JMBFS
Journal of Microbiology, Biotechnology and Food Sciences
International peer-reviewed scientific online journal

Published by Faculty of Biotechnology and Food Sciences

THE IMPACT OF ENDOCRINE DISRUPTIONS ON ANIMAL AND HUMAN ORGANISM

Kateryna Vanivska[1], Lucia Dianová[1], Marko Halo[1], Nikola Štefunková[1], Michal Lenický[1], Tomáš Slanina[1], Filip Tirpák[1,2], Tomáš Jambor[1], Norbert Lukáč[1], Robert Stawarz[3], Klaudia Jaszcza[4], Peter Massányi[1,3]

Address(es): Mgr. Kateryna Vanivska,
[1] Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Institute of Applied Biology, Trieda Andreja Hlinku 2, 94976 Nitra, Slovak Republic.
[2] University of Missouri, S141 ASRC, 920 East Campus Drive, Columbia, MO 65211-5300, USA.
[3] University of the National Education Commission, Krakow; Faculty of Exact and Natural Sciences, ul. Podchorążych 2, 30-084 Kraków, Poland.
[4] University of Agriculture in Krakow, Faculty of Animal Science, Department of Animal Physiology and Endocrinology, al. Mickiewicza 24/28, 30-059 Krakow, Poland.

*Corresponding author: vanivska.katya@gmail.com; xvanivska@uniag.sk

https://doi.org/10.55251/jmbfs.11855

ARTICLE INFO

Received 26. 9. 2024
Revised 27. 2. 2025
Accepted 11. 3. 2025
Published 1. 6. 2025

Regular article

OPEN ACCESS

ABSTRACT

Endocrine disruptors (EDCs) are chemicals that interfere with hormonal balance in both animals and humans, potentially leading to a wide range of health problems. This review explores how endocrine disruptors function, their sources, and their effects on human and animal health, including their impact on the reproductive system, metabolism, neuroendocrine function, and cancer progression. The aim of this review is to describe the mechanisms of action of endocrine disruptors, such as their interactions with hormonal receptors, induction of epigenetic changes, and effects on cell signaling pathways. Additionally, this work examines how endocrine disruptors influence physiological processes, evaluates the impact of nanoparticles on endocrine disruption, and discusses the body's defense mechanisms against these agents. Among the most well-known EDCs are bisphenol A (BPA) and phthalates, which have been linked to a wide range of health conditions. Recent studies have also highlighted the risks posed by nanoparticles, including microplastics and nanoplastics, which amplify endocrine disruption and disturb hormonal balance. Future research should focus on identifying molecular pathways affected by EDCs to mitigate their negative impact on the endocrine system.

Keywords: endocrine disruptors, endocrine system, hormones, nanoparticles

INTRODUCTION

Endocrine-disrupting chemicals (EDCs) are synthetic or natural substances that exert their effects through multiple mechanisms of action in the body. Some EDCs are capable of acting as 'hormone mimics,' deceiving organisms into thinking they are hormones. Others interfere with the body's natural hormones to fulfill their function. By changing the way hormones are made, metabolized, or stored in our bodies, some EDCs can increase or decrease hormone levels in the blood or even change the way that organism respond to different hormones **(Monneret, 2017; Yawer *et al.*, 2020)**.
The effects of endocrine disruptors are already evident at very low doses and exposure to them can have lifelong effects, which can lead to consequences for future generations. Endocrine disruptors are widely present in various industries, including manufacturing, food production, consumer goods, and environmental pollutants, as a result of their extensive use **(Diamanti-Kandarakis *et al.*, 2009)**.

THE IMPORTANCE OF THE ENDOCRINE SYSTEM IN THE ORGANISM

The endocrine system is one of the most important structures of the animal and human body, responsible for the production of hormones. Hormones are chemical substances that transmit well-defined signals to the body and thereby regulate the functioning of its various organs and systems **(Campbell & Jialal, 2024)**.
The endocrine system consists of central and peripheral components that work together as a unified system. The central endocrine organs are closely related to the organs of the central nervous system and coordinate the activity of other endocrine structures. Peripheral organs have a multifaceted effect on the body, enhance or weaken metabolic processes. There are also organs that combine endocrine function with exocrine function and a separate dissociated endocrine system, which is formed by a large group of isolated endocrinocytes scattered throughout the body's organs and systems **(Campbell & Jialal, 2024; Chrousos, 2007)**.
The central endocrine organs include the pituitary gland, pineal gland, and hypothalamus. The peripheral endocrine organs include the thyroid gland, parathyroid glands, adrenal glands, and prostate. Organs with both endocrine and exocrine functions include the testes, ovaries, and pancreas **(Campbell & Jialal, 2024; Lauretta *et al.*, 2019)**.
Each of these organs produces specific hormones that affect all aspects of the body's overall health and functioning **(Campbell & Jialal, 2024)**.
The main functions of the endocrine system are to regulate metabolism, growth and development, ensure the functioning of the reproductive system, and provide a stress response. The endocrine system supports absolutely all organs and vital functions of the entire body. For optimal health, hormones must be produced in the correct amounts and respond appropriately to physiological changes **(Brück, 1983; Campbell & Jialal, 2024)**.

SOURCES OF ENDOCRINE DISRUPTORS

Endocrine disruptors are chemicals or compounds that disrupt endocrine processes and that can affect the endocrine system. These disruptions lead to different developmental disorders, birth defects or cancer. Endocrine disruptors, which are present in many industrial and household products, prevent the body's natural hormones that regulate behavior, development, fertility, and homeostasis (normal cellular metabolism) from being synthesized, secreted, transported, bound, or excreted **(Anne & Raphael, 2000)**.
Endocrine disruptors are found in many everyday products, including some cosmetics, household chemicals, flame retardant-treated fabrics, food and beverage packaging, fragrances, toys, carpets, and pesticides. Contact with these chemicals can occur through air, food, skin, and water. It is not possible to completely avoid or eliminate EDCs, but it is possible to reduce exposure and the risk of health effects **(Diamanti-Kandarakis *et al.*, 2009)**.

MECHANISMS OF ACTION OF ENDOCRINE DISRUPTORS

The mechanism of action of endocrine disruptors is not entirely comprehended. Through the activation or antagonism of nuclear hormone receptors, EDCs can either promote or impede the metabolism of xenobiotic compounds and naturally occurring steroid hormones. By modifying the proteasome-mediated degradation of nuclear receptors and their coregulators, EDC influences the transcriptional activity of nuclear receptors **(Lee *et al.*, 2013)**.

Researchers have discovered that endocrine disruptors are able to:

- mimic, or partially mimic, naturally occurring hormones in the body, such as thyroid hormones, androgens (male sex steroids) and estrogens (female sex steroids), potentially leading to overstimulation;
- bind to a cell's receptor, similar to the way a key fits into a lock, and prevent the action of the hormone that occurs normally. The body then reacts improperly, and the regular signal is not produced. Anti-estrogen and anti-androgen compounds are two examples of substances that block hormones;
- affect or obstruct the body's natural hormone production or receptor function, for instance by changing the liver's metabolism of these hormones **(Combarnous & Nguyen, 2019)**.

These substances may have early-life impacts that do not show up until far later in life. Furthermore, under certain circumstances, these impacts may endure for several generations **(Duranova *et al.*, 2022; Lee *et al.*, 2013)**.

EFFECTS OF ENDOCRINE DISRUPTORS ON ANIMAL AND HUMAN HEALTH

Reproductive disorders

A combination of genetic factors, lifestyle, and environmental factors is responsible for the decline in fertility. It has been scientifically proven that because of many endocrine disruptors can mimic sex hormones, EDCs have the most negative impact on animal and human reproductive function. Chemicals that disrupt the endocrine system interact with each other, disrupting various endocrine axes, leading to serious dysfunctions of the gonads. Endocrine disruptors have the ability to alter embryonic development by interfering with sex steroid hormones. Synthetic estrogens, phytoestrogens, plasticizers, pesticides, and industrial chemicals are some of the disruptors that show both strong anti-androgenic and weak estrogenic effects. In germ cells, transgenerational epigenetic effects have also been seen, primarily via DNA methylation and epimutation **(Diamanti-Kandarakis *et al.*, 2009; Dutta *et al.*, 2023)**.

It has been determined that endocrine disruptors impede meiosis, follicle formation, and vitality during the development of the ovaries in animals. These substances have the potential to modify somatic cell genetic transcription during the early postnatal phase, delaying puberty. In both male and female, endocrine disruptor exposure might result in infertility issues. Research has connected exposure to endocrine disruptors to testicular dysgenesis, polycystic ovary syndrome, and hypotrophy **(Anne & Raphael, 2000)**.

One of the primary reasons of female infertility is the production of defective oocytes, which can be induced by EDCs aromatase inhibition. Furthermore, exposure throughout critical developmental stages, such as prenatal and neonatal periods, as well as childhood, has a greater impact on the reproductive system than exposure in adulthood **(Diamanti-Kandarakis *et al.*, 2009)**.

Among EDC-mediated male reproductive abnormal conditions are testicular cancer and cryptorchidism. These examples of abnormalities are similar in nature to EDC exposure in women. These negative results in combination with decreased sperm quality illustrate major risk factors for male reproductive health caused by EDC **(Laws *et al.*, 2021)**.

EDCs have an effect on the male reproductive system because they alter steroid hormones, which cause the prostate to develop and the Wolffian ducts to differentiate into the seminal vesicles, vas deferens, and epididymis. EDCs work as inhibitors of the enzymes aromatase and 5α-reductase, which are necessary for the biosynthetic process of estrogen and testosterone from androgens **(Dutta *et al.*, 2023)**.

The evaluation of sperm quality has become a key factor in predicting negative outcomes caused by EDCs. Recent studies on the effects of EDCs have confirmed that pesticide exposure reduces semen volume, increases pH, and alters sperm head morphology. *In vitro* studies associating phthalate exposure to decreased sperm motility in males from infertile couples, have been supported by human research. In addition to phthalates, exposure to bisphenol A affects plasma testosterone levels in both males and females, while hormones such as FSH are reduced, likely due to endocrine-disrupting activity **(Lahimer *et al.*, 2023; Mehrpour *et al.*, 2014)**.

Metabolic disorders

Various studies of diseases that are closely related to the impact of EDCs on metabolic diseases, such as obesity, type 2 diabetes and liver steatosis, are highlighting increasing scientific attention **(Haverinen *et al.*, 2021; Kokkoris & Pi-Sunyer, 2003)**.

It is scientifically established that metabolism occurs at the cellular level. The thyroid gland produces hormones that control the body's daily metabolism by controlling cellular functions. EDCs that are present in pesticides, food additives, plastics, and industrial waste can interfere with normal thyroid function, thereby disrupting metabolic processes **(Stiefel & Stintzing, 2023; Ylli *et al.*, 2000)**.

Research has demonstrated that certain EDCs, such as bisphenol A (BPA), which is present in a variety of consumer products, including water bottles and aluminum cans, disrupt the body's ability to regulate appetite and promote energy storage in adipose tissue **(Dalamaga *et al.*, 2024; Haverinen *et al.*, 2021)**.

EDCs have been shown to increase the expression of enzymes that either metabolize endogenous and exogenous compounds, changing the metabolic pathways by which these enzymes function in the body. EDCs can modify the activity of enzymes whose expression is implicated in the metabolism of steroids and sex hormones at the molecular level, initiating the complementary transcription through attached to basic nuclear receptors **(Dutta *et al.*, 2023; Puche-Juarez *et al.*, 2023)**.

Systematic reviews by Stojanoska *et al.* (2016), Song *et al.* (2016), **Rochester (2013)**, **Rancière *et al.* (2015)** and **Mustieles a Arrebola (2020)** have provided evidence connecting BPA exposure to metabolic syndrome and glucose metabolism issues. Additionally, emerging evidence suggests negative evidence of the impact of BPS on hypertension **(Jiang *et al.*, 2020; Haverinen *et al.*, 2021; Popoviciu *et al.*, 2023)**.

Recent meta-analyses by **Kim *et al.* (2019)** and **Ribeiro *et al.* (2020)** have confirmed a connection between obesity in both children and adults and BPA exposure. Preliminary studies on bisphenol substitutes suggest the same results, though data remain limited. Research by **Liu *et al.* (2019)** showed that BPF has some evidence of an association between obesity in children and adolescents, with stronger association among boys, which may indicate possible sex differences **(Haverinen *et al.*, 2021; Hinault *et al.*, 2023)**.

Neuroendocrine disorders

The endocrine and nervous systems are closely interconnected. The thyroid gland and the generation of thyroid hormones, which are essential for neurological development, are stimulated by the brain. Melatonin and cortisol represent hormones that control stress and sleep, also influence neurological function. These factors emphasize the importance of hormonal balance is for optimal neurological development and behavior **(Gore *et al.*, 2019)**.

However, endocrine-disrupting chemicals, which are present in numerous products are strongly associated with neurological diseases, can seriously damage the brain **(Gore, 2010)**.

The body's homeostatic functions – such as growth, reproduction, metabolism, energy balance, and stress response – are regulated by the central neuroendocrine systems. Signals from the central nervous system, particularly the hypothalamus, initiate these processes, which are subsequently transmitted by neuronal and endocrine effectors. Under normal conditions, the body's ability to respond to the environment is highly influenced by neuroendocrine systems, which provide communication between the brain and peripheral endocrine systems **(Gore, 2010; Patisaul, 2021)**.

Disruptions in neuroendocrine homeostasis due to EDC exposure, particularly during critical developmental stages, can lead to various disorders **(Gore *et al.*, 2019; Kabir *et al.*, 2015)**.

Growing evidence suggests that EDCs negatively affect central neuroendocrine systems. These systems are particularly vulnerable to endocrine disruption because they regulate and respond to hormone signals. Furthermore, since neuroendocrine cells function as neurons, they can rapidly react to external stimuli, including environmental factors. The neuroendocrine circuits within the hypothalamus are thus primed to mediate responses to environmental signals, such as endocrine disruptors. Research on the effects of environmental endocrine disruptors on neuroendocrine systems is becoming increasingly popular, with a major focus on the hypothalamic-pituitary-gonadal system's reproductive axis **(Gore, 2010; Gore *et al.*, 2019)**.

Furthermore, neurotransmitter systems that control neuroendocrine cells can be impacted by endocrine disruptors. Another mechanism of neuroendocrine disruption is the binding of polychlorinated biphenyls to serotonin, dopamine, and noradrenergic receptors. These neurotransmitters influence hypothalamic releasing factors that regulate the pituitary gland **(Ahn & Jeung, 2023; Gore, 2010; Kabir *et al.*, 2015)**.

According to the fact, endocrine disruptors can modify the quantity of specific cells in sexually dimorphic brain nuclei, such as calbindin-positive cells in the rat hypothalamus, leading to detrimental effects on the neuroendocrine system at the cellular level. These disruptions also include behavioral changes, including impairments in reproductive behavior in animals, which can reduce their ability to reproduce and influence mate selection. Such effects have evolutionary and ecological implications. Since the consequences of neuroendocrine disruption may be passed on to future generations, it is crucial to understand how and when these changes occur **(Ahn & Jeung, 2023; Gore, 2010)**.

Oncological diseases

Cancer development results from a complicated interaction of lifestyle, environmental influence, and genetic predisposition. The environment and certain occupations associated with high levels of chemical exposure are particularly linked to two-thirds of all malignant tumors **(Binkowski *et al.*, 2015; Calaf *et al.*, 2020; Madhu *et al.*, 2022)**.

Exposure to various chemicals, including metals, dyes, solvents, and silica, as well as pharmaceuticals such as synthetic estrogens, has been shown to contribute to carcinogenesis. Numerous carcinogens can also act as endocrine disruptors, influencing the initiation and progression of cancer across generations, according to research performed in cell and animal models, as well as findings from recent human studies **(Buoso *et al.*, 2020)**.

In addition to being implicated in the onset of specific malignancies, endocrine disruptors may also contribute to the growth, metastasis, or resistance to treatment of pre-existing cancers **(Monneret, 2017; Yilmaz *et al.*, 2020)**.

In females, exposure to endocrine disruptors has been linked to uterine and ovarian malignancies. Bisphenol A, present in beverage containers, cosmetics, food, and household items, can affect breast tissue and may be transferred from mother to child *in utero* and through breastfeeding **(Ahn & Jeung, 2023; Rachoń, 2015)**.

In males, even minimal exposure to BPA may increase the risk of prostate cancer. Certain endocrine disruptors can reprogram stem and progenitor cells, leading to a lifelong susceptibility to prostate cancer **(Ahn & Jeung, 2023)**.

Many malignancies beyond the reproductive system have a hormonal association. For example, bone cancer has been associated with growth hormone dysregulation, while thyroid-stimulating hormone (TSH), along with thyroid hormones T3 and T4, plays a significant role in thyroid cancer development **(Krashin *et al.*, 2019)**.

Exposure to phthalates has also been linked to adverse health outcomes. Male reproductive disorders associated with di(2-ethylhexyl) phthalate (DEHP) include reduced anogenital distance due to its anti-androgenic effects, lower testosterone and insulin-like factor-3 levels, and an increased risk of abnormal sperm production. Furthermore, DEHP exposure has been associated with increased levels of estrogen in pregnant women, a higher risk of developmental disorders, preterm birth, and autism spectrum disorders as a result of postnatal alterations in thyroid hormones **(Ahn & Jeung, 2023; Barakat *et al.*, 2020; National Academies of Sciences *et al.*, 2017)**.

Endocrine disruptors can modify hormone signaling pathways and exert epigenetic effects by interacting with receptors such as androgen receptors (AR), estrogen receptors (ER), and glucocorticoid receptors (GR). Moreover, these chemicals interfere with the aromatase enzyme, affecting the balance between androgens and estrogens, which is crucial for various physiological processes and may contribute to cancer development **(Buoso *et al.*, 2020)**. An increasing body of research indicates that endocrine disruptors significantly influence cancer risk, particularly in hormone-sensitive tumors such as breast and prostate cancer **(Ahn & Jeung, 2023; Rachoń, 2015)**.

EFFECTS OF NANOPARTICLES ON ENDOCRINE DISRUPTION

In recent years, microplastics (MPs) and nanoplastics (NPs) have significantly polluted the environment, posing detrimental effects on human health, particularly the mammalian endocrine system, reproductive health, and hormonal balance **(Ullah *et al.*, 2023; Vanivska *et al.*, 2024)**.

The hypothalamic-pituitary-gonadal axis regulates reproductive hormone control. Exposure to microplastics causes hormonal imbalances by altering serum FSH, LH, and testosterone levels, which leads to delayed gonadal maturation and reproductive disorders **(Koysombat *et al.*, 2023)**.

Studies indicate that microplastics also accumulate in female reproductive organs, including the ovaries and granulosa cells, which leads to reduced follicle growth, lower hormone levels, and abnormal folliculogenesis. Additionally, microplastics can induce fibrosis and apoptosis in granulosa cells through oxidative stress mechanisms. Acting as carriers of endocrine-disrupting chemicals, microplastics contribute to disorders such as infertility, precocious puberty, and polycystic ovary syndrome **(Dianová *et al.*, 2022; Halo Jr *et al.*, 2021; Iavicoli *et al.*, 2013; Ullah *et al.*, 2023)**.

Studies indicate that microplastics can bioaccumulate in mammalian testes and induce oxidative stress, leading to negative reproductive effects, such as impaired spermatogenesis and increased cell apoptosis. Particles smaller than 10 μm have been shown to reduce testosterone levels, impair sperm quality, and cause inflammation in the testes. Microplastics infiltrate testicular tissues, including Leydig cells, germ cells, and Sertoli cells, indicating their significant impact on reproductive health **(Iavicoli *et al.*, 2013; Urban *et al.*, 2024)**.

Nanoplastic exposure has been linked to alterations in testicular weight and sperm physiology, which include reduced sperm count and viability, morphological changes, and impaired spermatogenesis. Exposure during developmental stages accelerates the decline in sperm density and disrupts its normal arrangement within the seminiferous tubules **(Dagar & Bagchi, 2020; Ferrante *et al.*, 2022; Ullah *et al.*, 2023)**.

THE BODY'S DEFENSE MECHANISMS AGAINST ENDOCRINE DISRUPTORS

Endocrine disrupting chemicals (EDCs) pose a significant risk to both human and animal health, particularly through their impact on the immune system and metabolic processes **(Bansal *et al.*, 2017)**.

Immune cells, in particular macrophages and natural killer (NK) cells, actively recognize and respond to substances, as the immune system is the body's first line of defense. The immune system utilizes processes such as phagocytosis and cytokine production to counteract the effects of EDCs and reduce inflammation in the body **(DeWitt & Patisaul, 2018; Lodoen & Lanier, 2006)**.

Cytokine production is essential for maintaining the balance between pro- and anti-inflammatory signals. For instance, EDCs cause an inflammatory response, the body produces more anti-inflammatory cytokines to reduce inflammation. This reaction helps to prevent chronic inflammation **(Cicchese *et al.*, 2018; Schug *et al.*, 2011; Zhang & An, 2007)**.

In detoxification, the liver plays a central role through the action of the cytochrome P450 enzyme. Lipophilic EDCs are converted by the cytochrome into water-soluble forms, which can then be excreted via bile or urine **(Guarnotta *et al.*, 2022; Zhao *et al.*, 2021)**.

The impact of EDCs is also mediated by oxidative stress, which leads to the production of reactive oxygen species. This process involves enzymes such as glutathione peroxidase and superoxide dismutase (SOD), along with glutathione molecules, which work synergistically to protect cells from damage and maintain their integrity and functionality **(Afzal *et al.*, 2023; Kim *et al.*, 2022)**.

The gut microbiota also plays a crucial role in the metabolism of EDCs, as it influences both the absorption and toxicity of these substances.

Microbial populations can either biotransform EDCs into less harmful metabolites or enhance their excretion **(Hampl & Stárka, 2020)**.

Additionally, the circadian rhythms of the body are an important part of the defense systems against EDCs. The circadian system enables the body to adapt to various environmental substances, including the effects of EDCs. By synchronizing immune and metabolic processes with the light-dark cycle, the body can enhance its defenses against EDCs **(Gamble *et al.*, 2014)**.

CONCLUSIONS

Endocrine disrupting chemicals (EDCs) interfere with physiological processes in both animal and human body, posing significant health risks. This review focuses on the impact of endocrine disrupting chemicals (EDCs) on the immune system, gut microbiota, and circadian rhythms. EDCs have been associated with the development of various metabolic disorders, including obesity, diabetes, and related inflammatory conditions. EDCs have long-term effects on health through various mechanisms, including hormone receptor binding, oxidative stress generation, and interference with signaling pathways. The body's defense mechanisms such as immune response, detoxification processes, and circadian rhythms play a crucial role in counteracting the negative effects of EDCs. Understanding these pathways is essential for establishing therapeutic interventions to reduce their harmful effects. Further research should focus on detecting the cellular and molecular pathways affected by EDCs to mitigate their harmful effects on human health.

Acknowledgments: This research was funded by the Slovak Research and Development Agency Grant APVV-21-0168, APVV-20-0218, APVV-19-0243, by the Scientific Agency of the Slovak Republic VEGA No. 1/0698/22, and by the Cultural and educational grant agency KEGA023SPU-4/2022. Also, this work was funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V02-00043.

REFERENCES

Afzal, S., Abdul Manap, A. S., Attiq, A., Albokhadaim, I., Kandeel, M., & Alhojaily, S. M. (2023). From imbalance to impairment: The central role of reactive oxygen species in oxidative stress-induced disorders and therapeutic exploration. *Frontiers in Pharmacology*, *14*, 1269581. https://doi.org/10.3389/fphar.2023.1269581

Ahn, C., & Jeung, E.-B. (2023). Endocrine-Disrupting Chemicals and Disease Endpoints. *International Journal of Molecular Sciences*, *24*(6), 5342. https://doi.org/10.3390/ijms24065342

Anne, B., & Raphael, R. (2000). Endocrine Disruptor Chemicals. In K. R. Feingold, B. Anawalt, M. R. Blackman, A. Boyce, G. Chrousos, E. Corpas, W. W. de Herder, K. Dhatariya, K. Dungan, J. Hofland, S. Kalra, G. Kaltsas, N. Kapoor, C. Koch, P. Kopp, M. Korbonits, C. S. Kovacs, W. Kuohung, B. Laferrère, … D. P. Wilson (Eds.), *Endotext*. MDText.com, Inc. http://www.ncbi.nlm.nih.gov/books/NBK569327/

Bansal, A., Henao-Mejia, J., & Simmons, R. A. (2017). Immune System: An Emerging Player in Mediating Effects of Endocrine Disruptors on Metabolic Health. *Endocrinology*, *159*(1), 32–45. https://doi.org/10.1210/en.2017-00882

Barakat, R., Lin, P.-C., Park, C. J., Zeineldin, M., Zhou, S., Rattan, S., Brehm, E., Flaws, J. A., & Ko, C. J. (2020). Germline-dependent transmission of male reproductive traits induced by an endocrine disruptor, di-2-ethylhexyl phthalate, in future generations. *Scientific Reports*, *10*, 5705. https://doi.org/10.1038/s41598-020-62584-w

Binkowski, Ł. J., Rogoziński, P., Roychoudhury, S., Bruliński, K., Kucharzewski, M., Łaciak, T., Massanyi, P., & Stawarz, R. (2015). Accumulation of metals in cancerous and healthy tissues of patients with lung cancer in Southern Poland. *Journal of Environmental Science and Health, Part A*, *50*(1), 9–15. https://doi.org/10.1080/10934529.2015.964597

Brück, K. (1983). Functions of the Endocrine System. In R. F. Schmidt & G. Thews (Eds.), *Human Physiology* (pp. 658–687). Springer. https://doi.org/10.1007/978-3-642-96714-6_29

Buoso, E., Masi, M., Racchi, M., & Corsini, E. (2020). Endocrine-Disrupting Chemicals' (EDCs) Effects on Tumour Microenvironment and Cancer Progression: Emerging Contribution of RACK1. *International Journal of Molecular Sciences*, *21*(23), Article 23. https://doi.org/10.3390/ijms21239229

Calaf, G. M., Ponce-Cusi, R., Aguayo, F., Muñoz, J. P., & Bleak, T. C. (2020). Endocrine disruptors from the environment affecting breast cancer. *Oncology Letters*, *20*(1), 19–32. https://doi.org/10.3892/ol.2020.11566

Campbell, M., & Jialal, I. (2024). Physiology, Endocrine Hormones. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK538498/

Chrousos, G. P. (2007). Organization and Integration of the Endocrine System: The Arousal and Sleep Perspective. *Sleep Medicine Clinics*, *2*(2), 125–145. https://doi.org/10.1016/j.jsmc.2007.04.004

Cicchese, J. M., Evans, S., Hult, C., Joslyn, L. R., Wessler, T., Millar, J. A., Marino, S., Cilfone, N. A., Mattila, J. T., Linderman, J. J., & Kirschner, D. E. (2018). Dynamic balance of pro- and anti-inflammatory signals controls disease and limits pathology. *Immunological Reviews*, *285*(1), 147–167. https://doi.org/10.1111/imr.12671

Combarnous, Y., & Nguyen, T. M. D. (2019). Comparative Overview of the Mechanisms of Action of Hormones and Endocrine Disruptor Compounds. *Toxics*, *7*(1), 5. https://doi.org/10.3390/toxics7010005

Dagar, G., & Bagchi, G. (2020). Nanoparticles as Potential Endocrine Disruptive Chemicals. In S. K. Saxena & S. M. P. Khurana (Eds.), *NanoBioMedicine* (pp. 411–429). Springer. https://doi.org/10.1007/978-981-32-9898-9_17

DeWitt, J. C., & Patisaul, H. B. (2018). Endocrine disruptors and the developing immune system. *Current Opinion in Toxicology*, *10*, 31–36. https://doi.org/10.1016/j.cotox.2017.12.005

Diamanti-Kandarakis, E., Bourguignon, J.-P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M., Zoeller, R. T., & Gore, A. C. (2009). Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. *Endocrine Reviews*, *30*(4), 293–342. https://doi.org/10.1210/er.2009-0002

Dianová, L., Tirpák, F., Halo, M., Slanina, T., Massányi, M., Stawarz, R., Formicki, G., Madeddu, R., & Massányi, P. (2022). Effects of Selected Metal Nanoparticles (Ag, ZnO, TiO2) on the Structure and Function of Reproductive Organs. *Toxics*, *10*(8), 459. https://doi.org/10.3390/toxics10080459

Duranova, H., Fialkova, V., Valkova, V., Bilcikova, J., Olexikova, L., Lukac, N., Massanyi, P., & Knazicka, Z. (2022). Human adrenocortical carcinoma cell line (NCI-H295R): An *in vitro* screening model for the assessment of endocrine disruptors' actions on steroidogenesis with an emphasis on cell ultrastructural features. *Acta Histochemica*, *124*(5), 151912. https://doi.org/10.1016/j.acthis.2022.151912

Dutta, S., Sengupta, P., Bagchi, S., Chhikara, B. S., Pavlík, A., Sláma, P., & Roychoudhury, S. (2023). Reproductive toxicity of combined effects of endocrine disruptors on human reproduction. *Frontiers in Cell and Developmental Biology*, *11*, 1162015. https://doi.org/10.3389/fcell.2023.1162015

Ferrante, M. C., Monnolo, A., Del Piano, F., Mattace Raso, G., & Meli, R. (2022). The Pressing Issue of Micro- and Nanoplastic Contamination: Profiling the Reproductive Alterations Mediated by Oxidative Stress. *Antioxidants*, *11*(2), 193. https://doi.org/10.3390/antiox11020193

Gamble, K. L., Berry, R., Frank, S. J., & Young, M. E. (2014). Circadian Clock Control of Endocrine Factors. *Nature Reviews. Endocrinology*, *10*(8), 466–475. https://doi.org/10.1038/nrendo.2014.78

Gore A. C. (2010). Neuroendocrine targets of endocrine disruptors. *Hormones (Athens, Greece)*, *9*(1), 16–27. https://doi.org/10.14310/horm.2002.1249

Gore, A. C., Krishnan, K., & Reilly, M. P. (2019). Endocrine-disrupting chemicals: Effects on neuroendocrine systems and the neurobiology of social behavior. *Hormones and Behavior*, *111*, 7–22. https://doi.org/10.1016/j.yhbeh.2018.11.006

Guarnotta, V., Amodei, R., Frasca, F., Aversa, A., & Giordano, C. (2022). Impact of Chemical Endocrine Disruptors and Hormone Modulators on the Endocrine System. *International Journal of Molecular Sciences*, *23*(10), 5710. https://doi.org/10.3390/ijms23105710

Halo Jr, M., Bułka, K., Antos, P. A., Greň, A., Slanina, T., Ondruška, Ľ., Tokárová, K., Massányi, M., Formicki, G., Halo, M., & Massányi, P. (2021). The effect of ZnO nanoparticles on rabbit spermatozoa motility and viability parameters *in vitro*. *Saudi Journal of Biological Sciences*, *28*(12), 7450–7454. https://doi.org/10.1016/j.sjbs.2021.08.045

Hampl, R., & Stárka, L. (2020). Endocrine Disruptors and Gut Microbiome Interactions. *Physiological Research*, *69*(Suppl 2), S211–S223. https://doi.org/10.33549/physiolres.934513

Haverinen, E., Fernandez, M. F., Mustieles, V., & Tolonen, H. (2021). Metabolic Syndrome and Endocrine Disrupting Chemicals: An Overview of Exposure and Health Effects. *International Journal of Environmental Research and Public Health*, *18*(24), Article 24. https://doi.org/10.3390/ijerph182413047

Hinault, C., Caroli-Bosc, P., Bost, F., & Chevalier, N. (2023). Critical Overview on Endocrine Disruptors in Diabetes Mellitus. *International Journal of Molecular Sciences*, *24*(5), 4537. https://doi.org/10.3390/ijms24054537

Iavicoli, I., Fontana, L., Leso, V., & Bergamaschi, A. (2013). The Effects of Nanomaterials as Endocrine Disruptors. *International Journal of Molecular Sciences*, *14*(8), 16732–16801. https://doi.org/10.3390/ijms140816732

Kabir, E. R., Rahman, M. S., & Rahman, I. (2015). A review on endocrine disruptors and their possible impacts on human health. *Environmental Toxicology and Pharmacology*, *40*(1), 241–258. https://doi.org/10.1016/j.etap.2015.06.009

Kim, K., Kwon, J.-S., Ahn, C., & Jeung, E.-B. (2022). Endocrine-Disrupting Chemicals and Their Adverse Effects on the Endoplasmic Reticulum. *International Journal of Molecular Sciences*, *23*(3), 1581. https://doi.org/10.3390/ijms23031581

Kokkoris, P., & Pi-Sunyer, F. X. (2003). Obesity and endocrine disease. *Endocrinology and Metabolism Clinics of North America*, *32*(4), 895–914. https://doi.org/10.1016/S0889-8529(03)00078-1

Koysombat, K., Dhillo, W. S., & Abbara, A. (2023). Assessing hypothalamic pituitary gonadal function in reproductive disorders. *Clinical Science (London, England: 1979)*, *137*(11), 863–879. https://doi.org/10.1042/CS20220146

Krashin, E., Piekiełko-Witkowska, A., Ellis, M., & Ashur-Fabian, O. (2019). Thyroid Hormones and Cancer: A Comprehensive Review of Preclinical and Clinical Studies. *Frontiers in Endocrinology*, *10*, 59. https://doi.org/10.3389/fendo.2019.00059

Laws, M. J., Neff, A. M., Brehm, E., Warner, G. R., & Flaws, J. A. (2021). Endocrine disrupting chemicals and reproductive disorders in women, men, and animal models. *Advances in Pharmacology (San Diego, Calif.)*, *92*, 151–190. https://doi.org/10.1016/bs.apha.2021.03.008

Lahimer, M., Abou Diwan, M., Montjean, D., Cabry, R., Bach, V., Ajina, M., Ben Ali, H., Benkhalifa, M., & Khorsi-Cauet, H. (2023). Endocrine disrupting chemicals and male fertility: From physiological to molecular effects. *Frontiers in Public Health*, *11*, 1232646. https://doi.org/10.3389/fpubh.2023.1232646

Lauretta, R., Sansone, A., Sansone, M., Romanelli, F., & Appetecchia, M. (2019). Endocrine Disrupting Chemicals: Effects on Endocrine Glands. *Frontiers in Endocrinology*, *10*. https://doi.org/10.3389/fendo.2019.00178

Lee, H.-R., Jeung, E.-B., Cho, M.-H., Kim, T.-H., Leung, P. C. K., & Choi, K.-C. (2013). Molecular mechanism(s) of endocrine-disrupting chemicals and their potent oestrogenicity in diverse cells and tissues that express oestrogen receptors. *Journal of Cellular and Molecular Medicine*, *17*(1), 1–11. https://doi.org/10.1111/j.1582-4934.2012.01649.x

Lodoen, M. B., & Lanier, L. L. (2006). Natural killer cells as an initial defense against pathogens. *Current Opinion in Immunology*, *18*(4), 391–398. https://doi.org/10.1016/j.coi.2006.05.002

Madhu, N. R., Sarkar, B., Slama, P., Jha, N. K., Ghorai, S. K., Jana, S. K., Govindasamy, K., Massanyi, P., Lukac, N., Kumar, D., Kalita, J. C., Kesari, K. K., & Roychoudhury, S. (2022). Effect of Environmental Stressors, Xenobiotics, and Oxidative Stress on Male Reproductive and Sexual Health. In S. Roychoudhury & K. K. Kesari (Eds.), *Oxidative Stress and Toxicity in Reproductive Biology and Medicine: A Comprehensive Update on Male Infertility Volume II* (pp. 33–58). Springer International Publishing. https://doi.org/10.1007/978-3-031-12966-7_3

Mehrpour, O., Karrari, P., Zamani, N., Tsatsakis, A. M., & Abdollahi, M. (2014). Occupational exposure to pesticides and consequences on male semen and fertility: A review. *Toxicology Letters*, *230*(2), 146–156. https://doi.org/10.1016/j.toxlet.2014.01.029

Monneret, C. (2017). What is an endocrine disruptor? *Comptes Rendus Biologies*, *340*(9), 403–405. https://doi.org/10.1016/j.crvi.2017.07.004

National Academies of Sciences, E., Studies, D. on E. and L., Toxicology, B. on E. S. and, & Toxicity, C. on E.-R. L.-D. (2017). Phthalates and Male Reproductive-Tract Development. In *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals*. National Academies Press (US). https://www.ncbi.nlm.nih.gov/books/NBK453249/

Patisaul, H. B. (2021). Chapter Four - Endocrine disrupting chemicals (EDCs) and the neuroendocrine system: Beyond estrogen, androgen, and thyroid. In L. N. Vandenberg & J. L. Turgeon (Eds.), *Advances in Pharmacology* (Vol. 92, pp. 101–150). Academic Press. https://doi.org/10.1016/bs.apha.2021.03.007

Popoviciu, M. S., Paduraru, L., Nutas, R. M., Ujoc, A. M., Yahya, G., Metwally, K., & Cavalu, S. (2023). Diabetes Mellitus Secondary to Endocrine Diseases: An Update of Diagnostic and Treatment Particularities. *International Journal of Molecular Sciences*, *24*(16), 12676. https://doi.org/10.3390/ijms241612676

Puche-Juarez, M., Toledano, J. M., Moreno-Fernandez, J., Gálvez-Ontiveros, Y., Rivas, A., Diaz-Castro, J., & Ochoa, J. J. (2023). The Role of Endocrine Disrupting Chemicals in Gestation and Pregnancy Outcomes. *Nutrients*, *15*(21), 4657. https://doi.org/10.3390/nu15214657

Rachoń, D. (2015). Endocrine disrupting chemicals (EDCs) and female cancer: Informing the patients. *Reviews in Endocrine and Metabolic Disorders*, *16*(4), 359–364. https://doi.org/10.1007/s11154-016-9332-9

Schug, T. T., Janesick, A., Blumberg, B., & Heindel, J. J. (2011). Endocrine Disrupting Chemicals and Disease Susceptibility. *The Journal of Steroid Biochemistry and Molecular Biology*, *127*(3–5), 204–215. https://doi.org/10.1016/j.jsbmb.2011.08.007

Ullah, S., Ahmad, S., Guo, X., Ullah, S., Ullah, S., Nabi, G., & Wanghe, K. (2023). A review of the endocrine disrupting effects of micro and nano plastic and their

associated chemicals in mammals. *Frontiers in Endocrinology*, *13*, 1084236. https://doi.org/10.3389/fendo.2022.1084236

Urban, I., Štefunková, N., Jaszcza, K., & Massanyi, P. (2024). Development and application of zinc nanoparticles in the medical field. *Journal of Microbiology, Biotechnology and Food Sciences*, *14*(1), Article 1. https://doi.org/10.55251/jmbfs.11061

Vanivska, K., Dianová, L., Jr, M. H., Štefunková, N., Lenický, M., Slanina, T., Tirpák, F., Ivanič, P., Stawarz, R., & Massányi, P. (2024). Toxicity of nanoparticles on animal and human organism: Cell response. *Journal of Microbiology, Biotechnology and Food Sciences*, *14*(1), Article 1. https://doi.org/10.55251/jmbfs.10844

Yawer, A., Sychrová, E., Labohá, P., Raška, J., Jambor, T., Babica, P., & Sovadinová, I. (2020). Endocrine-disrupting chemicals rapidly affect intercellular signaling in Leydig cells. *Toxicology and Applied Pharmacology*, *404*, 115177. https://doi.org/10.1016/j.taap.2020.115177

Yilmaz, B., Terekeci, H., Sandal, S., & Kelestimur, F. (2020). Endocrine disrupting chemicals: Exposure, effects on human health, mechanism of action, models for testing and strategies for prevention. *Reviews in Endocrine and Metabolic Disorders*, *21*(1), 127–147. https://doi.org/10.1007/s11154-019-09521-z

Ylli, D., Sidhu, S., Parikh, T., & Burman, K. D. (2000). Endocrine Changes in Obesity. In K. R. Feingold, B. Anawalt, M. R. Blackman, A. Boyce, G. Chrousos, E. Corpas, W. W. de Herder, K. Dhatariya, K. Dungan, J. Hofland, S. Kalra, G. Kaltsas, N. Kapoor, C. Koch, P. Kopp, M. Korbonits, C. S. Kovacs, W. Kuohung, B. Laferrère, … D. P. Wilson (Eds.), *Endotext*. MDText.com, Inc. http://www.ncbi.nlm.nih.gov/books/NBK279053/

Zhang, J.-M., & An, J. (2007). Cytokines, Inflammation, and Pain. *International Anesthesiology Clinics*, *45*(2), 27. https://doi.org/10.1097/AIA.0b013e318034194e

Zhao, M., Ma, J., Li, M., Zhang, Y., Jiang, B., Zhao, X., Huai, C., Shen, L., Zhang, N., He, L., & Qin, S. (2021). Cytochrome P450 Enzymes and Drug Metabolism in Humans. *International Journal of Molecular Sciences*, *22*(23), 12808. https://doi.org/10.3390/ijms222312808