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## Endocrine disruptors in foods: Overlooked factors contributing to the prevalence of obesity

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**Abstract:** Endocrine disruptors, also known as endocrine-disrupting chemicals, could mimic or interfere with the body's hormones. Indeed, naturally occurring endocrine disruptors have been widely identified in daily foods. Moreover, industrialisation has resulted in increasing synthetic endocrine disruptors being produced and used as food additives or in food package materials, which makes exposure to endocrine disruptors become more common. Although the safety of synthetic chemicals has been extensively evaluated before entering into the food industry, increasing evidence has also highlighted that long-lasting exposure might influence long-term metabolic outcomes and be associated with the prevalence of obesity. Therefore, this review summarised the sources, detection methods, obesogenic effects and possible mechanisms of endocrine disruptors commonly found in foods, as well as discussed possible underlying mechanisms by which endocrine disruptors contribute to the increased risk of obesity. In conclusion, the review may provide useful information for understanding the association between endocrine disruptors and obesity, which could provide a new angle of view for preventing obesity prevalence.

**Keywords:** endocrine disruptor; food additive; obesity; metabolic disorder

Endocrine disruptors, also known as endocrine-disrupting chemicals (EDCs), are a type of exogenous substances or mixtures which can influence the function(s) of the endocrine system and cause adverse health effects on the (sub)populations or their descendants. The adverse effects include changes in morphology, physiology, growth, reproduction, development, or lifespan, caused by weakened functional capacity or increased susceptibility to environmental influences (Rousselle et al. 2013). The Yusho rice oil poisoning incident is a well-known incident in which food contaminated

with endocrine disruptors, including a mixture of polychlorinated biphenyls, polychlorinated dibenzofurans (PCDFs), and polychlorinated quaterphenyls (PCQs), affected nearly 14 000 people (Masuda et al. 1998; Yoshida et al. 2009) with more than 500 dead.

Nowadays, endocrine disruptors are widely found in food, which may have a profound impact on human health (Cwiek-Ludwicka and Ludwicki 2014; González-Castro et al. 2011). The best-known property of endocrine disruptors is their hormone-like effects (Vandenberg et al. 2020). In recent years, the neurobe-

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havioral toxicity of endocrine disruptors has also been revealed, which may result from their actions on nerves *via* endocrine signals (Xu and Yin 2019). Particularly, the obesogenic effects of endocrine disruptors have drawn great attention from researchers in the last decades due to the prevalence of obesity (Andújar et al. 2019; Blanco et al. 2020). For example, bisphenol A (BPA), a widely used plasticiser in food packaging, increased the risk of precocious puberty, obesity, and type 2 diabetes mellitus (Mirmira and Evans-Molina 2014). In this article, we will summarise the detection methods, obesogenic effects, and possible mechanisms of endocrine disruptors commonly found in foods.

## ENDOCRINE DISRUPTORS IN FOODS

Endocrine disruptors can affect organisms at low doses and may synergistically exert their potential adverse effects. Indeed, this was often overlooked and could complicate determining accurate safety thresholds for endocrine disruptors in the daily diet (Kortenkamp 2014; Vandenberg 2019). Furthermore, studies also showed that the effects of endocrine disruptors are not only influenced by the dosage and frequency of exposure but also related to exposure in different periods of human life (Maffini et al. 2006). Even short-term exposure during important periods of human development (e.g. pregnancy, lactation, infants, and toddlers) may cause long-lasting and profound effects. For example, higher BPA exposure in early childhood was associated with excess child adiposity (Vafeiadi et al. 2016). A recent study also showed that selected EDCs could induce steroidogenesis in follicular granulosa cells, highlighting their potential impacts

on female reproduction and fertility (Luongo et al. 2022). Thus, assessing the public health effects of daily exposure to endocrine disruptors *via* foods is in great need.

Various synthetic chemicals are endocrine disruptors or have potential endocrine-disrupting activity. Pesticides, herbicides, fungicides, veterinary drugs, and food packaging components together with natural compounds and heavy-metal pollutants are endocrine disruptors commonly found in food (Table 1) (Muncke 2009; Kowalska et al. 2016; Ahmad et al. 2017; Lee et al. 2019; Cederroth et al. 2020). The endocrine disruptors that attract the most attention are the EDCs in food packaging, especially plastic packaging. For example, BPA and phthalates, widely used in the production of plastic packaging, have been found to possess potential health risks (le Maire et al. 2009; Schecter et al. 2010; Rudel Ruthann et al. 2011; Yang et al. 2019c; Darbre 2020).

The main sources of endocrine disruptors in food are crop, meat, water pollution, and food packaging chemicals (Figure 1). The use of pesticides mainly causes crop pollution (Boon et al. 2008; Jensen et al. 2013; Al-Nasir et al. 2020; Qin et al. 2021), reclaimed water (Wang et al. 2018; Wu et al. 2020) during crop growth and heavy-metal pollution in the soil (Gall et al. 2015; Rai et al. 2019). Organophosphorus pesticides (OPPs) and organochlorine pesticides (OCPs), cyfluthrin, chlorpyrifos-methyl, propionamide, thiabendazole, triazophos, endosulfan and imidazole are insecticides commonly detected in fruits and vegetables (Schilirò et al. 2011; Li et al. 2018; Yang et al. 2019a; Martyniuk et al. 2020). Natural compounds, phytoestrogens (Cederroth et al. 2012) and mycotoxins (Kowalska et al. 2016) can also cause crop pollution. Similarly, veterinary drugs (Lee et al. 2019)

Table 1. Types of endocrine-disrupting chemicals (EDCs) commonly found in food

Sources	Types of EDCs
Insecticide	organochlorine pesticides (DDT and its metabolites), organophosphorus pesticides (Triazophos, Chlorpyrifos), pyrethroids (Fenvalerate, Cypermethrin, Permethrin, etc.), dioxins, organotin compounds, Imidacloprid
Herbicide	antiandrogenic herbicides (Mesotrione, Hexazone, etc.), glyphosate-based herbicides
Fungicide	Triadimefon, Triclosan
Veterinary drugs	Cefuroxime, Cymiazole, Trenbolone, Zeranol, Phoxim, Altrenogest and Nandrolone, etc.
Food packaging	bisphenol A and its analogues, phthalates (diethylhexyl phthalate, dibutyl phthalate, butyl benzyl phthalate, diethyl hydroxylamine), diethylstilbestrol, polychlorinated biphenyls, perfluorinated compounds, alkylphenols (nonylphenol, octylphenol, etc.)
Natural com	mycoestrogens (Zearalenone, Alternaria toxin, etc.), phytoestrogens (soy isoflavones, etc.)
Heavy-metal pollutants	mercury (Hg) and complexes, cadmium (Cd) and complexes, lead (Pb) and complexes

DDT – dichlorodiphenyltrichloroethane

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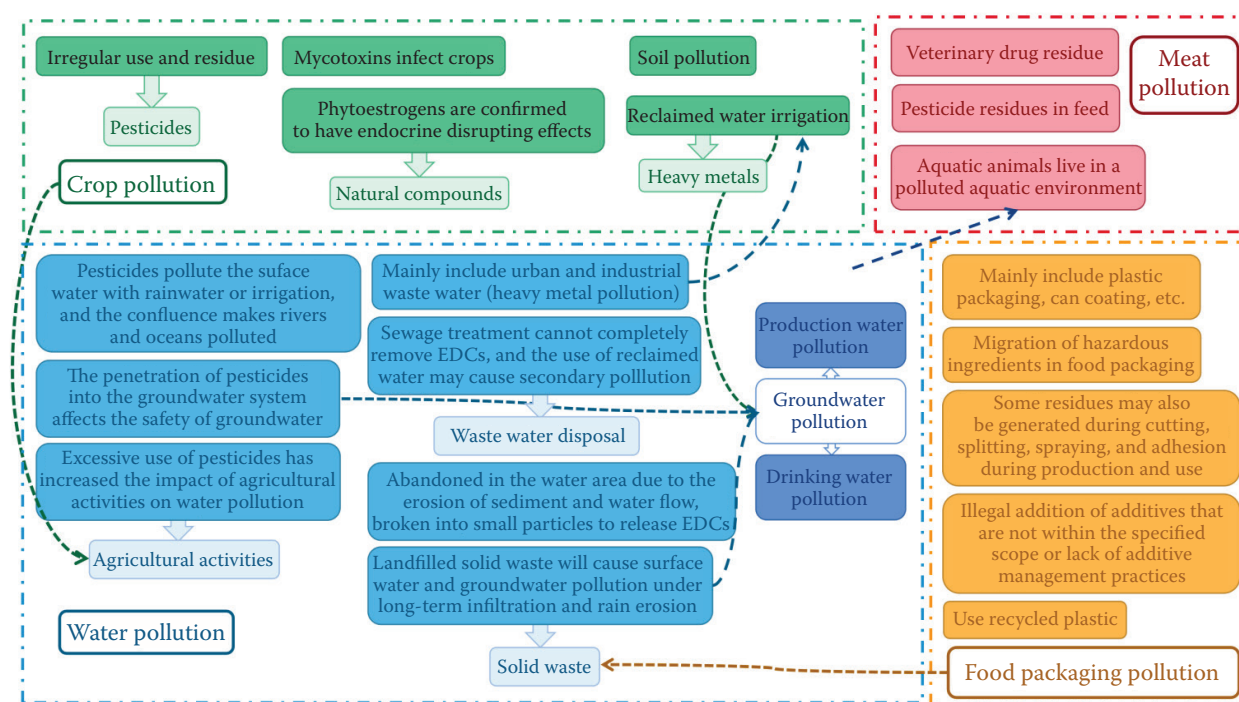


Figure 1. Main sources of endocrine-disrupting chemicals (EDCs) in food

and animal feed contaminated with endocrine disruptors (Walorczyk 2007) are the main sources of meat contamination. Wastewater discharge (Jiang et al. 2020; Kasonga et al. 2021) will cause pollution of drinking water (Wee and Aris 2017), and it will also contaminate crops and aquatic organisms (fish, shellfish, etc.) (Álvarez-Muñoz et al. 2015). In recent decades, the endocrine disruptor pollution resulting from the wide use of plastic packaging (Duan et al. 2020) and aluminium can coatings (Fattore et al. 2015; González et al. 2020) in the food industry has attracted increasing attention. The release of harmful components from packaging during long-term storage worsens the situation. Using recycled plastics will further increase pollution (Xu et al. 2020). Therefore, it is necessary to conduct effective surveillance of EDCs and develop accurate, rapid and low-cost detection methods to reduce the adverse impact of EDCs.

## METHODS FOR DETECTING ENDOCRINE DISRUPTORS

**Pretreatment and extraction methods.** Because endocrine disruptors are often present at trace levels in food, preprocessing and extraction are normally necessary for quantifying endocrine disruptors. Currently, solid-phase extraction (SPE), solid-phase microextraction (SPME), liquid-liquid extraction (LLE), and liquid-phase microextraction (LPME) are several common

extraction methods for endocrine disruptor identification. For instance, BPA and its analogues in food cans were reported to be successfully separated by SPME for migration analysis (Viñas et al. 2010). LLE has been used to extract phthalates and heavy-metal pollutants from espresso coffee and its packaging (De Toni et al. 2017), while hollow-fibre LPME has been used to extract phthalates from water samples (González-Sálamo et al. 2018). In addition to conventional extraction methods, several novel extraction methods have also been developed in recent years. For example, ultrasound-assisted extraction with continuous solid-phase extraction (SPE) and gas chromatography-mass spectrometry (GC-MS) were developed to determine multiple EDCs simultaneously (Hejji et al. 2021). Effervescent tablets have been used for microextraction phenolic endocrine disruptors in beverages (Jing et al. 2020). Graphene oxide (Fe-alg-MGO) magnetic beads encapsulated in iron cross-linked alginate have been used as adsorbents to extract BPA from water samples (Tasmia et al. 2020). Solid-phase MIP-SPE sorbents, made by synthesising a molecularly imprinted polymer as extraction sorbent for SPE, were used with high-performance liquid chromatography and ultraviolet detection for analysing pesticides (Arias et al. 2020), and a novel composite material, Fe<sub>3</sub>O<sub>4</sub>@N-RGO, was used as an adsorbent to extract bisphenol endocrine disruptors from carbonated beverages (Li et al. 2019).

**Detection methods.** As illustrated above, the endocrine disruptors in foods may come from various sources and include both natural and human-made chemicals. Particularly, all these endocrine disruptors may function synergistically. However, current regulations are mainly focused on synthetic chemicals with endocrine-disrupting activity being introduced during the food manufacturing process. Therefore, fast and accurate detection methods would play an important role in determining (or evaluating) the overall contents of endocrine disruptors in food, which may provide useful information to avoid excessive intake and thus prevent hazards such as obesity.

Laboratory analysis of endocrine disruptors is primarily done by GC-MS and liquid chromatography-mass spectrometry (LC-MS). For instance, GC-MS was reported to quantify bisphenols in canned food as well as to determine phthalates and heavy metals in food packaging (De Toni et al. 2017; Cunha et al. 2020) while LC-MS was successfully used for the analysis of BPA in fruit juices, and phthalates in fish fillets (Gallo et al. 2019; Panio et al. 2020). Although these detection methods are accurate, sensitive, and precise, they often require expensive equipment and complicated procedures. Thus, more convenient and affordable assays are in great need. Electrochemical sensors are considered promising alternatives because they are rapid, accurate and less costly. Different materials have been explored to develop elec-

trochemical sensors to improve detection results, especially novel nanomaterials (Gallo et al. 2019; Panio et al. 2020). For instance, nanocarbon-modified electrochemical sensors were reported to be able to detect BPA at 5 nM (Jiang et al. 2021). Electrochemical sensors with nanocomposites composed of black phosphorus and porous graphene also showed good selectivity and stability for accurately detecting BPA in plastic package materials (Cai et al. 2019). In addition, paper-based electrochemical sensors with carbon black (a carbon-based nanomaterial) can detect BPA at 0.03  $\mu\text{M}$  levels in drinking water with low cost and high sensitivity (Jemmeli et al. 2020). Novel methods make detecting EDCs more convenient, less costly, and more accurate.

## MECHANISM OF ENDOCRINE DISRUPTORS CAUSING OBESITY

Plenty of scientific literature has shown endocrine disruptors to have adverse effects in animal models and exponentially harmful effects in humans. The association between endocrine disruptors and obesity has been widely studied. Several underlying mechanisms by which endocrine disruptors lead to the increased risk of obesity have been explored, including regulating nuclear receptors linked pathway, non-nuclear receptor linked pathway, hypothalamic-pituitary axis and inducing oxidative stress (Figure 2).

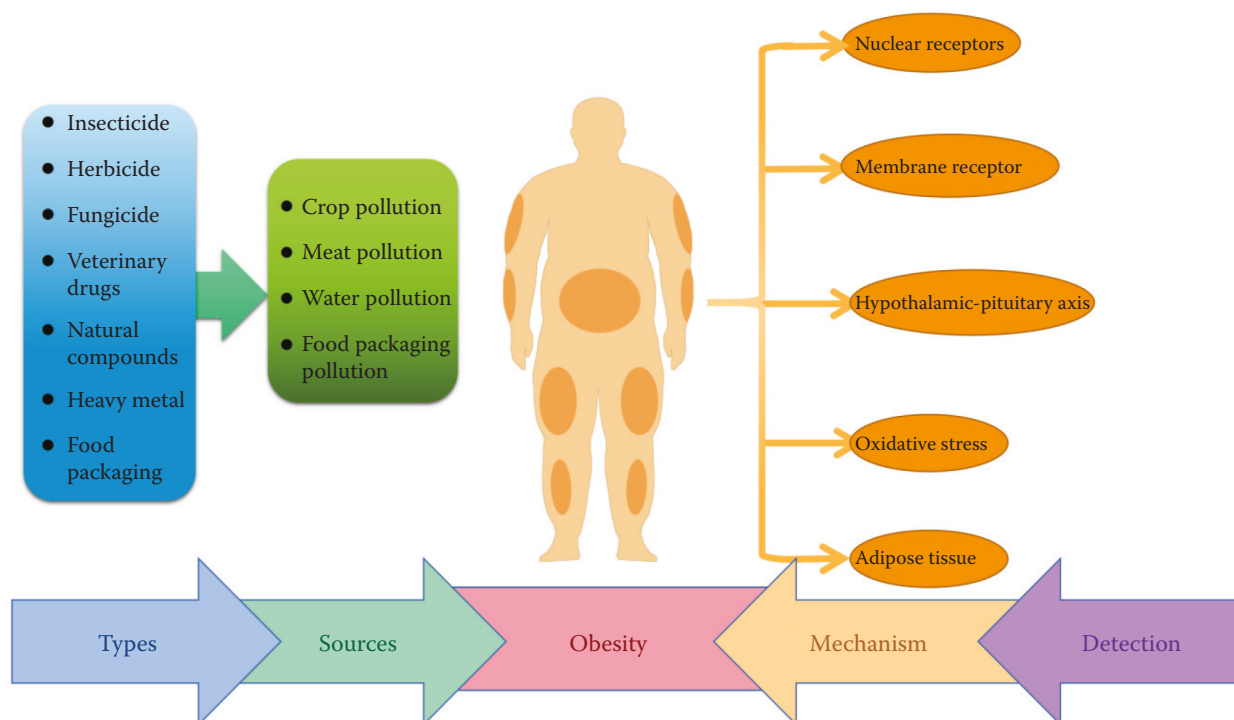


Figure 2. The potential association between endocrine disruptors and obesity



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**Nuclear receptors.** Endocrine disruptors interact with nuclear receptors (NRs) and regulate signal transduction (Table 2). Increasing evidence shows that NRs have important roles in obesity. For example, BPA, bisphenol F (BPF), and bisphenol S (BPS) increase estrogen receptor (ER) activity and decrease androgen receptor (AR) activity (Park et al. 2020; Qiu et al. 2021). Notably, ERs may modulate regional adiposity with ER $\alpha$  limiting adipose accumulation and ER $\beta$  counteracting the effect of ER $\alpha$  (Gavin et al. 2013). Endocrine disruptors such as BPA, BPF, and BPS activate both ER $\alpha$  and ER $\beta$ , but their activation responses are imbalanced, which may be the underlying mechanisms of their profound effects on metabolism. In male mice, ARs profoundly affect energy balance, and decreasing AR activation causes obesity (Fan et al. 2005). Therefore, the inhibitory effects on AR activity may also contribute to the obesogenic effects of BPA and its analogues.

Peroxisome proliferator-activated receptors  $\gamma$  (PPAR $\gamma$ ) is one of the principal adipogenic factors at the centre of a complex network of transcription factors that regulate the differentiation of 3T3-L1 preadipocytes to adipocytes (Farmer 2006; Chinchu et al. 2020). Notably, BPS and phthalates have been shown to regulate PPAR $\gamma$  and influence fat formation and accumulation (Desvergne et al. 2009; Martínez et al. 2020), while organotin compounds also affect the transactivation activity of PPAR $\gamma$  (Kanayama et al. 2005).

Furthermore, some pesticides can interact with the aryl hydrocarbon receptor (AhR), thyroid receptor (TR), and mineralocorticoid receptor (MR) (Ghisari et al. 2015; Zhang et al. 2018a). Among these nuclear receptors, AhR affects lipogenesis in the liver and adipose tissue (Bock 2020). Meanwhile, *in vitro* studies also found that TR antagonism contributes to adipogenic effects (Kassotis et al. 2019), and there is *in vivo*

Table 2. Nuclear receptors (NRs) interact with endocrine-disrupting chemicals (EDCs)

NRs	EDCs
Estrogen receptor (ER)	BPA and its analogues (BPF, BPS) have estrogenic and anti-androgenic effects, and their mixture had higher endocrine-disrupting activity at lower concentrations (Park et al. 2020).
	Heavy metals show high estrogenicity in estrogen receptor-dependent on transcriptional expression assay steam (Choe et al. 2003).
	ERs may modulate regional adiposity with ER $\alpha$ limiting adipose accumulation and ER $\beta$ counteracting the effect of ER $\alpha$ (Gavin et al. 2013).
Androgen receptor (AR)	Imidacloprid binds to AR to disrupt the endocrine system and affects reproductive health in mice (Yuan et al. 2020).
	BPA, BPF, and BPS decrease AR activity (Qiu et al. 2021).
	In male mice, ARs profoundly affect energy balance, and decreasing AR activation causes obesity (Fan et al. 2005).
Peroxisome proliferator-activated receptors (PPARs)	BPA can affect mRNA expression of all forms of PPAR in the liver and testes (Sharma et al. 2019).
	BPA and BPS can induce the expression of PPAR $\gamma$ and its target genes in macrophages, and it may affect lipid metabolism due to the connection of macrophages with fat and liver cells (Gao et al. 2020).
	PPAR $\gamma$ is one of the principal adipogenic factors at the centre of a complex network of transcription factors that regulate the differentiation of 3T3-L1 preadipocytes to adipocytes (Farmer 2006; Chinchu et al. 2020).
	BPS and phthalates have been shown to regulate PPAR $\gamma$ and influence fat formation and accumulation (Desvergne et al. 2009; Martínez et al. 2020).
	Organotin compounds affect the transactivation activity of PPAR $\gamma$ (Kanayama et al. 2005).

Table 2. To be continued

NRs	EDCs
Thyroid hormone receptors (TRs)	<p>Triazophos binds strongly to TRs, affecting the normal physiological function of the receptor and interfering with its natural ligands (Li et al. 2019).</p> <p>4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene, which is the metabolite of BPA, binds with TRs better than BPA because of structural similarity with thyroid hormones (Sheikh 2020).</p> <p>Some pesticides can interact with aryl hydrocarbon receptor (AhR), TR, and mineralocorticoid receptor (MR) (Ghisari et al. 2015; Zhang et al. 2018a).</p> <p>Among these nuclear receptors, AhR affects lipogenesis in the liver and adipose tissue (Bock 2020).</p> <p><i>In vitro</i> studies found that TR antagonism contributes to adipogenic effects (Kassotis et al. 2019).</p> <p>There is <i>in vivo</i> and <i>in vitro</i> evidence that MR exerts a pro-adipogenic role by inhibiting UCP1 expression in brown adipocytes (Kuhn et al. 2019).</p>
Glucocorticoid receptors (GR) and mineralocorticoid receptors (MR)	<p>Several EDCs could promote adipogenesis by increasing GR activity (Neel et al. 2013; Sargis et al. 2010).</p> <p>Pb is a heavy metal with endocrine disruptor activity. Pb(NO<sub>3</sub>)<sub>2</sub> showed both anti-glucocorticoid and anti-mineralocorticoid activities.</p> <p>Several heavy metal compounds (including BaCl<sub>2</sub>, CoCl<sub>2</sub>, CuCl<sub>2</sub>, Pb(NO<sub>3</sub>)<sub>2</sub>, LiCl, SnCl<sub>2</sub>, ZnCl<sub>2</sub>, CdCl<sub>2</sub>, MnCl<sub>2</sub>) also show an inhibitory effect on GR transactivation or an antagonistic effect on MR activity (Zhang et al. 2018b).</p>
Estrogen-related receptors (ERRs)	<p>BPA can bind specifically to ERR<math>\gamma</math>, but the physiological relevance needs to be further determined because the target gene and natural ligand of ERR<math>\gamma</math> are unclear (Takayanagi et al. 2006).</p>
Progesterone receptor (PR)	<p>Some common EDCs (DDT and its metabolites, nonylphenol, etc.) show anti-progestin activity due to their binding with human PR, and it may have negative effects on pregnancy and reproduction (Viswanath et al. 2008).</p> <p>A molecular docking study reported the binding affinity of chlorpyrifos and human PR (Hazarika et al. 2020).</p> <p>Increased expression of PR mRNA during mid-pregnancy was found to be associated with lipogenic activity (Rodríguez-Cuenca et al. 2006).</p>
Retinoid X receptor (RXR)	<p>The organotins induced 11<math>\beta</math>-HSD2 expression and activity in JEG-3 placenta cells by activating RXR<math>\alpha</math>, which will cause development problems in the fetus (Inderbinen et al. 2020).</p>
Pregnane X receptor (PXR)	<p>Poly- and perfluorinated compounds can activate human PXR and result in many human diseases (Zhang et al. 2017).</p> <p>Insecticide cis-bifenthrin activation of the pregnane X receptor was reported to increase hepatic lipid synthesis and decrease lipid metabolism, which promoted the accumulation of lipids in the liver (Xiang et al. 2018).</p>
Aryl hydrocarbon receptor (AhR)	<p>Monoethylhexyl phthalate can induce the expression of AhR, which is not conducive to human breast health.</p>

BPA – bisphenol A; BPF – bisphenol F; BPS – bisphenol S; DDT – dichlorodiphenyltrichloroethane

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and *in vitro* evidence that MR exerts a pro-adipogenic role by inhibiting UCP1 expression in brown adipocytes (Kuhn et al. 2019).

Similarly, glucocorticoid receptor (GR) activity was also proven to be correlated with the metabolism activity of adipocytes, and several EDCs could promote adipogenesis by increasing GR activity (Sargis et al. 2010; Neel et al. 2013). Besides, a molecular docking study reported the binding affinity of chlorpyrifos and human progesterone receptor (PR) (Hazarika et al. 2020). Indeed, increased expression of PR mRNA during mid-pregnancy was found to be associated with lipogenic activity (Rodríguez-Cuenca et al. 2006). Additionally, insecticide cis-bifenthrin activation of the pregnane X receptor was reported to increase hepatic lipid synthesis and decrease lipid metabolism, which promoted the accumulation of lipids in the liver (Xiang et al. 2018). In summary, as many nuclear receptors are closely related to obesity, the interaction between EDCs and NRs is worthy of attention.

**Membrane receptors.** EDCs also interact with several non-nuclear receptors (Levin and Hammes 2016) (Table 3). For instance, membrane estrogen receptor (mER), androgen receptor (mAR), and progesterone receptor (mPR) could be activated by a range of endocrine disruptors and they play vital roles in energy metabolism. Membrane ER $\alpha$  transduces specific signals in 3T3-L1 progenitors and initiates interactions between membrane ER $\alpha$  and nuclear ER $\alpha$  that inhibit PPAR $\gamma$  expression and adipogenesis (Ahluwalia et al. 2020). Activation of membrane ER $\alpha$ , without involvement of nuclear ER $\alpha$ , was found to decrease triglyceride concentration and expression of mRNAs associated with lipid synthesis in differentiated bone marrow stem cells and 3T3-L1 cells in wild-type mice (Pedram et al. 2015).

**Hypothalamic-pituitary axis.** The hypothalamic-pituitary (HP) axis of the neuroendocrine system in-

cludes the hypothalamus, pituitary gland and endocrine organs such as thyroid and adrenal glands and gonads. The changes in HP activity were proven to be tightly associated with the development of obesity, while endocrine disruptors may exert their obesogenic effects *via* regulating the hypothalamic-pituitary-thyroid (HPT) activity (Table 4). Studies in zebrafish larvae found that exposure to di(2-ethylhexyl) phthalate (DEHP) resulted in changes in gene expression associated with the activity of the HPT axis (Jia et al. 2016). Similarly, BPF changed the expression of genes associated with the hypothalamic-pituitary-gonadal (HPG) axis (Yang et al. 2019b) and ER expression (Baghel and Srivastava 2020) in zebrafish. A human study also revealed that the presence of BPA in the urine of pregnant women was associated with the abnormal hypothalamic-pituitary-adrenal (HPA) axis function (Giesbrecht et al. 2016). Besides, prenatal ethanol exposure has been shown to increase the high blood glucose and high blood lipid sensitivity in the offspring of high-fat diet-induced adult male mice *via* influencing the HPA axis (Xia et al. 2014). Taken together, EDCs can induce changes in the hypothalamic-pituitary axis that may be linked to obesity.

**Oxidative stress.** Excessive endogenous reactive oxygen species (ROS) were identified as belonging among the most important factors causing various chronic diseases including obesity (Paithankar et al. 2021). The level of ROS that exceeds the capacity of endogenous antioxidant systems will cause oxidative stress that damages health (Nilsson and Liu 2020). Many EDCs in food, such as heavy metals, plasticisers, pesticides and others increase the production of ROS or lower the endogenous antioxidant activity. ROS influenced the differentiation of mesenchymal stem cells to adipocytes (Kanda et al. 2011). For instance, a deficiency of catalase leading to an excess of H<sub>2</sub>O<sub>2</sub> concentration in tissues could

Table 3. Membrane receptors interact with endocrine-disrupting chemicals (EDCs)

Membrane receptors	EDCs
Membrane estrogen receptors (mESR)	Xenoestrogens (including OCP, nonylphenol, BPA, coumestrol, DES, and heavy metal ions) can signal through mESR, and both rapid physiological changes and longstanding epigenetic modifications may be induced by EDC (Rosenfeld and Cooke 2019).
Membrane androgen receptors (mARs)	Several pesticides at relatively low concentrations disrupt rapid androgen signalling in the transfection of prostate cancer PC-3 cells <i>in vitro</i> through the membrane androgen receptor (Thomas and Dong 2019).
Membrane progesterone receptor (mPR)	DES and its analogues bound to mPR $\alpha$ can act as agonists (Tokumoto et al. 2007).

BPA – bisphenol A; DES – diethylstilbestrol; OCP – organochlorine pesticides

Table 4. Endocrine-disrupting chemicals (EDCs) regulate the activity of the hypothalamic-pituitary axis

Hypothalamic-pituitary axis	EDCs
Hypothalamic-pituitary-thyroid (HPT) axis	<p>Perfluorooctane sulfonate changes the expression levels of genes and disrupts the stability of thyroid hormone levels in the HPT axis (Shi et al. 2009).</p> <p>Studies in zebrafish larvae found that exposure to di(2-ethylhexyl) phthalate resulted in changes in gene expression associated with the activity of the HPT axis (Jia et al. 2016).</p>
Hypothalamic-pituitary-gonadal (HPG) axis	<p>BPA exposure during the perinatal and postpartum periods changes the transcript levels of Kiss-1/GnRH and steroidogenic enzymes in the HPG axis in mice (Xi et al. 2011).</p> <p>BPF changed the expression of genes associated with the HPG axis (Yang et al. 2019b).</p>
Hypothalamic-pituitary-adrenal (HPA) axis	<p>Perfluorooctane sulfonate affects the mRNA and protein expression levels of CRF1r and GR gene to inhibit the HPA axis (Salgado-Freiría et al. 2018).</p> <p>A human study also revealed that the presence of BPA in the urine of pregnant women was associated with abnormal HPA axis function (Giesbrecht et al. 2016).</p> <p>Prenatal ethanol exposure has been shown to increase the high blood glucose and high blood lipid sensitivity in the offspring of high-fat diet-induced adult male mice <i>via</i> influencing the HPA axis (Xia et al. 2014).</p>

BPA – bisphenol A; BPF – bisphenol F

significantly increase the body weight and the risk of developing diabetes (Shin et al. 2020). Therefore, EDCs-induced oxidative stress could also contribute, at least partially, to their obesogenic effects.

## DISCUSSION

Until now, the use of EDCs in the food industry has become increasingly common. Growing evidence points out the non-unneglectable endocrine disruptive effects of long-term exposure to EDCs. Food has become a major route for pollutants to enter the body. In recent years, studies of the relationship between EDCs and obesity have increased. This review mainly discussed the sources of EDCs commonly found in food, the detection methods, and their association with obesity. Particularly, understanding the mechanism underlying the obesogenic activity of EDCs might provide novel ideas for obesity prevention. The subsequent studies may focus on the low-dose and synergistic effects of EDCs upon long-term exposure and exploration of safe alternative substances for the food industry. Meanwhile, accurate, rapid and cost-effective detection methods for identifying

and quantifying EDCs from daily foods are in great need. Besides, developing cost-effective, environmentally friendly, and highly effective methods for quickly removing endocrine disruptor pollutants also draws great attention. For instance, a zeolitic imidazolate framework (ZIF-8) magnetic porous nanocomposite has been successfully synthesised for the fast and simultaneous removal of microplastics and plastic-derived endocrine disruptors (Pasanen et al. 2023). In summary, the relationship between obesity (and its related diseases) and endocrine disruptors is worthy of our attention to ensure food safety and people's health.

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