasing concentrations in soil and water all over the world. Concern has been expressed regarding the entry of estrogens into the human food chain which in turn relates to how plants take up and metabolism estrogens.
Objectives: In this review we explore the environmental fate of estrogens highlighting their release through effluent sources, their uptake, partitioning and physiological effects in the ecological system. We draw attention to the potential risk of intensive modern agriculture and waste disposal systems on estrogen release and their effects on human health. We also highlight their uptake and metabolism in plants.
Methods: We use MEDLINE and other search data bases for estrogens in the environment from 2005 to the present, with the majority of our sources spanning the past five years. Published acceptable daily intake of estrogens (μg/L) and predicted no effect concentrations (μg/L) are listed from published sources and used as thresholds to discuss reported levels of estrogens in the aquatic and terrestrial environments. Global levels of estrogens from river sources and from Waste Water Treatment Facilities have been mapped, together with transport pathways of estrogens in plants.
Results: Estrogens at polluting levels have been detected at sites close to waste water treatment facilities and in groundwater at various sites globally. Estrogens at pollutant levels have been linked with breast cancer in women and prostate cancer in men. Estrogens also perturb fish physiology and can affect reproductive development in both domestic and wild animals. Treatment of plants with steroid estrogen hormones or their precursors can affect root and shoot development, flowering and germination. However, estrogens can ameliorate the effects of other environmental stresses on the plant.
Conclusions: There is published evidence to establish a causal relationship between estrogens in the environment and breast cancer. However, there are serious gaps in our knowledge about estrogen levels in the environment and a call is required for a world wide effort to provide more data on many more samples sites. Of the data available, the synthetic estrogen, ethinyl estradiol, is more persistent in the environment than natural estrogens and may be a greater cause for environmental concern. Finally, we believe that there is an urgent requirement for inter-disciplinary studies of estrogens in order to better understand their ecological and environmental impact.

Contents

Abbreviations: E1, estrone; E2, estradiol; 17β-E2, 17β-estradiol; 17α-E2, 17α-estradiol; E3, estriol; EE2, ethinyl estradiol; CAFOs, concentrated animal feeding operations; WWTPs, waste water treatment plants; MSH, mammalian sex hormones; CAT, catalase; POX, peroxidase; MSTPs, municipal sewage treatment plants; GLU, glucuronide; SUL, sulfate; STPs, sewage treatment plants; BW, body weight; PNEC, predicted-no-effect concentration; NOEL, no-observed-adverse-effect; JECFA, Joint Expert Committee on Food Additives; ADI, average daily intake; ROS, reactive oxygen species; SOD, superoxide dismutase; CAT, catalase; GPX, guaiacol peroxidase; AsA-GSH, ascorbate glutathione; APX, ascorbate peroxidase; MDHAR, mono dehydro ascorbate reductase; DHAR, dehydroascorbate reductase; GR, glutathione reductase; AsA, ascorbate; GSH, glutathione; VTG, vitellogenin; IOP, intraocular eye pressure; HRT, hormone replacement therapy.

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1. Introduction

Estrogens are biologically active hormones that are derived from cholesterol and released by the adrenal cortex, testes, ovary and placenta in humans and animals. Estrogenic compounds have also been found in plants (Hamid and Eskicioglu, 2012; Ying et al., 2002). Steroid estrogens can be classified as natural or synthetic hormones (Fig. 1) and can act as endocrine disrupting chemicals (EDCs).

Natural steroidal estrogens (also known as the C18 steroidal group) share the same tetracyclic molecular framework comprising four rings, one phenolic group, two cyclohexane and one cyclo-pentane ring (Fig. 1). Structural differences within the C18 group lie in the configuration of the D-ring at positions C16 and C17. For example, estrone (E1) has a carbonyl group on C17, 17β-estradiol (E2) has a hydroxyl group on C17, whilst estriol (E3) has two alcohol groups on C16 and C17 (Fig. 1). The C17 hydroxyl group of the E2 can either point downward or upward on the molecular plane, forming either the α- or β-compound. Conjugated estrogens, which are also potential environmental hazards, are formed by esterification of free estrogens by glucuronide and sulfate groups at the position(s) of C3 and/or C17 (Hamid and Eskicioglu, 2012; Khanal et al., 2006).

Understanding the physiochemical properties of steroidal estrogens compounds is crucial in order to resolve their fate in soil and water systems. The distribution of organic pollutants between water and other natural solids are often considered as a partitioning process between the aqueous and organic phase. The water partition coefficient (K_{ow}), is the ratio of the concentration of a compound in n-octanol and water under equilibrium conditions at a particular temperature. Compounds with a high molecular weight and a high log K_{ow} of >5 are easily adsorbed to sediments and can be primarily removed by coagulation. Estrogens are expected to be absorbed onto the solid phases due to their significant log K_{ow} (Pal et al., 2010). Accordingly, among the estrogens E2 has the highest hydrophobicity but all steroidal estrogens are moderately hydrophobic (log $K_{ow} = 2.4$–4.0), nonvolatile (vapor pressure 9×10^{-13}–3×10^{-8} Pa), weak acids ($pK_a = 10.3$–10.8) (see Table 1). These coefficients including K_d can be used to evaluate the fate of the organic compounds during experiments, thus avoiding an expensive and time-consuming analysis. Furthermore, they provide a calculation method to estimate the percentage of a substance being absorbed onto solid phase, which is finally discharged to the environment, and that which is dissolved in the liquid phase (Carballa et al., 2008).

Generally, unconjugated estrogens or free estrogens are not very soluble in water; EE2 is the least soluble. At pH 7, the order of aqueous solubility was E1 (one OH group) to E2 (two OH groups) and then EE2 with the added ethinyl groups at 17α-position on the D ring; solubility appeared to be the same at pH 4 and 7. However, solubility can be pH-dependent because, for example, at pH 10, relative solubility of estrogens are higher (Shareef et al., 2006).

The world's human population of about 7 billion discharges approximately 30,000 kg/yr. of natural steroidal estrogens (E1, E2, and E3) and an additional 700 kg/yr. of synthetic estrogens (EE2) solely from birth control pill practices. However, the possible release of estrogens to the environment from livestock is much higher. For example, in the United States and European Union, the annual estrogen discharge by livestock, at 83,000 kg/yr., is more than twice the rate of human discharge. Indeed, possible causal relationships have been established between concentrated animal feeding operations (CAFOs) and the detection of estrogens in the aquatic environment (Shrestha et al., 2012). Clearly, natural estrogens in animal and human waste pose a serious risk to the environment. This risk is heightened by the application of animal manure or sludge bio-solids to agriculture lands, being an alternative nutrient source for organic farming, a widely adopted practice in modern agriculture (Xuan et al., 2008). Indeed, application of animal manure to agricultural land has been identified as a main source of estrogens in the environment (Arnon et al., 2008).

Given the serious threat posed by estrogens as pollutants, our aim, here, is to provide a comprehensive account of their environmental impact for human and eco-environmental health perspectives. We have carried out an exhaustive search of the published literature and paid

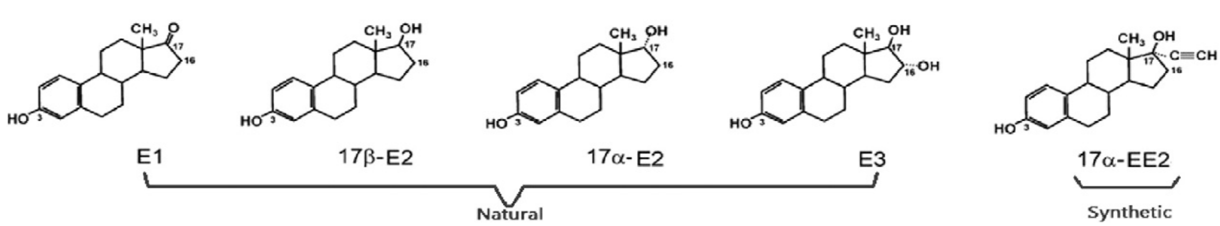

Fig. 1. Chemical structure of natural and synthetic estrogenic compounds. Key: E1, estrone; 17β-E2, 17β-estradiol; 17α-estradiol; E3, estriol; 17α-EE2, ethinyl estradiol.