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Abstract

Several environmental chemicals are classified as endocrine-disrupting chemicals (EDCs). Many of them have an impact on reproductive functions and sex hormones because of their estrogenic and/or antiandrogenic properties. Phthalates and bisphenol A (BPA) are two well-known EDCs. They are abundant in the environment. Phthalates are usually classified as antiandrogens, whereas BPA is considered as estrogen-like EDC and xenoestrogen. Other than their endocrine-disrupting effects, these two chemicals are also known to have genotoxic and epigenetic effects. Besides, they are hepatotoxic and have substantial effects on other organs/systems (thyroid, kidney, neuroendocrine system, immune system, etc.). In this chapter, we will mainly focus on the toxic effects of different phthalate esters and BPA by discussing their availability in the environment, mechanism and mode of actions, their biotransformation and reproductive effects, and their effects on other systems (hepatic, renal, etc.). Besides, we discuss epidemiological studies that are conducted to reveal their effects on the reproductive and endocrine systems. This chapter provides the readers a compact piece of knowledge on these abundant substances and helps them to understand the action of these substances at the molecular and cellular levels.

Keywords: endocrine-disrupting chemical, antiandrogen, xenoestrogen, phthalate, bisphenol A

1. Introduction

Exposure to environmental chemicals, particularly in early life, is among the substantial risks for developmental programming of different diseases in adult life of humans. In a report by
World Health Organization (WHO), it was estimated that more than 13 million deaths were caused by environmental exposures each year. Moreover, this report also proposed that nearly one third of mortality and morbidity can be due to environmental causes in underdeveloped or developing countries [1].

Many environmental exposures to different chemical, physical, or biological agents can interact with genetic and epigenetic mechanisms and affect the normal growth and development. Among those exposures, endocrine-disrupting chemicals (EDCs) are of particular concern, as humans are abundantly exposed to these chemicals by various means in every period of life. According to the U.S. Environmental Protection Agency (EPA), an EDC was defined as “an exogenous agent that interferes with synthesis, secretion, transport, metabolism, binding action, or elimination of natural bloodborne hormones that are present in the body and are responsible for homeostasis, reproduction, and developmental process” [2]. Several well-known environmental chemicals are classified as EDCs. Many of them act on reproductive functions because of their estrogenic and/or antiandrogenic properties.

In the present chapter, we will mainly focus on the toxic effects of different phthalate esters and bisphenol A (BPA), which are the most abundant environmental chemicals. We will discuss their availability in the environment, mechanism and mode of actions, biotransformation, and effects on reproductive systems and other organs (hepatic, renal, etc.) in different periods of life. Besides, we will address the epidemiological studies that are conducted on these chemicals.

2. Availability of endocrine disrupting chemicals in the environment

EDCs are available in polyvinyl chloride (PVC) plastics, polycarbonate materials (type 7 plastics), epoxy resins, medical devices [intravenous (i.v.) bags, dialysis bags, surgical implants, dental fillings sealants], pharmaceuticals (enteric coatings of pharmaceutical pills and nutritional supplements), consumer products (make-up products, fragrances, nail polish, lotions, creams, baby products, soaps, liquid soaps shampoos, conditioners, hair sprays), children’s toys, children products (modeling clay, waxes, paints), printing inks, paints, household products (detergents, softeners, surfactants), construction materials (including floorings and PVC windows, wood floor finishes, cements, caulking in buildings), insulating fluids (transformer oils) for transformers and capacitors, lubricating oils, stabilizing additives in flexible PVC coatings of electrical cables and electronic components, textiles (footwear, raincoats, picture printed shirts), vacuum pump fluids, pesticides (insecticides), and flame retardants and, most importantly, in food (packaging materials and in the inner lining of food cans) [3–5].

3. Classification of EDCs

From a toxicological perspective, EDCs can be classified according to their sources or their modes of action.
In the first classification, EDCs can be grouped as [6, 7]:

a. natural (e.g., phytoestrogen: genistein and coumestrol) and
b. synthetic [e.g., phthalates, BPA, polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins; dichlorodiphenyltrichloroethane (DDT), vinclozolin, and diethylstilbestrol (DES)] compounds.

In the second classifications, EDCs can be classified as [8, 9]:

a. EDCs that affect reproductive system
b. EDCs that affect pancreas
c. EDCs that affect thyroid
d. EDCs that effect Central nervous system
e. EDCs that affect other systems

The significant effects of EDCs on hormones are suggested to be:

a. Increasing or decreasing effect on the production of hormones (these substances may mimic naturally occurring hormones such as estrogens, androgens, or thyroid hormones or they may potentially cause the overstimulation of hormonal pathways within the body),
b. Increasing or decreasing effect on the transportation of hormones,
c. Increasing or decreasing effect on the metabolism of hormones,
d. Increasing or decreasing effect on the elimination of hormones,
e. Agonistic or antagonistic effect on the target cells of the hormones (by binding to a receptor within a cell and blocking the functions of endogenous hormones; i.e., acting as antiestrogens and antiandrogens), and
f. Altering the homeostatic systems of the organisms and causing their miscommunication or irresponsiveness to their own physiology and the environment.

4. Modes/mechanisms of actions of EDCs

a. Effect on hormone, nuclear, and nonnuclear receptors: Our understanding of the mechanisms by which EDCs exert their effect has grown. EDCs were originally thought to exert actions primarily through nuclear hormone receptors [i.e., estrogen receptors (ERs), androgen receptors (ARs), progesterone receptors, thyroid receptors (TRs), and retinoid receptors]. However, recent basic and mechanistic researches show that the underlying mechanisms of their toxicity are much wider than originally envisioned. Thus, other than nuclear receptors, EDCs may also act via nonnuclear steroid hormone receptors (e.g., membrane ERs), nonsteroid receptors (e.g., neurotransmitter receptors such as serotonin...

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