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REVIEW PAPER

THE CHALLENGE OF ENDOCRINE DISRUPTING COMPOUNDS (EDCS) IN THE CURRENT ENVIRONMENT FOR PUBLIC HEALTH*

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Abstract

The article presents the current knowledge on the health risks concerning the exposure to Endocrine Disrupting Compounds (EDCs) present in the environment. The pollution of the natural environment with chemical compounds of industrial origin or from the development of new technologies is inherently linked with the use of substances harmful to the human health, such as polychlorinated biphenyls, dioxins, pesticides, fungicides, herbicides, components of plastic products, pharmaceutical drugs, agents with antimicrobial properties and flame retardants. These compounds are classified as EDCs, a group of substances able to modulate the activity of the endocrine system and contributing to the development of reproductive anomalies in both human and animal organisms. A major source of EDCs exposure for people is food and drinking water, which become contaminated when chemical substances spread with precipitation, landfill leachate, and industrial wastewater. The environment has long been treated as a disposal site for substances classified as waste or the byproducts of production processes by man and his economy. One of the dangers people have become aware of in the last decade are endocrine disrupting compounds. As the name would suggest, this type of environmental pollution affects the organism's endocrine system and what is even more detrimental, disrupts the endocrine balance. They can, imperceptibly and outside of the victim's consciousness, affect the develop-

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ment of people and other living organisms from the moment of conception, causing irreversible damage. Thus, there exists a need to monitor, analyze and limit the existence of dangerous chemical compounds such as EDCs in water, soil, air and food.

Keywords: endocrine disrupting compounds (EDCs), environment, health consequences, public health.

INTRODUCTION

Endocrine disrupting compounds are chemical substances causing disorders of the endocrine system, which are present in the environment and food normally or as a contaminant. (Soto, Sonnenschein 2010, Rutkowska et al. 2015).

There are various definitions in literature that outline the nature of EDCs. And thus, the World Health Organisation (WHO) defines the EDCs as "exogenous substances or mixtures that alter the function(s) of the endocrine system and consequently cause adverse effects in an intact organism, its progeny, or (sub)populations" (Damstra et al. 2002), while the European Union's (EU) definition states that "EDCs are exogenous substances that cause adverse health effects in an intact organism, or its progeny, secondary to changes in endocrine function. A potential EDC is a substance that possesses properties that might be expected to lead to endocrine disruption in an intact organism" (European Commission 1996). As far as the Environmental Protection Agency (EPA, USA) is concerned, EDCs are "exogenous agents that interfere with the synthesis, secretion, transport, metabolism, binding action, or elimination of natural blood-borne hormones that are present in the body and are responsible for homeostasis, reproduction, and developmental processes" (Kavlock et al. 1996).

EDCs include, e.g., phytoestrogens, metalloestrogens, bisphenol A, phthalates, dioxins, pharmaceuticals, hormones, steroids, polychlorinated biphenyls and pesticides, detergents and industrial chemicals (Ortega et al. 2012, Rutkowska et al. 2015, Dawid et al. 2016).

EDCs existed and continue to exist and there is no reason to believe that their emission to society, which has detrimental effects on the health of people and animals, has ceased. Every day, we are exposed to them while eating, breathing polluted air and drinking contaminated water (Langauer-Lewowicka, Pawlas 2015, Rutkowska et al. 2015, Ochwanowska et al. 2019, Bąk-Badowska et al. 2021).

Possible health consequences of exposure to EDCs are determined by a multitude of factors. Examples include the source of exposure or the age of the person suffering the exposure. The younger the body, the more susceptible it is to their effects. The subjection of a fetus in a mother's womb to EDCs may cause development anomalies and epigenetic changes. It ought to be noted that endocrine disruptors are active in concentrations smaller

than the toxic dose. Moreover, it has to be taken into consideration that a long period of time can pass between the exposure to the compounds and the appearance of the first symptoms of disease. The human body is not usually just exposed to one substance, but compounds of different substances which may act synergically or antagonistically with each other (Faniband et al. 2014, Mitro et al. 2015, Rutkowska et al. 2015, Chmielewski et al. 2020*b*, Christensen et al. 2021). Table 1 outlines sources of EDCs (Włodarczyk-Makuła 2019).

Table 1

Sources of EDCs (modified)

Source	Application	Compound/Substance
Surface runoff from agricultural lands	chloroorganic and organophosphate pesticides and insecticides	DDT and isomers, aldrin, dieldrin, lindane, atrazine, permethrin and their metabolites
Surface runoff from livestock farming land	pharmaceutical products used in veterinary medicine	natural and synthetic hormones (estrone, estradiol, ethinyl estradiol, testosterone)
Landfill leachate	chemical industry	organochlorines: PCDD, PCB
Ports	substances preventing algae growth	tributyltin
Urban and industrial wastewater	surfactants	alkylphenols nonylphenol
Chemical industry wastewater	plasticizers	dibutyl phthalate, benzyl butyl phthalate
Pulp industry wastewater	raw material for production plant material	phytoestrogens isoflavones

PRESENCE OF EDCS IN THE ENVIRONMENT

In the recent years, the identification and determination of the level of water contamination by EDCs have become the subject of even more in-depth research. Conventional wastewater treatment plants are not fully adjusted to complete elimination of these compounds; therefore, EDCs can be found in wastewater, surface waters and even in drinking water (in quantities of ng l^{-1} or μg l^{-1}).

Amongst chemicals known as EDCs, there are polychlorinated biphenyls, dioxins, perfluoroalkylated substances, solvents, phthalates (Shea 2003), bisphenols BPA (Howdeshell et al. 1999), dichlorodiphenyldichloroethylene (DDE) (Longnecker 2002), organophosphate and chloroorganic pesticides (Gore 2002) and polybrominated diphenyl ethers (PBDE) – Chevrier et al. (2010).

Both surface and ground waters are the source of water supply for inhabitants of towns and villages, and the problem of limiting the load of those micro-contaminations in treated wastewater has become all the more valid (Tadeo et al. 2012).

EDCs spread into the environment mostly from anthropogenic sources. The effectiveness of ECD removal in classic processes of sewage treatment results in their presence in both surface and ground waters. EDCs are also spread into the environment as a result of landfill burning and the disposal of medical waste. In turn, the presence of those compounds in waters causes disorders in the development of water habitat populations, which also affects the health of animals and people (Molins-Delgado et al. 2016, Ismail et al. 2017, Song et al. 2018, Cao et al. 2020, Chmielewski et al. 2020, 2020*a*).

EDCs identified in aquatic habitats are a significant threat to the organisms inhabiting them, to animals that drink contaminated water and feed on those organisms as well as to people who are at the end of the food chain (Esteban et al. 2014, Kudlek et al. 2015).

The increase in the consumption of pharmaceutical drugs has further exacerbated the problem of pharmaceutical compounds present in water habitats (Gworek et al. 2020). Studies have shown that both surface and ground waters suffer the pollution by trace levels of pharmaceuticals (Kudlek et al. 2015). Table 2 shows selected concentrations of pharmaceutical products found in environmental samples.

Table 2

Pharmaceuticals determined in environmental samples

Pharmaceutical	Specimen component analysed/ Analyte	Sample origin	Concentration	Reference
Analgesic and anti-inflammatory	ibuprofen	river water	0.087 μg l^{-1}	Winkler et al. (2001)
		surface waters	0.1-1.0 μg l^{-1}	Buser et al. (1998)
		raw wastewater	143 μg l^{-1}	Santos et al. (2005)
Antibiotics	Sulfamethoxazole	raw wastewater	1,464 +/-203 ng l^{-1}	Luczkiewicz et al. (2013)
	roxithromycin		161+/-0 ng l^{-1}	
	trimethoprim		482+/-116 ng l^{-1}	
	clarithromycin		1,416+/-401 ng l^{-1}	
Antiepileptic drugs	carbamazepine	raw wastewater	2.1 μg l^{-1}	Santos et al. (2005)
Contrast agent	iopromide	raw wastewater	27.0 μg l^{-1}	Felis et al. (2005)
	iopamidol		2.20 μg l^{-1}	

Source: the authors.

EFFECT OF EDCS ON HEALTH

The detrimental effect of EDCs on the human health is the subject of a multitude of scientific reports. Those conclude that they contribute to many illnesses and disabilities to a significant degree. (Trasande et al. 2015, Chmielewski et al. 2016, 2019, 2020, 2020*a*, 2020*b*).

Studies show that EDCs were found in the human body in the adipose tissue, as well as in body fluids, such as amniotic fluid, serum, urine, and milk (Rudkowski 2013, Rutkowska et al. 2015, Quinete et al. 2016, Kulik-Kupka et al. 2017).

These EDCs have been shown to interfere with a variety of endocrine pathways, including oestrogen (Takeuchi et al. 2005), androgen (Takeuchi et al. 2005), thyroid (Zoeller et al. 2005), retinol (Colborn 2003), aryl hydrocarbon, and peroxisome proliferator-activated receptor pathways (Desvergne et al. 2009).

EDCs are chemical compounds that show an ability to interact with the endocrine system and modulate its activity. Whether a compound is classified as an EDC depends on the way they affect living organisms rather than their chemical structure (Soto et al. 1995).

EDCs may cause developmental disorders, endocrine system disorders, disruption of reproduction, increased risk of developing cancers, disorders of the activity of the immune and nervous systems, obesity and changes in behaviour (Ćwiek-Ludwicka, Ludwicki 2014, Langauer-Lewowicka, Pawlas 2015, DeWitt, Patisaul 2018, Chmielewski et al. 2020*c*, 2020*d*, Miranowicz-Dzierżawska 2021, Zapór 2021).

Table 3 presents an evaluation of relationships between EDC exposure and possible health outcomes (Trasande et al. 2015).

Epidemiological research shows that the exposure of an organism to EDCs is related to the occurrence of diabetes, problems with the cardiovascular and nervous system, obesity and even cancer (Vandenberg et al. 2013, Nagle et al. 2015).

Chemical substances affecting the endocrine system which disrupt the oestrogen pathway, including bisphenol A (BPA), synthetic oestrogen, diethylstilboestrol (DES), 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), constitute a potential risk factor contributing to the increase in the incidence of breast cancer (Jenkins et al. 2012, Tomczyńska et al. 2016).

EDCs, which include BPA and its halogen derivatives which have been found in human serum, are included as factors affecting the development of ovary cancer. Literature data give information on the effect of BPA on the development of cancer cells in the ovaries (Hoffmann et al. 2018).

Table 4 shows the effect of pesticides on the functioning of the endocrine system.

Table 3

Evaluations of Exposure-Outcome Relationships (modified)

Exposure	Outcome	Probability of causation (%)
PBDEs	IQ loss and intellectual disability	70-100
Organophosphate pesticides	IQ loss and intellectual disability	70-100
DDE	childhood obesity	40-69
DDE	adult diabetes	20-39
Di-2-ethylhexylphthalate	adult obesity	40-69
Di-2-ethylhexylphthalate	adult diabetes	40-69
BPA	childhood obesity	20-69
PBDEs	testicular cancer	0-19
PBDEs	cryptorchidism	40-69
Benzyl and butyl phthalates	male infertility, resulting in increased assisted reproductive technology	40-69
Phthalates	low t, resulting in increased early mortality	40-69
Multiple exposures	ADHD	20-69
Multiple exposures	autism	20-39

Abbreviation: ADHD, attention-deficit hyperactivity disorder.

Table 4

Select pesticides causing the disorders of the endocrine system

Type of pesticide	Biological effects	References
Permethrin	thyroid activity disruption, testosterone synthesis disruption, effect on the process of spermatogenesis	Saito et al. (2017)
Dichlorodiphenyl--trichloroethane (DDT)	breast tumours, decrease of sperm quality, precocious puberty	Soto, Sonnenschein (2015)
Carbendazim	androgenic action, effect on the hypothalamic-pituitary-gonadal axis, changes in hormone levels [mainly: testosterone, lutropin (LH), follicle-stimulating hormone (FSH)], lipid metabolism disorder in the liver, dysbiosis in the intestine	Liu et al. (2019)
Vinclozolin	androgenic action, decrease in estradiol concentration, changes in sexual behaviour, changes in the methylation of the genetic material in sperm cells	Nilsson et al. (2018)

Source: the authors.

CONCLUSION

The civilization and industrial growth entail an uncontrolled increase in the emission of EDCs into the environment, related to human activity. These compounds are shown by studies to have the ability to modulate the activity of the endocrine system while also contributing to the development of reproductive anomalies. Properties of these compounds, which are toxic to both humans and animals, make them an issue of interest for those engaged in what is widely understood as public health policy. There is no doubt that EDCs should be monitored in terms of their spread in the environment, and in the future, the object of interest of government authorities responsible for environmental protection and disease prophylaxis in general public.

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