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Review

A review on endocrine disruptors and their possible impacts on human health

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ABSTRACT

Endocrine disruption is a named field of research which has been very active for over 10 years, although the effects of endocrine disruptors in wildlife have been studied mainly in vast since the 1940s. A large number of chemicals have been identified as endocrine disruptors and humans can be exposed to them either due to their occupations or through dietary and environmental exposure (water, soil and air). Endocrine disrupting chemicals are compounds that alter the normal functioning of the endocrine system of both humans and wildlife. In order to understand the vulnerability and risk factors of people due to endocrine disruptors as well as the remedies for these, methods need to be developed in order to predict effects on populations and communities from the knowledge of effects on individuals. For several years there have been a growing interest on the mechanism and effect of endocrine disruptors and their relation with environment and human health effect. This paper, based on extensive literature survey, briefly studies the progress mainly in human to provide information concerning causative substances, mechanism of action, ubiquity of effects and important issues related to endocrine disruptors. It also reviews the current knowledge of the potential impacts of endocrine disruptors on human health so that the effects can be known and remedies applied for the problem as soon as possible.

Contents

Abbreviations: APE, alkylphenol ethoxylate; AR, androgen receptor; BaP, benzo[a]pyrene; BFR, brominated flame retardants; BPA-bisphenol A, (BPA); CD36, cluster of differentiation 36; CNS, central nervous system; DBP, di-n-butyl phthalate; DDD, 1,1-dichloro-2,2-di(chlorophenyl)ethane; DDT, 1,1,1-trichloro-2,2-di(chlorophenyl)ethane; DEHP, di(2-ethylhexyl) phthalate; DES, diethylstilbestrol; DIDP, diisodecyl phthalate; DNA, deoxyribonucleic acid; DNHP, di-n-hexyl phthalate; DnOP, di-n-octyl phthalate; ED, endocrine disruptor; EDC-, endocrine disrupting chemicals; ER, estrogen receptor; EPA, U.S. Environmental Protection Agency; FD&C, federal food drug and cosmetic act; FFA, free fatty acid; HBCDD, hexabromocyclododecane; HCB, hexachlorobenzene; IL-1β, interleukin 1 beta; IL-10, interleukin 10; IRS-1, insulin receptor substrate 1; NAT, N-acetyltransferase; NIEHS, National Institute of Environmental Health Sciences; NIS, sodium/iodide symporter; NP, nonylphenol; MFO, mixed functional oxidase; PAH, polycyclic aromatic hydrocarbon; PBB, polybrominated biphenyls; PBDE, polybrominated diphenyl ethers; PCB, polychlorinated bisphenols; PCDF, polychlorinated dibenzofuran; PCOS, polycystic ovary syndrome; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonate; POP, persistent organic pollutant; PPAR, peroxisome proliferator activated receptor; PTU, 6-propyl-2-thiouracil; STP, sewage treatment plant; T3, triiodothyronine; T4, thyroxine; TCDD, tetrachlorodibenzo-p-dioxin; TGF-β, transforming growth factor beta; TNF-α, tumor necrosis factor alpha; TPO, thyroperoxidase; TR, thyroid receptor; TSH, thyroid stimulating hormone; WHO, World Health Organization; UNEP, United Nations Environment Programme.

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1. Introduction

1.1. What are endocrine disruptors?

An endocrine-disrupting compound has been defined by the U.S. Environmental Protection Agency (EPA) as 'an agent that interferes with the synthesis, secretion, transport, binding, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development and/or behaviour' (Kavlock et al., 1996). Simplified, this means that endocrine disruptors are chemicals, or chemical mixtures, that interfere with normal hormone function.

EDCs are highly heterogeneous (Blumberg, 2009; Grun, 2010) and can be classified in the following two ways.

A. They can be classified in two categories (Diamanti-Kandarakis et al., 2009):
   (i) Those that occur naturally.
      • Natural chemicals found in human and animal food (e.g. phytoestrogen: genistein and coumestrol) and
   (ii) Those that are synthesized. These can be further grouped as follows:
      • Synthetic chemicals used as industrial solvents or lubricants and their byproducts (e.g. polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins)
      • Plastics (e.g. bisphenol A (BPA))
      • Plasticizers
      • Pesticides (e.g. dichlorodiphenyltrichloroethane (DDT))
      • Fungicide (e.g. vinclozolin) and
      • Some pharmaceutical agents (e.g. diethylstilbestrol (DES)).
B. The EDCs can also be grouped according to their origins (Caliman and Gavrilescu, 2009):
   (i) Natural and artificial hormones (e.g. fitoestrogens, 3-omega fatty acids, contraceptive pills and thyroid medicines).
   (ii) Drugs with hormonal side effects (e.g.naproxen, metoprolol and clofibrate).
   (iii) Industrial and household chemicals (e.g.phthalates, alkylphenoletoxilate detergents, fire retardants, plasticizers, solvents, 1,4-dichloro-benzene and polychlorinated bis-phenols (PCBs).
   (iv) Side products of industrial and household processes (e.g., polycyclic aromatic hydrocarbons (PAHs), dioxins, pentachlorobenzene).

However, from different observations, endocrine disruptors can also be categorized into three groups apart from the classification based on occurrence according to Gore, et al.

(i) *Pesticides*: Pesticides are usually designed in such a way so that they can be highly sensitive toward the reproductive and neural systems of the organisms. But the similarity of these processes with normal human physiological system indicates that these chemicals can also affect normal human body. The pesticides that are used commonly include DDT and chlorpyrifos (Gore et al., 2014).

DDT has a long history as an endocrine disruptor. The compound was once used randomly as a pesticide in the agricultural sectors, in production of crops and livestock, in household, gardens, public places and institutions, but because of its hazardous nature it was banned few years back. However, the compound is still in use in some countries. DDT can interfere with thyroid, estrogen, androgen, rennin-angiotensin, insulin and neuroendocrine systems which can directly influence the reproductive, cardiovascular and metabolic systems of human body. These have obviously made it one of the most potential candidates of endocrine disruptors (Gore et al., 2014).

Organophosphorus pesticides are the most commonly used insect killer and chloropyrifos is a unique example of this class of insecticides. The insecticide is used in both in household and agriculture sectors to control pests such as cockroaches, flies, termites, fire ants, mosquitoes. However, it is confirmed from studies that the compound is highly toxic since it has a huge effect on nervous systems (Gore et al., 2014).

(ii) *Chemicals in products*: EDC is present in the products that we use in our day to day life, starting from the products that include children products, electronics, personal care products, textile/clothing to building contact materials. However, in most of the cases, we are not aware of these facts since it is not always included in their chemical compound list. This is a matter of concern since there is a huge possibility of these chemicals to be released into the environment and come in contact with us. Also in the children's product where EDCs are mainly found, it is always seen that the children might pick up those products and put them into their mouth. Apart from these, EDCs are frequently found in personal care products starting from toothpaste, the products that we apply on our skin, soaps, in which antimicrobial agents are used. However for ease of understanding we may subclass this class into two groups: children's product and electronics (Gore et al., 2014).

Lead is a natural compound and is being regularly used in mining, smelting, refining, leaded petrol (gasoline), lead-acid batteries, paints, jewellery, children's products and in many other products. The children are the potential candidates of lead poisoning, since the amount they ingest per unit body weight is obviously higher, they may ingest high quantity of them and also they do not have a fully developed blood-brain