DOI: 10.26599/FSHW.2026.9251001

Contents lists available at SciOpen

Food Science and Human Wellness

journal homepage: https://www.sciopen.com/journal/2097-0765

China Food Publishing Co.

The regulatory role of gut microbiota in energy metabolism disorders of distal organs by emerging contaminants

Yunting Li[1#], Haitao Ma[1#], Ling Cai[2], Haojun Zhang[3]*, Junling Wang[1]*

[1]*Department of Toxicology, School of Public Health, Lanzhou University, Lanzhou, 730000, China.*

[2]*Gansu Provincial Hospital, No.204 Donggang West Road, Lanzhou, 730000, China.*

[3]*Affiliated Hospital of Northwest Minzu University/The Second People's Hospital of Gansu Province, Lanzhou, 730000, China.*

ABSTRACT: Emerging contaminants (ECs) are a significant category of newly recognized pollutants with potential risks to human health. Human are exposed to ECs via several ways including air, food, and water. The gut microbiota (GM) and its metabolites can be closely linked to multi-organ energy metabolism in the body. Despite substantial studies on the health impacts induced by ECs, a comprehensive understanding of the pathways through which ECs influence gut-target organ energy metabolism remains absent. This study demonstrates that ECs disrupt GM balance, which subsequently triggers systemic inflammation through the nuclear factor kappa-B (NF-κB)/janus kinase-signal transducer and activator of transcription (JAK-STAT) pathways, induces insulin resistance (IR) by inhibiting insulin receptor substrate 1 (IRS1) phosphorylation, and impairs bile acid (BA) metabolism via farnesoid X receptor (FXR) signaling dysregulation. Ultimately, these mechanisms lead to abnormal energy metabolism in multiple organs including the liver, brain, and reproductive system. In addition, probiotics hold promising application potential in alleviating the harmful metabolic effects induced by ECs. By modulating the composition of the GM, enhancing intestinal barrier function, reducing inflammation, and producing metabolic products, probiotics are expected to restore metabolic homeostasis in distant organs. Therefore, this review explores the potential interactions between ECs and the energy metabolism of gut-target organs. It summarizes the detrimental effects of ECs-induced GM, consolidates possible mechanistic pathways linking GM disruption to abnormal energy metabolism, discusses probiotics as potential interventions to support preventive strategies, and suggests that Future research should focus on developing personalized and combined probiotic intervention strategies, and further elucidate their mechanisms of action, in order to fully exploit the health-protective potential of probiotics.

Keywords: emerging contaminants; gut-energy metabolism; probiotics

1. Introduction

Emerging contaminants (ECs) are compounds that present in various environmental media. Exposure to ECs can occur via inhalation, cutaneous contact, and dietary consumption (Zhan, 2023). Notable ECs, including antibiotics, bisphenol, microplastics, and et al., exhibit possible hazards to human health (Shao et al., 2021), mainly focus on neurotoxicity, endocrine disruption, immunotoxicity, reproductive toxicity, and hepatotoxicity (Smital, 2008). Multiple studies have identified substantial correlations between ECs

[#]These authors contribute to this paper equally, they are co-first authors.
***Corresponding author**
haozi_523@163.com, wangjl@lzu.edu.cn

Received 8 June 2025
Received in revised from 26 August 2025
Accepted 7 November 2025

exposure and metabolic impairment, and disruptions to gut microbiota (GM), highlighting its potential impacts on health (Fu et al., 2019; SARGIS, 2023).

These pollutants can directly harm the gut environment in several ways. On one hand, ECs can damage the tight junctions between intestinal cells, weakening the gut barrier and making it more permeable (Dmytriv et al., 2024). On the other hand, they may alter the pH and redox balance inside the intestinal lumen, disrupting normal physiological conditions (Zhao et al., 2021). Such a disturbed gut environment not only directly impairs nutrient absorption and local immunity but also sets the stage for subsequent microbial imbalance.

GM is comprised of a variety of microorganisms, with bacteria playing a prominent role. The primary bacterial phyla can be categorized into *Bacteroidetes*, *Proteobacteria*, and *Firmicutes*. GM regulates several physiological functions (Burgos-Aceves et al., 2024) and then significantly influences metabolomics, including immune responses, hormone regulation, and impacts on distant organs (Zhao et al., 2024). Exposure to ECs can disrupt GM through altering its quantity and function, ultimately resulting in dysbiosis (Bao et al., 2015). This perturbation can further affect energy metabolism in both the gastrointestinal tract and remote organs (Kakakhel et al., 2023). Based on previous research, it suggested that GM may contribute to organ impairment by altering energy metabolism pathways, supporting

the concept of the gut-energy metabolism axis, which is fundamentally defined as the bidirectional interaction and regulation between the gut and systemic energy homeostasis through multiple pathways. This axis involves the GM, intestinal barrier function, gut-derived metabolites, and various host physiological systems. It plays a critical role in maintaining energy intake, storage, expenditure, and overall metabolic health (Stojanović, Ozren, et al., 2022).

Recent research suggests that GM dysbiosis might impair the intestinal barrier and allow microbial components to reach distant organs, contributing to disease development (Gruener et al., 2023; Schoeler and Caesar, 2019). Additionally, exposure to ECs has been linked to significant metabolic imbalances within GM (Li et al., 2016). Furthermore, commensal bacteria experience oxidative stress damage, which then leads to certain adverse effects on target organs (Montenegro et al., 2023). However, limited evidence has been given to how GM changes affect energy metabolism in target organs, and the key metabolic pathways remain unexplored (Ray, 2014).

Probiotics have been confirmed to exert beneficial effects in counteracting the harmful impacts of ECs (Dahiya et al., 2024). In recent years, researchers have actively explored the potential of probiotics in alleviating damage induced by exogenous chemical pollutants (Abdolmaleki et al., 2022), with particular focus on the mechanisms by which probiotics regulate GM to improve the metabolic functions of target organs (Sarlak et al., 2021). Probiotics, mainly consisting of beneficial microorganisms such as *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, exert multiple health-promoting effects by modulating GM composition, enhancing intestinal barrier integrity, suppressing inflammatory responses, and producing bioactive metabolic products (Ni et al., 2023). These actions contribute to alleviating GM dysbiosis caused

by ECs exposure and restoring metabolic homeostasis in distant organs. Emerging evidence further indicates that probiotics can regulate host energy metabolism by influencing mitochondrial function, lipid oxidation, and glucose utilization in peripheral tissues (Song et al., 2023). However, the key signaling pathways involved in these processes remain insufficiently summarized and require further systematic investigation.

The previous researches have not sufficiently emphasized alterations in the energy metabolism of target organs following exposure to ECs, leading to limited discussion of key pathways and potential therapies. This study explores how EC-induced dysbiosis affects the energy metabolism of distant organs, referred to as the gut-energy metabolism axis. Moreover, it summarizes the underlying mechanisms and proposes the potential role of probiotics in enhancing distal organ function after intervention.

2.Interactions between ECs and GM

2.1 Common ECs and effects

Currently, there is no international consensus on the classification of ECs, which can permeate into all aspects of human life and negatively impact multiple organs. Table 1 lists the classification of ECs, exposure methods, and relevant health risks.

Table 1 Classification of emerging pollutants

Emerging contaminants	Classification	Source of contaminant	Health hazards	Reference
Antibiotics	Sulfonamides, macrolides (MA), tetracyclines, fluoroquinolones	Farming wastewater, municipal sewage discharge, medical waste, agricultural activities, industrial production discharges	Bacterial and environmental antibiotic resistance leads to treatment failures and deaths.	(Ben et al., 2019)
Hormones	Estrone (E1), estradiol (E2), estriol (E3), phytoestrogens, progestins (P4)	Industrial production, daily life, medical waste, agricultural activities.	Systemic hypersensitivity, inhibition of enzymes responsible for central nervous system functioning	(Keerthanan et al., 2021)
Antipyretic and analgesic (medicine)	Acetaminophen (APAP), Ibuprofen (IBU)	Medical waste, personal medicines and care products, municipal sewage discharges, farming wastewater	Cardiovascular risk	(Wong et al., 2005)
Doping (in athletics)	Amphetamines, cocaine (coke), caffeine,	Pharmacogenetic intake, foodborne Intake, external additions	Poor mental health, violence, injury, sexually transmitted infections, Risk of bloodborne viruses and harm to the fetus	(Farrell et al., 2019)
Contrast medium	Odinated X-ray contrast media, gadolinium-based contrast agents.	Medical wastewater, Municipal Wastewater Treatment Plant,Direct Discharge	Cytotoxicity, genotoxicity and developmental toxicity	(Yan et al., 2024)
Bisphenol	Bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol AF (BPAF)	Industrial production, Plastic products, Wastewater treatment plants, Food and beverages, Personal care products	Cumulative poison	(Gopal et al., 2021)
Phthalate ester	Di(2-ethylhexyl) phthalate (DEHP), Dibutyl phthalate (DBP), Diphenyl Phthalate (DPHP), Dihexyl phthalate (DnHP), Di(2-methoxy)ethyl phthalate (DEHP), Diallyl Phthalate (DAP), Octyldecyl phthalate (ODP),	Industrial production and processing, Consumer products, Agriculture, Environmental media, Medical waste	Anti-estrogenic/androgenic Effects, reduced fertility	(Huang et al., 2022)

	Didecyl phthalate (DIDP), Diisopentyl phthalate (DIPP)			
Triclosan	/	Personal care products, Medical products, Textiles and Plastic Products,Agriculture	Cumulative poison	(Gopal et al., 2021)
Perfluorinated chemical compound	Perfluorocarboxylic acids (PFCA), perfluorosulfonates (PFAS)	Industrial production discharge, product use	Mainly developmental toxicity, hepatotoxicity, neurotoxicity, reproductive toxicity	(Lau et al., 2004; Zeng et al., 2019)
Poly fluoric chemical compound	Hydroxypolyfluoride (PVDF), chlorinated polyfluorinated compounds (PFCs)	Industrial production discharge, product use	Obesity, asthma, immunotoxicity, cardiovascular toxicity	(Zhang et al., 2023)
New brominated flame retardants (NBFRs)	Decabromodiphenyl ethane (DBDPE), 1,2-Bis(2,4,6-tribromophenoxy)ethane (BTBPE), tetrabromoethylcyclohexane (TBECH), tris(2,3-dibromo propyl) isocyanurate (TBC)	Industrial production, product use, environmental migration, waste disposal, international trade	Altered thyroid function, liver and kidney damage, neurodevelopmental toxicity, endocrine toxicity, damage to nerve cells and tissues	(Chen et al., 2019; Feiteiro et al., 2021; Dong et al., 2015)
Microplastic	Polystyrene (PS), polyethylene terephthalate (PET), polyethylene (PE), polyvinyl chloride (PVC)	Household products,packaging materials,textiles, industrial products, marine activities, atmospheric deposition, sewage Discharge	Hemolysis, disruption of cell membranes, intestinal inflammation, induces chronic respiratory disease, depression, liver damage, obesity, cancer	(Choi et al., 2020; Chmielewski et al., 2022)
An engineering project nanomaterials	Silver-engineered nanomaterials (Ag ENMs),zinc oxide-engineered nanomaterials(ZnO ENMs), titanium dioxide-engineered nanomaterials.(TiO2 ENMs)	Industrial production, commercial distribution	Inflammation of the cardiovascular system, respiratory symptom level inflammation, lung inflammation	(Ferdous et al., 2019; Schulte et al., 2019; Pini et al., 2016)

2.2 Ecological interaction between ECs and GM

GM is a complex and dynamic community of microorganisms that has recently been recognized as a "vital organ". It communicates with other organs through neurological, endocrine, immune, and metabolic pathways, playing a key role in various physiological functions, including metabolism, barrier homeostasis, inflammation, and hematopoiesis. (Ahlawat et al., 2021).

The interaction between GM and exogenous compounds can generally be divided into three main mechanisms: direct absorption and utilization, metabolism through the liver, and alternations in the structure and abundance of the GM community and interactions (Li et al., 2024).

Meanwhile, GM plays a crucial role in metabolizing ECs through various metabolic processes. Although most environmental toxins do not directly target GM, some pollutants can enter the human body and interact with it in multiple ways. Several studies have revealed that exposure to ECs can disrupt GM composition, leading to changes such as dysfunction of energy metabolism, reduced nutrition absorption, and a weakened immune system (Wang et al., 2024; Zhang et al., 2020; Zhang et al., 2015).

2.3 GM Dysbiosis Induced by ECs

ECs may disrupt GM, and further lead to dysbiosis, ecological homeostasis, and adverse health outcomes in humans. Therefore, investigating their mechanisms of ECs-GM interaction is essential (Zhao et al., 2024).

ECs affect both the composition and abundance of GM (Sun et al., 2019). Previous studies indicated that intestinal epithelial lesions increase with prolonged exposure time and ECs concentration, however, the fraction of microbial community composition and abundance varied significantly (Sun et al., 2019; Zhang et al., 2023). Similarly, a pharmacological study found that patients with ECs-induced peripheral neuropathy have higher serum deoxycholic acid levels and an elevated relative abundance of Clostridium (Zhong, 2022). These findings suggested that the dynamic balance of GM populations was severely disrupted after exposure to ECs. Further research shows that ECs can interact with GM.

ECs and their metabolites could interact with GM and disrupt their normal metabolic activities. One study demonstrated that ECs contribute to GM dysbiosis, intestinal barrier dysfunction, and metabolic disturbances (Jin et al., 2019). Another investigation observed that the short-chain fatty acids (SCFA) produced by GM increased significantly in adult offspring after maternal exposure to DBDPE. This suggests that DBDPE treatment affects gut microbial composition and modifies the metabolic function within the gut ecosystem (Zhang et al., 2023). These findings highlight that ECs can be detrimental to the metabolic health of the host.

Beyond metabolic disruption, ECs can directly damage intestinal tissues, causing mucosal irritation, inflammation, and other physiological disturbances. For example, PFCA exposure has been linked to tissue damage by reducing GM diversity (Jiao et al., 2023). Similarly, transcriptome analysis following BPS exposure revealed abnormal gene expression in the intestinal mucosal barrier, contributing to inflammation (Li et al., 2024).

3. GM-Mediated Energy Metabolism Influence of ECs

3.1 GM-Mediated Energy Metabolism Influence of ECs

ECs disrupt systemic energy metabolism through multiple pathways, altering key metabolites (Li et al., 2023; Provencher et al., 2022; Ratelle et al., 2020) and inducing oxidative stress, inflammation, and cell death (Lebeau-Roche et al., 2023; Marie and Gallet, 2022; Zhang et al., 2022a). These dose-dependent effects (Assiri et al., 2024) impair hepatic lipid metabolism, mitochondrial function, and nucleic acid synthesis (Sun et al., 2024; Cayer et al., 2024), ultimately leading to multi-organ metabolic dysfunction. Importantly, ECs also disrupt energy homeostasis by impairing GM, which acts as a critical intermediary, as shown in models such as mussels (Dumas et al., 2020). Further mechanistic studies and targeted interventions are urgently needed.

To investigate how ECs impact energy metabolism through GM, a comprehensive literature search was conducted using PubMed, Web of Science, and Scopus. The search strategy incorporated Medical Subject Headings (MeSH) terms to refine results based on inclusion and exclusion criteria. This review aims to assess the impact of ECs on distant organs by examining their interactions with GM, particularly through the metabolism of key bridging molecules. Emission standards are detailed in Table 2, and the search results are summarized in Table 3.

The present studies indicated the importance of bridge chemicals in metabolomics, which connects the GM and the distal organs that collectively regulate the organism.

Table 2 Emission standards

Key Considerations	Inclusion criteria	Exclusion criteria
Research approach	Animal studies	No animal studies, human studies, in vitro, or ex vivo studies
Exposure method	ECs Exposure	No ECs exposure
Control subjects	Control subjects	No control group
Result	Through the bridge, substance reflecting on the influence of GM, distal systems	Only reflects intestinal damage

Table 3 Effects of emerging contaminants on distal organs via GM

Target organ	Emerging contaminants	Animal model（including animal, age, exposure group, exposure duration, exposure dose）	Changes in GM	Bridge metabolites	Energy metabolism	Reference
Gut	Microplastics (MP)	18 Kunming mice; 8 weeks old; 6 groups; 1 week exposure; dose 20 mg/mL (Different MP per group)	↑: Diversity of GM in the exposed group, Mycobacteriaceae, Thick-walled Mycobacteriaceae, Ruminalococcaceae, Trichosporonaceae.	Triglyceride	Inflammatory cells of gut↑	(Xie et al., 2022)
	Microplastics (MP)	36 female ICR mice; 8 weeks old; 3 groups; 30 days exposure; dose:0, 0.002, and 0.2 μg/d, respectively	↑: Mycobacteriophage; ↓: Thick-walled Mycobacteriophage.	Amino acids, lipopolysaccharides, proteins	exposure group amino acid of gut metabolism↑	(Sun et al., 2021)
	Broad-spectrum antibiotics such as ampicillin,streptomycin, and clindamycin	40 male mice (C57BL6) 20 ± 2 g; 4 groups; 2 week exposure; exposed groups received receiving antibiotic drinking water containing 1 mg/ml	↑: Anaplasma phylum, Aspergillus phylum; ↓: Bacterial diversity and abundance, Filamentous, Actinomycetes.	Bile acids	Multiple bile acids in the enterohepatic circulation are affected	(Liu et al., 2020)
	TP (tretinoin), ampicillin, metronidazole, vancomycin and neomycin sulfate	TP: male C57BL/6J mice; 6-8 weeks old; 2 groups; exposed to 600 μg/kg TP ,5 days. Antibiotics (ABX): 200 mg/kg (100 mg/kg for vancomycin), 5 days	Alteration of gut microbial composition and structure; ↓:Abundance of Lactobacillus rhamnosus.	Bile acids	Unconjugated BAs in the cecum contents↓, lactobacilli abundance was negatively correlated with unconjugated bile acid content	(Hu et al., 2024)
	Microplastics (MP)	15 zebrafish ; 6 months of age or older; 3 groups; 14 days exposure; 300, 600 mg/L drinking water	↑: Rhizobiaceae, Xanthobacteraceae; ↓: exposure groups Enterobacteriaceae, Cetobacteriaceae.	Transcriptomics	hepatocyte injury	(Tian et al., 2024)
Liver	Ceftriaxone	32 male C57BL/6J mice; 8 weeks old; 4 groups; 8 weeks exposure, exposed groups received a 6.8 mg/L penicillin G in drinking water	↑: Opportunistic pathogens, Klebsiella, Morganella; ↓: Probiotics, Bifidobacterium, Lactobacillus.	Bile acids, indole, erucic acid	Affect the bacterial composition, alter the faecal metabolome.	(Hill et al., 2014)
	Ceftriaxone sodium	48 male C57BL/6J mice; 4 weeks old; 2 groups; 8 days exposure; exposure group received ceftriaxone sodium solution 400 mg/mL, 0.2 mL per dose	↑: Parasutterella, Akkermansia, Warty Microbacteria, Ascomycota; ↓: Parasutterella, Lachnospiraceae_NK4A136_group, Thick-walled Bacteria, Deferribacterota, Patesicibacteria.	Bile acids, amino acids	Alter intestinal metabolism, resulting in hepatic metabolic disorders	(Lai et al., 2023)

	Sulfamethoxazole (SMX)	1000 largemouth bass juveniles; mean weight 30.65 ± 0.02 g; 3 groups; 8 weeks exposure, two levels of sulfamethoxazole (0, 0.3%)	↑: Cetobacterium, Brevinema； ↓: Exposed group Pleslomonas, Mangrovibacter, Shewanella, Enterococcus, Bifidobacterium, Aurantimicrobium.	Bile acids	Oxidative stress, inflammation↑, apoptosis↑	(Xie et al., 2020)
	Antibiotics, anticoagulants	SD female and male rats; 6 weeks old; 3 groups; amoxicillin to establish an intestinal dysbiosis model (90 mg/kg); exposure groups warfarin sodium (0.2 mg/Kg), dabigatran (20 mg/kg) and rivaroxaban (2.6 mg/kg)	↑: Ascomycota phylum; ↓: Thick-walled phylum, Anaplasma phylum.	Amino acids	Affect the expression of heparanase and P-gp, transport and metabolism of oral anticoagulants.	(Chen et al., 2022)
Liver	Perfluorooctane sulfonate (PFOS)	ICR mice; 4-5 weeks old; 4 groups (n=8-11); 14-day exposure; doses of 1 mg/kg, 5 mg/kg, and 10 mg/kg	↑: Bacteroides spp. Allobaculum; ↓: Lactobacillus spp, Enterococcus spp.	Amino acids	One hundred sixteen hepatic metabolites and 23 faecal metabolites differed.	(Jiang et al., 2022)
	Perfluorobutane sulfonate (PFBS)	24 male C57BL/6 mice; 8 weeks old; 4 groups; 6 weeks exposure; 50 μg/L	↑: Enterococcus ; ↓: Akkermansia, Lactobacillus.	Amino acids	39 metabolites↓	(Liu et al., 2023)
	Cadmium and nano plastics (NPs)	300 bass; mean initial weight: 14.67 ± 0.08 g; 4 groups; 7 and 9 days exposure; 10 μg/L Cd, 100 μg/L NPs	↑: Thick-walled phylum, Tenereus, Aspergillus, Enterobacteriaceae; ↓: Clostridiaceae, Mycoplasma.	Antioxidant indicators	MDA↑,the liver oxidative stress and oxidative damage↑	(Chen et al., 2023)
	Polybrominated diphenyl ethers (PBDE)	8week C57BL/6J mice bred for three generations resulted (n=5);exposed until 15 months of age; dose 57 mg/kg	↓: intestinal tight junction protein transcripts; altered intestinal environment and dysregulation of inflammation-related metabolites	Diastase	lipid metabolizing enzymes↓, genes involved in microbial endocytosis in hepatocytes↑	(Lim et al., 2024)
	Diethyl (2-ethylhexyl) phthalate (DEHP)	56 ICR mice; 3 weeks old; 7 groups; 6 weeks exposure; 1000 mg/kg bw/day	↑:Exposure group Mycobacterium avium.	Hormones	↑: T-SOD, CuZn-SOD, MDA	(Lu et al., 2024)
Liver	Quercetin Nanoparticles (QNP)	240 Nile tilapia; 40 ± 0.45 g; 4 groups; 60 days exposure; 400 mg QNPs/kg diet	↑: Total GM, Aeromonas.	Hormones	↓: CAT, SOD, GSH	(Farag et al., 2023)
Brian	Antibiotics	16 male NIH Swiss mice; 8 weeks old; 2 groups; 30 days exposure; ampicillin (1 mg/ml),	↓: GM interact with Toll-like receptors.	Amino acids	MyD88 expression↓	(Johnson and Burnet, 2020)

		vancomycin (5 mg/ml), neomycin (10 mg/ml), metronidazole (10 mg/ml) and amphotericin-B (0.1 mg/ml)				
Reproduction	Diethyl (2-ethylhexyl) phthalate (DEHP)	30 female ICR mice; 4 weeks old; 3 groups; 30 days exposure; doses of 500 and 1500 mg/kg	↑: Exposed group Thick-walled bacillus phylum;↓: Anaplasma phylum, Actinobacillus phylum, Epsilon phylum.	Amino acids, short-chain fatty acids	165 metabolites↓, 65 metabolites↑	(Fu et al., 2021)
	Bisphenol A	60 male C57BL/6j; 7 weeks old; 6 groups; 6 weeks exposure; 50 mg/kg b.w/d	↑: Exposure group E. faecalis, Parasutterella; ↓: Heterobacterium spp., H. pylori, Mycobacterium avium.	Bile acids, amino acids	Altered KEGG pathway, BA metabolism in arginine and proline metabolism	(Wu et al., 2024)
Reproduction	Diethyl (2-ethylhexyl) phthalate (DEHP)	36 BALB/c mice; 4 weeks old; 6 groups; 4 weeks exposure; 400 μg/L	Differences in the composition of bacteria at the genus level changed significantly	Short-chain fatty acid	↓: Acetic acid, butyric acid concentrations, SCFA; ↑: hepatic TG, plasma LDL	(Teng et al., 2024)
Kidney	Triclosan (TCS)	16 C57BL/6J male mice; 7-8 weeks old; 2 groups; 10 weeks exposure; dose 50 mg/kg	↑: Exposed group Thick-walled phylum, Actinobacteria phylum, ↓: Anaplasma phylum, Cyanobacteria phylum, Patescibacteria, Warty Microbacteria phylum.	Fatty acids	↑: MDA; ↓: SOD, TCHO	(Zhuang et al., 2024)

Note: ↑means upregulation while↓indicates downregulation

3.2 Mechanism of the Gut-metabolic axis

Although the processes of ECs in metabolomics and their harmful effects on distal organs have been the focus of attention, the precise mechanisms remain incompletely explored. The gut-metabolism axis might play a key role in this process.

3.2.1 Microbial molecular correlation patterns（MAMPs）

The gut acts as an immunological organ, serving as a physical barrier against substances (Chassaing et al., 2014). It also has adaptive and innate immune cells that protect against infections. The GM contributes to the maturation of the immune response, with Microbial Molecular Correlation Patterns (MAMPs) serving as key immune signaling components (Patten and Collett, 2013).

Exposure to ECs can compromise the intestinal barrier, allowing macromolecules such as lipopolysaccharides (LPS) to enter the bloodstream (Liu et al., 2021). This subsequently triggers immune responses by activating dendritic cells, macrophages, and neutrophils, leading to the release of inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukins-1 (IL-1) and interleukins-6 (IL-6) (Fleshner, 2013; Nakkarach et al., 2021). These cytokines can interact with afferent neurons and cross the blood-brain barrier (BBB), activating microglia and causing inflammation. This process primarily triggers systemic inflammation via the nuclear factor kappa-B (NF-κB) pathway, influences fatty acid metabolism through the janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway, and governs energy metabolism through the activation of Adenosine 5’-monophosphate (AMP)-activated protein kinase (AMPK) and mammalian target of rapamycin (mTOR) pathways (Hotamisligil, 2006). Ultimately, these disruptions lead to changes inpro-inflammatory gene expression, metabolic imbalances, and insulin resistance (IR), altering both fatty acid and glucose metabolism.

3.2.2 Insulin resistance (IR)

IR is a key characteristic of various chronic metabolic disorders. Research suggests that changes in the GM, inflammation, and immune system dysfunction play crucial roles in its development (Petersen and Shulman, 2018). Studies have indicated that exposure to ECs has been linked to IR, which in turn exacerbates GM imbalance. This imbalance is marked by reduced microbial diversity, lower abundance of beneficial bacteria, and structural abnormalities within the microbial community (Li et al., 2024b).

ECs’ exposure has been shown to significantly alter GM composition, leading to an increase in pro-inflammatory bacteria associated with gut barrier dysfunction. Specifically, there is a rise in the abundance of opportunistic pathogenic bacteria such as *Haemophilus, bilophila* and *Wadsworthia* in the feces. At the same time, the LPS level is increased in exposed individuals, binding to lipopolysaccharide-binding proteins in the bloodstream. These complexes interact with clusters of differentiation 14 (CD14) receptors, forming trimers that signal through Toll-like and pattern-recognition receptors (Neves et al., 2013). This process activates multiple inflammatory signaling pathways, leading to a systemic chronic inflammatory response (WRIGHT et al., 1990). As a result, there is an increased expression of pro-inflammatory cytokines, including IL-1 and TNF-α, which disrupt insulin signaling. TNF-α

contributes to IR by inhibiting the phosphorylation of serine residues in insulin receptor substrate 1 (IRS1), resulting in elevated blood glucose levels (Cseh et al., 2000). Overall, exposure to ECs frequently disrupts GM balance and induces systemic inflammatory responses, both of which contribute to metabolic disorders linked to impaired energy regulation.

3.2.3 Bile acids (BA)

It has been observed that exposure to ECs impacts GM metabolism, including changes in BA, which plays a key role in regulating energy metabolism. A recent study has discovered that BA can influence GM composition by modulating the abundance of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium* (Ridlon et al., 2020). Some secondary BA, such as deoxycholic acid (DCA), may contribute to gut dysbiosis and inflammatory bowel disease (IBD) by increasing the prevalence of harmful bacteria like *Enterococcus*. In contrast, lithocholic acid (LCA) can inhibit pathogenic bacteria like Escherichia coli while promoting beneficial anaerobic bacteria such as *Bacteroides*, thereby supporting gut health (Collins et al., 2023).

Beyond their impact on microbial composition, BA also significantly influence the host metabolism via their metabolic byproducts. SCFA, produced as a result of BA metabolism, can cross the intestinal barrier into the bloodstream, altering the host's metabolic status. Additionally, secondary BA activates G protein-coupled receptors and nuclear receptors in the gut, regulating cholesterol metabolism, glucose-lipid metabolism, and other physiological processes (Fleishman and Kumar, 2024).

Exposure to ECs disrupts BA homeostasis by affecting the abundance and composition of the host GM, reducing ileal BA reabsorption and increasing hepatic BA production (Zhao et al., 2024b). A study has shown that long-term exposure to ECs strengthens the expression of *Cyp8b1*, a crucial enzyme in CA synthesis, and *Cyp7a1*, a rate-limiting enzyme. Meanwhile, the ileal expression of *Fgf15*, a regulator of *Cyp7a1*, was significantly reduced. This feedback mechanism normally prevents excessive BA accumulation, which could otherwise cause liver and organ damage (Gadaleta and Moschetta, 2019).

Long-term EC exposure may also increase BA hydrophobicity, promoting cholesterol transport from the gut to the liver and leading to elevated cholesterol levels and chronic metabolic disorders. This process involves the regulation of cholesterol metabolism and the activation of the farnesoid X receptor (FXR). An increase in hydrophobic BA, such as DCA, might trigger a feedback response in the liver to enhance cholesterol conversion, helping maintain BA balance (Calkin and Tontonoz, 2010). However, long-term exposure to ECs might alter FXR function, affecting BA synthesis, cholesterol synthesis, and clearance (Gao et al., 2018). Additionally, these BA might also affect fatty acid production and lipid metabolism by modifying GM composition (Russell, 2003), ultimately leading to energy metabolism disturbances in various organs.

3.3 Intestinal-energy metabolism on target organs

Liver

Exposure to ECs disrupts gut microbiota balance, reduces mucus secretion, and impairs tight junction proteins, significantly increasing intestinal permeability. As a result, this facilitates the accumulation of LPS

in the bloodstream, triggering inflammatory responses that ultimately cause liver damage (Liu et al., 2021). Additionally, excessive LPS synthesis, combined with a deficiency in secondary BA, leads to the formation of α-keto acids, amines, and carbon dioxide during amino acid metabolism, which can further harm the body. Simultaneously, smaller ECs can also accumulate in the liver and blood vasculature, impairing insulin signaling pathways by downregulating IRS1 and phosphatidylinositol-3-kinase (PI3K) expression, thereby contributing to insulin resistance and organ dysfunction (Huang et al., 2022). In conclusion, ECs influence multiple metabolic pathways in the liver, resulting in metabolic abnormalities and hepatic damage (Zhang et al., 2022).

Brain

ECs exposure strengthens the activity of superoxide dismutase and catalase in the liver and intestine while diminishing acetylcholinesterase activity in the brain (Zhang et al., 2022b). These disruptions contribute to BA irregularities, which can impact neurodevelopment (Lai et al., 2023). In the context of metabolic diseases, ECs exposure or stress-induced inflammation can influence the activation of microglial cells, thereby modifying signaling in the hypothalamus. These conditions can lead to hyperphagia, obesity, insulin resistance (Rosin and Kurrasch, 2018), and ultimately long-term cognitive effects and other behavioral alterations.

Reproductive System

Exposure to ECs can reduce estrogen levels, cause immune dysfunction, and trigger inflammation, leading to alterations in gut metabolites, including BA (McCallum et al., 2017). These changes might ultimately contribute to the formation of uterine fibroids (Vineetha et al., 2023) and negatively affect offspring growth and development (Blake et al., 2022). In males, higher EC exposure correlates with decreased scrotal circumference and total sperm motility (Solaiman et al., 2009). Endocrine-disrupting ECs, commonly found in contaminated food and water, have been widely studied as obesogens. Their effects may include prenatal weight gain, IR (Podratz et al., 2020), pancreatic β-cell dysfunction, and reduced sperm quality.

Other organs

At the same time, ECs exposure has been linked to various degrees of damage across multiple organs (Zhao et al., 2024c). For example, disruptions in cholesterol metabolism, arginine biosynthesis, and bile secretion pathways have been observed in both infected and antibiotic-treated groups (Li et al., 2022). These findings highlight the systemic impact of ECs on energy metabolism and overall health.

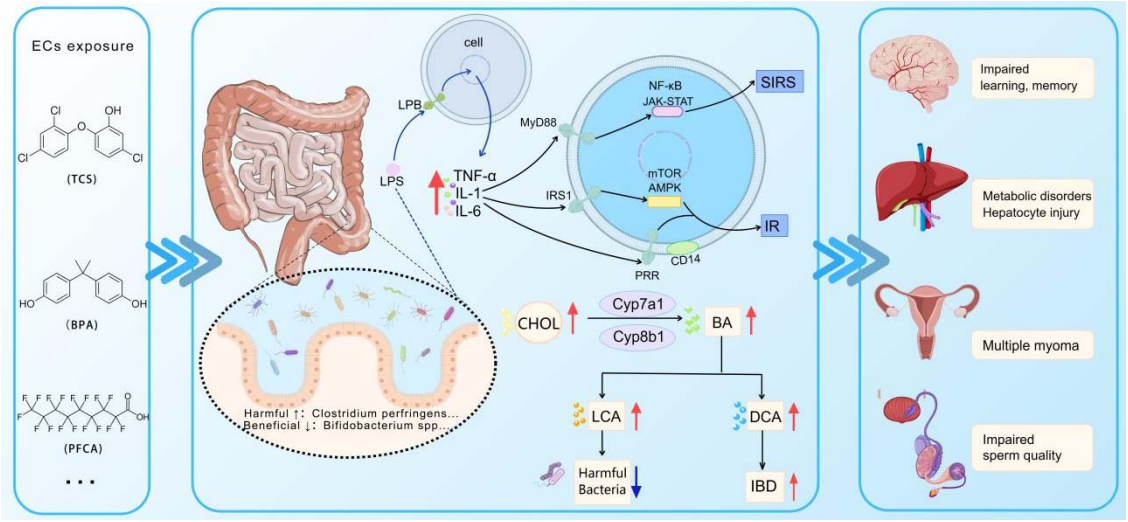

Figure 1. Effects of ECs on multiple organs via GM.

3.4 Summary

To systematically elucidate the mechanisms by which ECs disrupt multi-organ metabolism via GM, a summary Table 4 was constructed. It compares GM alterations, key metabolic pathway changes, and functional impairments in major target organs following EC exposure.

Table 4 Comparative Responses of Different Organs in the ECs/GM/Energy Metabolism Axis

Target Organ	Major ECs Types	GM Alterations	Key Bridging Metabolites	Energy Metabolism Dysregulation	Typical Mechanisms
Gut	Microplastics, Antibiotics	Diversity ↓, Pathogenic bacteria ↑	SCFA, Amino acids	Local inflammation ↑, Amino acid metabolism disorder	Mucosal barrier damage, Immune activation
Liver	Various ECs, Antibiotics, PFCs	Probiotics ↓, BA-metabolizing bacteria disorder	BA, Amino acids	Lipid accumulation ↑, β-oxidation ↓, Gluconeogenesis disorder	BA–FXR axis disruption, Mitochondrial dysfunction
Brain	Antibiotics	GM–Toll-like receptor interaction ↓	Amino acids	Neurotransmitter imbalance, Energy supply deficiency	Neuroinflammation, Microglial activation
Reproductive System	Phthalates, Bisphenol A	Firmicutes ↑/ Actinobacteria ↓	Bile acids, SCFA	Sex hormone synthesis disorder, Oocyte energy deficiency	Endocrine–metabolic crosstalk disruption

Note: ↑means upregulation while↓indicates downregulation

4. GM-Mediated Antagonism of Emerging Pollutants by Probiotics

4.1 Probiotics

Probiotics are live microorganisms that provide health benefits to the host when consumed in sufficient amounts (Hill et al., 2014). Many studies have demonstrated that probiotics have the ability to mediate bridging molecules and counteract the harmful effects of ECs.

4.2 Physicochemical Functions of Probiotics

Probiotics have been playing an increasingly significant role in environmental remediation, particularly in the bioremediation of pollutants, where they exhibit unique advantages. In terms of biodegradation, probiotics are capable of decomposing organic pollutants such as petroleum hydrocarbons and pesticides through metabolic activity, as well as removing inorganic contaminants like heavy metals via biosorption on their cell surfaces (Huixiong et al., 2024). Additionally, probiotics possess the ability to biotransform pollutants into less toxic or non-toxic substances, effectively reducing environmental risks (Reshu et al., 2024). Studies have demonstrated that probiotics rely on a combination of enzymatic degradation, biosorption, and ecological modulation to enhance the efficiency of pollutant transformation and removal (Arshad et al., 2024). Recent research also indicates that probiotics, as crucial biological regulators of host GM, play a key role in mitigating the adverse effects of emerging pollutants on intestinal health.

4.3 GM-Mediated Antagonism of Emerging Pollutants by Probiotics

4.3.1 Improvement of Gut Condition

Probiotics can effectively alleviate disruptions in gut barrier integrity and microbiota metabolic homeostasis induced by emerging pollutants by modulating gut microbial ecology and enhancing barrier functions, thus demonstrating considerable potential in ecological safety and intestinal protection (Wang et al., 2021). Specifically, probiotics suppress pathogenic and harmful bacteria through competitive exclusion while promoting the proliferation of beneficial microbes, thereby restoring microbiota composition and maintaining microbial homeostasis (Song et al., 2023). Moreover, probiotics can upregulate the expression of tight junction proteins, improve their localization and distribution, repair pollutant-induced intestinal barrier damage, reduce gut permeability, and minimize the translocation of endotoxins and pollutants (Distrutti et al., 2013). Additionally, by enhancing mucus layer secretion, probiotics form a physical barrier that effectively prevents pathogens and harmful substances from contacting epithelial cells, thereby further preserving barrier integrity (GAO et al., 2013).

4.3.2 Antioxidant and Anti-inflammatory Effects

Exposure to emerging pollutants often triggers excessive production of free radicals, leading to oxidative stress, cellular structural damage, and disrupted physiological functions. Studies indicate that probiotics can reduce oxidative stress by upregulating the activity of various antioxidant enzymes, such as glutathione peroxidase (GPX), superoxide dismutase (SOD), and catalase (CAT), thereby scavenging free radicals, decreasing reactive oxygen species (ROS) levels, and protecting hepatic and intestinal tissues

(Qinqin et al., 2024). Concurrently, probiotics can inhibit pollutant-induced activation of inflammatory pathways, including NF-κB and AMPK signaling, thereby reducing the expression of pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1, and ameliorating chronic inflammatory states (Qinqin et al., 2024).

4.3.3 Promotion of Pollutant Metabolism and Excretion

Certain probiotic strains facilitate the metabolism and excretion of pollutants through mechanisms such as binding, degradation, and modulation of BA metabolism, effectively reducing pollutant accumulation within the host. In cholesterol metabolism, for instance, administration of various doses of *Lactobacillus casei Zhang* and its fermented dairy products in rats significantly lowered hepatic total cholesterol and triglyceride levels, increased fecal total bile acid content, and modulated serum apolipoprotein levels, suggesting an indirect regulatory effect on cholesterol absorption and excretion via BA metabolism (Zhang, 2011). Furthermore, some probiotics can enhance heavy metal excretion by modulating the enterohepatic circulation. Oral administration of Lactobacillus plantarum, for example, has been shown to increase cadmium excretion and alleviate its accumulation and toxicity in vivo. Notably, docosahexaenoic acid (DHA) has also been reported to promote cadmium detoxification by restoring Parabacteroides abundance in the intestines of cadmium-exposed mice (Jianzhen et al., 2023).

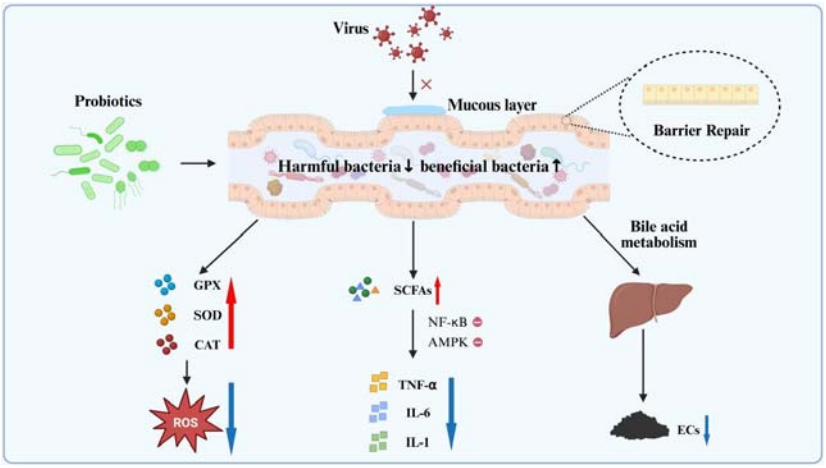

Figure 2. Probiotics antagonize emerging pollutants by GM

4.3.4 Restoration of Disrupted Intestinal Metabolites

Recent studies demonstrate that probiotics mitigate pollutant-induced metabolic toxicity and organ dysfunction through modulation of gut-derived metabolites. Specifically, *Akkermansia muciniphila* converts primary to secondary BA via bile salt hydrolase activity, activating FXR and G protein-coupled bile acid receptor 1 (TGR5) signaling pathways to regulate hepatic lipid metabolism and reproductive hormone homeostasis (Cui, X. et al, 2025). *Lactobacillus rhamnosus GG* generates SCFA that activate G protein-coupled receptors 41/43 (GPR41/GPR43) and suppress histone deacetylase activity, thereby enhancing intestinal barrier integrity and reducing NF-κB-mediated testicular inflammation (Zhen, H. et al., 2024). Multi-strain formulations of *Lactobacillus plantarum* confer multi-organ protection through BA metabolic remodeling, acetylcholine precursor synthesis, and tight junction protein upregulation (Razzaq, A. et al., 2024). A systematic summary of these mechanisms is presented in Table 5.

Table 5 Beneficial Effects of Probiotics in Antagonizing ECs

Probiotics	Regulating intermediates	Energy metabolism	Improvement of distal organs	Reference
P. freudenreichii freudenreichii B3523 (PF) and P. freudenreichii shermanii B4327 (PS)	BA	The involvement of the gut-liver axis influences liver damage and metabolic disturbances resulting from ECs exposure.	Liver disease	(Nair and Johny, 2018)
Bacillus subtilis (bacillus subtilis)	Amino acids	the gut microbiota is capable of modifying and converting primary bile acids into secondary bile acids through dehydroxylation reactions.	Liver disease	(Zhang et al., 2024)
Baker's yeast (BY), Chrysomycin (CTC)	Amino acids	Serum glutamic oxalacetic transaminase (GOT)↑	Liver disease	(Çelyk et al., 2003)
Commercial Probiotics Hypro-calves	Amino acids	blood IgA↑and serum CD4↑	Skeleton	(Karamzadeh-Dehaghani et al., 2021)
Mucinophilic Ackermannia (genus of bacteria)	BA	Grow in the presence of bile salts	Reproduction	(Asadi et al., 2022)
Lactobacillus plantarum ATG-K2, ATG-K6 and ATG-K8	BA	↑:antibacterial activity, bile salt hydrolase activity, hydrogen peroxide production	Reproduction	(Beck et al., 2019)
Lactobacillus plantarum strain Tensia	Amino acids	↑： L-histidine, L-glutamine, L-ornithine, L-arginine, or L-lysine	Reproduction	(Songisepp et al., 2012)
Lactobacillus rhamnosus, Lactobacillus plantarum	SCFA	A restored balance of short-chain fatty acids (SCFAs)	Reproduction	(Wu et al., 2024)
Probiotics SLAB51	Amino acids	oxidative stress↓	Brain, liver	(Wu et al., 2024)
Lactobacillus plantarum TW1-1	Antioxidant indicators	hyper-permeability↓, serum lipopolysaccharide level↑	Reproduction	(Tian et al., 2019)
Lactobacillus plantarum DP189	Acetylcholine ACh (amine-related vitamin B complex)	oxidative stress↓,inflammatory response↓, a rebound in the release of acetylcholine.	Cranial nerves	(Wang et al., 2024)
Lactobacillus, Bifidobacterium	SCFA	glutathione↑, malonaldehyde contents↓, indicated the improved oxidative status.	Intestinal tract	(Song et al., 2018)
Lactobacillus acidophilus	Amino acids	alanine transaminase, aspartate aminotransferase, albumin, creatinine, and urea were significantly different in treated and non-treated animals.	Cytotoxicity	(Khalifa et al., 2023)

Note: ↑means upregulation while↓indicates downregulation

4.4 Future Perspectives

Despite the promising potential of probiotics in mitigating the toxicity of emerging pollutants, their precise mechanisms of action and optimal application strategies remain to be elucidated. Considering individual variations in GM composition, personalized probiotic interventions represent a crucial future research direction to achieve targeted reduction of pollutant toxicity. Additionally, combined intervention strategies incorporating probiotics with other measures might exert synergistic protective effects. For example, studies have shown that co-administration of vitamin D and probiotics can enhance protection against cadmium toxicity. Furthermore, the screening, identification, and application of novel probiotic strains with superior pollutant metabolism capacity and organ-protective functions hold significant scientific value and practical potential in fields such as food safety and environmental remediation. In-depth investigation of the mechanisms by which probiotics modulate pollutant toxicity and organ function through GM regulation, BA metabolism, and the gut-organ axis will be crucial for the rational application of probiotics. Of particular note, probiotics also possess broad prospects in emerging applications, such as the development of functional endophytic colonization systems to prevent polycyclic aromatic hydrocarbon contamination in agricultural products, which offer both market potential and investment value, providing new research avenues for the diversified application of probiotics.

In conclusion, future research should prioritize the development of personalized and combined probiotic intervention strategies and elucidate their underlying mechanisms, thereby maximizing the health-protective functions of probiotics in safeguarding human health.

Conclusion

Despite more evidence provided by recent ECs researches, significant gaps remain in understanding their metabolic impact across multiple organs. Most studies focus on the outcomes of ECs' exposure and the potential benefits of probiotics, but few investigate the specific metabolic pathways involved in multi-organ dysfunction. This review synthesizes current literature to highlight how ECs induce metabolic disruptions through the gut-metabolism axis. By providing a detailed analysis of these mechanisms, our study offers a more comprehensive understanding of ECs-related toxicity and helps bridge the existing knowledge gap in multi-organ metabolic dysfunction.

Ethical Approval

Not applicable.

Funding

This research was supported by the National Natural Science Foundation of China under Grant 72064002, Gansu Key Research and Development Programmes under Grant No.25YFFA028, Gansu Natural Science Foundation under Grant No.25JRRA668, and the Fundamental Research Funds for the Central Universities under Grant lzujbky-2024-14 and lzujbky-2025-it59.

Data and Materials availability

No data and materials was used for the research described in the article.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose including employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

Reference

Abdolmaleki, K., et al., 2022. Emerging technologies in combination with probiotics for aflatoxins removal: an updated review. International Journal of Food Science and Technology. 57, 5712-5721.

Ahlawat, S., et al., 2021. Gut–organ axis: a microbial outreach and networking. Letters in Applied Microbiologyletters in Applied Microbiology. 72, 636-668.

Arshad, I., et al., 2024. A review on the synergistic approaches for heavy metals bioremediation: harnessing the power of plant-microbe interactions. Lahore Garrison University Journal of Life Sciences. 8, 268-286.

Asadi, A., et al., 2022. The probiotic properties and potential of vaginal lactobacillus spp. Isolated from healthy women against some vaginal pathogens. Letters in Applied Microbiology. 74, 752-764.

Assiri, M. A., et al., 2024. Electronic cigarette vapor disrupts key metabolic pathways in human lung epithelial cells. Saudi Pharmaceutical Journal. 32,101897.

Bao, L. J., et al., 2015. Global trends of research on emerging contaminants in the environment and humans: a literature assimilation. Environmental Science and Pollution Research. 22, 1635-1643.

Beck, B. R., et al., 2019. Whole genome analysis of lactobacillus plantarum strains isolated from kimchi and determination of probiotic properties to treat mucosal infections by candida albicans and gardnerella vaginalis. Frontiers in Microbiology. 10,433.

Ben, Y., et al., 2019. Human health risk assessment of antibiotic resistance associated with antibiotic residues in the environment: a review. Environmental Research. 169, 483-493.

Blake, B. E., et al., 2022. Transcriptional pathways linked to fetal and maternal hepatic dysfunction caused by gestational exposure to perfluorooctanoic acid (pfoa) or hexafluoropropylene oxide-dimer acid (hfpo-da or genx) in cd-1 mice. Ecotoxicology and Environmental Safety. 248,114314.

Burgos-Aceves, M. A., et al., 2024. Effect of emerging pollutants on the gut microbiota of freshwater animals: focusing on microplastics and pesticides. Science of the Total Environment. 948,174809.

Calkin, A. C., Tontonoz, P., 2010. Liver x receptor signaling pathways and atherosclerosis. Arteriosclerosis Thrombosis and Vascular Biology. 30, 1513-1518.

Cayer, L., et al., 2024. An integrated multi-omics analysis of the effects of the food processing-induced contaminant 2-monochloropropane-1,3-diol (2-mcpd) in rat heart. Archives of Toxicology.

Çelyk, K., et al., 2003. Reduction of toxic effects of aflatoxin b1 by using baker yeast (saccharomyces cerevisiae) in growing broiler chicks diets. Revista Brasileira De Zootecnia-Brazilian Journal of Animal Science. 32, 615-619.

Chassaing, B., et al., 2014. Mammalian gut immunity. Biomedical Journal. 37, 246-58.

Chen, M. S., et al., 2023. Combined effects of cadmium and nanoplastics on oxidative stress, histopathology, and intestinal microbiota in largemouth bass (micropterus salmoides). Aquaculture. 569, 739363.

Chen, T., et al., 2019. Thyroid function and decabromodiphenyl ethane (dbdpe) exposure in chinese adults from a dbdpe manufacturing area. Environment International. 133, 105179.

Chen, W. J., et al., 2022. Changes in the gut microbiota may affect the clinical efficacy of oral anticoagulants. Frontiers in Pharmacology. 13, 860237.

Chmielewski, J., et al., 2022. Microplastic in the environment. The role of education in raising social awareness of the handling of plastic waste. Journal of Elementology. 27, 31-45.

Choi, D., et al., 2020. In vitro chemical and physical toxicities of polystyrene microfragments in human-derived cells. Journal of Hazardous Materials. 400, 123308.

Collins, S. L., et al., 2023. Bile acids and the gut microbiota: metabolic interactions and impacts on disease. Nature Reviews Microbiology. 21, 236-247.

Cseh, K., et al., 2000. The role of tumour necrosis factor (tnf)-α resistance in obesity and insulin resistance. Diabetologia. 43, 525-525.

Cui, X. et al., 2025. Recent advances in gut microbiota-mediated regulation of fat deposition and metabolic disorders. Microbiome Research Reports. 4(3), 31.

Dahiya, P., et al., 2024. Guardians of the gut: harnessing the power of probiotic microbiota and their exopolysaccharides to mitigate heavy metal toxicity in human for better health. Probiotics and Antimicrobial Proteins.1-17.

Distrutti, E., et al., 2013. Probiotics vsl#3 protect against development of visceral pain in murine model of irritable bowel syndrome. Plos One. 8(5), e63893.

Dmytriv, Tetiana R., et al., 2024. Intestinal barrier permeability: the influence of gut microbiota, nutrition, and exercise. Frontiers in physiology 15, 1380713.

Dong, Z., et al., 2015. Tris-(2,3-dibromopropyl) isocyanurate induces depression-like behaviors and neurotoxicity by oxidative damage and cell apoptosis in vitro and in vivo . The Journal of Toxicological Sciences. 40, 701-709.

Dumas, T., et al., 2020. Metabolomics approach reveals disruption of metabolic pathways in the marine bivalve mytilus galloprovincialis exposed to a wwtp effluent extract. Science of the Total Environment. 712, 136551.

Farag, M. R., et al., 2023. Effect of quercetin nanoparticles on hepatic and intestinal enzymes and stress-related genes in nile tilapia fish exposed to silver nanoparticles. Biomedicines. 11(3), 663.

Farrell, M., et al., 2019. Responding to global stimulant use: challenges and opportunities. The Lancet. 394, 1652-1667.

Feiteiro, J., et al., 2021. Health toxicity effects of brominated flame retardants: from environmental to human exposure. Environmental Pollution. 285, 117475.

Ferdous, Z., et al., 2019. Pulmonary exposure to silver nanoparticles impairs cardiovascular homeostasis: effects of coating, dose and time. Toxicology and Applied Pharmacology. 367, 36-50.

Fleishman, J. S., Kumar, S., 2024. Bile acid metabolism and signaling in health and disease: molecular mechanisms and therapeutic targets. Signal Transduction and Targeted Therapy. 9, 97.

Fleshner, M., 2013. Stress-evoked sterile inflammation, danger associated molecular patterns (damps), microbial associated molecular patterns (mamps) and the inflammasome. Brain, Behavior, and Immunity. 27, 1-7.

Fu, J., et al., 2019. Metabolomic profiling of zebrafish (danio rerio) embryos exposed to the antibacterial agent triclosan. Environmental Toxicology and Chemistry. 38, 240-249.

Fu, X. F., et al., 2021. Di-(2-ethylhexyl) phthalate exposure induces female reproductive toxicity and alters the intestinal microbiota community structure and fecal metabolite profile in mice. Environmental Toxicology. 36, 1226-1242.

Gadaleta, R. M., Moschetta, A., 2019. Metabolic messengers: fibroblast growth factor 15/19. Nature Metabolism. 1, 588-594.

GAO, K., et al., 2013. Functions of intestinal epithelial barriers modulated by probiotics and mechanisms. Chinese Journal of Animal Nutrition.1,1936-1945.

Gao, X., et al., 2018. Yangonin protects against cholestasis and hepatotoxity via activation of farnesoid x receptor in vivo and in vitro. Toxicology and Applied Pharmacology. 348, 105-116.

Gopal, C. M., et al., 2021. Seasonal occurrence and risk assessment of pharmaceutical and personal care products in bengaluru rivers and lakes, india. Journal of Environmental Chemical Engineering. 9, 105610.

Gruener, N., et al., 2023. Pivotal role of intestinal microbiota and intraluminal metabolites for the maintenance of gut-bone physiology. International Journal of Molecular Sciences. 24(6), 5161.

Hill, C., et al., 2014. The international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology. 11, 506-514.

Hotamisligil, G. S., 2006. Inflammation and metabolic disorders. Nature. 444, 860-867.

Huang, D. J., et al., 2022. Polystyrene microplastic exposure induces insulin resistance in mice via dysbacteriosis and pro-inflammation. Science of the Total Environment. 838, 155937.

Huang, P., et al., 2022. Cumulative risk assessment and exposure characteristics of parabens in the general taiwanese using multiple hazard indices approaches. Science of the Total Environment. 843, 156821.

Hu, S., et al., 2024. Lactobacillus rhamnosus gg ameliorates triptolide-induced liver injury through modulation of the bile acid-fxr axis. Pharmacological Research. 206, 107275.

Huixiong, L., et al., 2024. Microbial consortium degrading of organic pollutants: source, degradation efficiency, pathway, mechanism and application. Journal of Cleaner Production. 451, 141913.

Jiang, L. L., et al., 2022. The role of fecal microbiota in liver toxicity induced by perfluorooctane sulfonate in male and female mice. Environmental Health Perspectives. 130(6), 067009.

Jiao, X., et al., 2023. Toxic effects of perfluorocaproic acid (pfhxa) on crucian carp (carassius auratus) and the response of the intestinal microbial community. Comparative Biochemistry and Physiology C-Toxicology & Pharmacology. 271, 109683.

Jianzhen, L., et al., 2023. Docosahexaenoic acid promotes cd excretion by restoring the abundance of parabacteroides in cd-exposed mice. Molecules. 28, 4217.

Jin, Y. X., et al., 2019. Impacts of polystyrene microplastic on the gut barrier, microbiota and metabolism of mice. Science of the Total Environment. 649, 308-317.

Johnson, K., Burnet, P., 2020. Opposing effects of antibiotics and germ-free status on neuropeptide systems involved in social behaviour and pain regulation. Bmc Neuroscience. 21, 1-14.

Kakakhel, M. A., et al., 2023. Deciphering the dysbiosis caused in the fish microbiota by emerging contaminants and its mitigation strategies-a review. Environmental Research. 237, 117002.

Karamzadeh-Dehaghani, A., et al., 2021. Combined effect of probiotics and specific immunoglobulin y directed against escherichia coli on growth performance, diarrhea incidence, and immune system in calves. Animal. 15(2), 100124.

Keerthanan, S., et al., 2021. Pharmaceutical and personal care products (ppcps) in the environment: plant uptake, translocation, bioaccumulation, and human health risks. Critical Reviews in Environmental Science and Technology. 51, 1221-1258.

Khalifa, E., et al., 2023. Silver nanoparticles synthesized by probiotic bacteria and antibacterial role in resistant bacteria. Amb Express. 13(1), 140.

Lai, C. Z., et al., 2023. Long-term effects on liver metabolism induced by ceftriaxone sodium pretreatment*. Environmental Pollution. 335, 122238.

Lau, C., et al., 2004. The developmental toxicity of perfluoroalkyl acids and their derivatives. Toxicology and Applied Pharmacology. 198, 231-241.

Lebeau-Roche, E., et al., 2023. Time and dose-dependent impairment of liver metabolism in gasterosteus aculeatus following exposure to diclofenac (dcf) highlighted by lc-hrms untargeted metabolomics. Science of the Total Environment.858, 159801.

Li, G. L., et al., 2023. The toxicological effect on pak choi of co-exposure to degradable and non-degradable microplastics with oxytetracycline in the soil. Ecotoxicology and Environmental Safety. 268, 115707.

Li, H. T., et al., 2022. Gut microbiota and metabolome description of antibiotic-treated neonates from parturients with intrauterine infection. Frontiers in Cellular and Infection Microbiology. 12, 817832.

Li, H., et al., 2016. The influence of gut microbiota on drugmetabolismand toxicity. Expert Opinion On Drug Metabolism & Toxicology. 12, 31-40.

Li, S. Q., et al., 2024. Bisphenol s exposure induces intestinal inflammation via altering gut microbiome. Food and Chemical Toxicology. 190, 114830.

Li, Y., et al., 2024. Effects of polycyclic aromatic hydrocarbons on the gut-testis axis. Ecotoxicology and Environmental Safety. 280, 116539.

Lim, J. J., et al., 2024. Single-cell transcriptomics unveiled that early life bde-99 exposure reprogrammed the gut-liver axis to promote a proinflammatory metabolic signature in male mice at late adulthood. Toxicological Sciences. 200, 114-136.

Liu, L. L., et al., 2020. Naturally occurring tpe-ca maintains gut microbiota and bile acids homeostasis via fxr signaling modulation of the liver-gut axis. Frontiers in Pharmacology. 11, 12.

Liu, S., et al., 2023. Novel insights into perfluorinated compound-induced hepatotoxicity: chronic dietary restriction exacerbates the effects of pfbs on hepatic lipid metabolism in mice. Environment International. 181, 108274.

Liu, Y., et al., 2021. Loss of vagal integrity disrupts immune components of the microbiota-gut-brain axis and inhibits the effect of lactobacillus rhamnosus on behavior and the corticosterone stress response. Neuropharmacology. 195, 108682.

Lu, Z., et al., 2024. Oyster peptide-zinc complex ameliorates di-(2-ethylhexyl) phthalate-induced testis injury in male mice and improving gut microbiota. Foods. 13(1), 93.

Marie, B., Gallet, A., 2022. Fish metabolome from sub-urban lakes of the paris area (france) and potential influence of noxious metabolites produced by cyanobacteria. Chemosphere. 296, 134035.

McCallum, E. S., et al., 2017. in situ exposure to wastewater effluent reduces survival but has little effect on the behaviour or physiology of an invasive great lakes fish. Aquatic Toxicology. 184, 37-48.

Montenegro, J., et al., 2023. Exploring the influence of gut microbiome on energy metabolism in humans. Advances in Nutrition. 14, 840-857.

Nair, D., Johny, A. K., 2018. Characterizing the antimicrobial function of a dairy-originated probiotic, propionibacterium freudenreichii, against multidrug-resistant salmonella enterica serovar heidelberg in turkey poults. Frontiers in Microbiology. 9, 1475.

Nakkarach, A., et al., 2021. Anti-cancer and anti-inflammatory effects elicited by short chain fatty acids produced by escherichia coli isolated from healthy human gut microbiota. Microbial Cell Factories. 20, 36.

Neves, A. L., et al., 2013. Metabolic endotoxemia: a molecular link between obesity and cardiovascular risk. Journal of Molecular Endocrinology. 51, R51-R64.

Ni, Y. H., et al., 2023. Bifidobacterium and lactobacillus improve inflammatory bowel disease in zebrafish of different ages by regulating the intestinal mucosal barrier and microbiota. Life Sciences. 324:121699.

Patten, D. A., Collett, A., 2013. Exploring the immunomodulatory potential of microbial-associated molecular patterns derived from the enteric bacterial microbiota. Microbiology. 159, 1535-1544.

Petersen, M. C., Shulman, G. I., 2018. Mechanisms of insulin action and insulin resistance. Physiological Reviews. 98, 2133-2223.

Pini, M., et al., 2016. Human health characterization factors of nano-tio2 for indoor and outdoor environments. International Journal of Life Cycle Assessment. 21, 1452-1462.

Podratz, P. L., et al., 2020. Disruption of fertility, placenta, pregnancy outcome, and multigenerational inheritance of hepatic steatosis by organotin exposure from contaminated seafood in rats. Science of the Total Environment. 723, 138000.

Provencher, J. F., et al., 2022. 44-year retrospective analysis of ultraviolet absorbents and industrial antioxidants in seabird eggs from the canadian arctic (1975 to 2019). Environmental Science & Technology. 56, 14562-14573.

Qinqin, L., et al., 2024. Mechanism of probiotics in the intervention of colorectal cancer: a review. World Journal of Microbiology and Biotechnology. 40:306.

Ratelle, M., et al., 2020. Polycyclic aromatic hydrocarbons (pahs) levels in urine samples collected in a subarctic region of the northwest territories, canada. Environmental Research. 182, 109112.

Ray, K., 2014. Gut microbiota: microbial metabolites feed into the gut-brain-gut circuit during host metabolism. Nature Reviews. Gastroenterology & Hepatology. 11, 76-76.

Razzaq, A. et al., 2024. Role of lactobacillus probiotics in gut health and food safety: Mechanisms for contaminant reduction and applications in food products. Food Science & Applied Microbiology Reports. 3(2), 08–125.

Reshu, C., et al., 2024. Biotechnological strategies for remediation of arsenic-contaminated soils to improve soil health and sustainable agriculture. Soil &Amp; Environmental Health. 2, 100061.

Rosin, J. M., Kurrasch, D. M., 2018. Bisphenol a and microglia: could microglia be responsive to this environmental contaminant during neural development? American Journal of Physiology-Endocrinology and Metabolism. 315, E279-E285.

Russell, D. W., 2003. The enzymes, regulation, and genetics of bile acid synthesis. Annual Review of Biochemistry. 72, 137-174.

SARGIS, R. M., 2023. Selenoproteins in arsenic-induced metabolic dysfunction.NIH RePORTER.

Sarlak, Z., et al., 2021. Bioremediation of organophosphorus pesticides in contaminated foodstuffs using probiotics. Food Control. 126, 108006.

Schoeler, M., Caesar, R., 2019. Dietary lipids, gut microbiota and lipid metabolism. Reviews in Endocrine & Metabolic Disorders. 20, 461-472.

Schulte, P. A., et al., 2019. A systematic review of human studies and epidemiological investigations. Scandinavian Journal of Work, Environment & Health. 45, 217-238.

Shao, et al., 2021. Progress in the study of interactions between microplastics and other emerging pollutants. Environmental Science And Technology. 44, 214-222.

Smital, T., Acute and chronic effects of emerging contaminants. In: D. Barcelo, M. Petrovic, Eds.), 2008, pp. 105-142.

Solaiman, S. G., et al., 2009. Feeding performance and blood parameters of male goat kids fed easiflo® cottonseed. Small Ruminant Research. 81, 137-145.

Song, R., et al., 2018. Nanocomposite of half-fin anchovy hydrolysates/zinc oxide nanoparticles exhibits actual non-toxicity and regulates intestinal microbiota, short-chain fatty acids production and oxidative status in mice. Marine Drugs. 16(1), 23.

Songisepp, E., et al., 2012. Safety of a probiotic cheese containing lactobacillus plantarum tensia according to a variety of health indices in different age groups. Journal of Dairy Science. 95, 5495-5509.

Song, X. R., et al., 2023. Role of intestinal probiotics in the modulation of lipid metabolism: implications for therapeutic treatments. Food Science and Human Wellness. 12, 1439-1449.

Stojanović, O., et al., 2022. Intestinal plasticity and metabolism as regulators of organismal energy homeostasis. Nature Metabolism. 4(11), 1444–1458.

Sun, H. Q., et al., 2021. Effects induced by polyethylene microplastics oral exposure on colon mucin release, inflammation, gut microflora composition and metabolism in mice. Ecotoxicology and Environmental Safety. 220, 112340.

Sun, Y., et al., 2019. Activation of aryl hydrocarbon receptor by dioxin directly shifts gut microbiota in zebrafish. Environmental Pollution. 255, 113357.

Sun, Z. C., et al., 2024. Tissue damage, antioxidant capacity, transcriptional and metabolic regulation of red drum sciaenops ocellatus in response to nanoplastics exposure and subsequent recovery. Ecotoxicology and Environmental Safety. 273, 116175.

Teng, M. M., et al., 2024. Effects of bbibp-corv vaccine on gut microbiota and short-chain fatty acids in mice exposed to bis (2-ethylhexyl) phthalate and dioctyl terephthalate. Environment International. 190, 108851.

Tian, R., et al., 2024. Mechanism insights into the histopathological changes of polypropylene microplastics induced gut and liver in zebrafish. Ecotoxicology and Environmental Safety. 280, 116537.

Tian, X. Z., et al., 2019. lactobacillus plantarum tw1-1 alleviates diethylhexylphthalate-induced testicular damage in mice by modulating gut microbiota and decreasing inflammation. Frontiers in Cellular and Infection Microbiology. 9, 221.

Vineetha, K. K., et al., 2023. The gut microbiota: a novel player in the pathogenesis of uterine fibroids. Reproductive Sciences. 30, 3443-3455.

Wang, B., et al., 2024. Environmental and sublethal concentrations of polystyrene nanoplastics induced antioxidant system, transcriptomic responses, and disturbed gut microbiota in oyster magallana hongkongensis. Journal of Agricultural and Food Chemistry. 72, 13581-13592.

Wang, J., et al., 2024. Oxidized/unmodified-polyethylene microplastics neurotoxicity in mice: perspective from microbiota-gut-brain axis. Environment International. 185, 108523.

Wang, X. Z., et al., 2021. Probiotics regulate gut microbiota: an effective method to improve immunity. Molecules. 26(19), 6076.

Wong, D. R., et al., 2005. Cardiovascular hazard and non-steroidal anti-inflammatory drugs. Current Opinion in Pharmacology. 5, 204-210.

WRIGHT, S. D., et al., 1990. Cd14, a receptor for complexes of lipopolysaccharide (lps) and lps binding-protein. Science. 249, 1431-1433.

Wu, J. Y., et al., 2024. Mixed probiotics modulated gut microbiota to improve spermatogenesis in bisphenol a-exposed male mice. Ecotoxicology and Environmental Safety. 270, 115922.

Xie, L. L., et al., 2022. Intestinal flora variation reflects the short-term damage of microplastic to the intestinal tract in mice. Ecotoxicology and Environmental Safety. 246, 114194.

Xie, S. W., et al., 2020. Interactions between dietary lipid levels and chronic exposure of legal aquaculture dose of sulfamethoxazole in juvenile largemouth bass micropterus salmoides. Aquatic Toxicology. 229, 105670.

Yan, H., et al., 2024. Occurrence of iodinated contrast media (icm) in water environments and their control strategies with a particular focus on iodinated by-products formation: a comprehensive review. Journal of Environmental Management. 351, 119931.

Zhan, 2023. Classification of emerging pollutants and progress of research on their detection technologies. Environmental Science And Technology. 46, 81-87+101.

Zhang, et al., 2023. Progress in research on the health effects of emerging environmental pollutants. Toxicology. 37, 43-48+53.

Zhang, G. X., et al., 2023. Associated long-term effects of decabromodiphenyl ethane on the gut microbial profiles and metabolic homeostasis in sprague-dawley rat offspring. Environment International. 172, 107802.

Zhang, M., et al., 2023. The effect of polychlorinated biphenyls extracted from offshore sediments on the intestinal epithelium and microflora of zebrafish. International Journal of Environmental Science and Technology. 20, 12731-12740.

Zhang, P., et al., 2020. Toxicological responses of carassius auratus induced by benzophenone-3 exposure and the association with alteration of gut microbiota. Science of the Total Environment. 747, 141255.

Zhang, S., et al., 2015. Subchronic exposure of mice to cadmium perturbs their hepatic energy metabolism and gut microbiome. Chemical Research in Toxicology. 28, 2000-2009.

Zhang, Y., et al., 2024. bacillus subtilis improves antioxidant capacity and optimizes inflammatory state in broilers. Animal Bioscience. 37, 1041-1052.

Zhao, F., et al., 2024. Interactions between gut microbiota and emerging contaminants exposure: new and profound implications for human health. Environmental Research Communications. 6(7), 072001.

Zhao, G. P., et al., 2021. Nitrogen contaminants damage on intestinal epithelial tight junctions: a review. Environmental Chemistry Letters, 19(6), 4549-4561.

Zhong, Mechanism of intestinal flora/bile acids/TGR5/CCR5 signalling pathway involved in paclitaxel-induced peripheral neuropathy. China Medical University, 2022.

Zhang, Z. Y., 2011. Effects of dietary probiotic Lactobacillus casei Zhang on hepatic lipid metabolism in rats fed a high-fat diet. Scientia Agricultura Sinica, 45(5), 943–950.

Zhen, H. et al., 2024. Fructooligosaccharides for Relieving Functional Constipation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Foods, 13(24), 3993.

Zhuang, J. S., et al., 2024. Effects of chronic triclosan exposure on nephrotoxicity and gut microbiota dysbiosis in adult mice. Ecotoxicology and Environmental Safety. 271, 115866.

Zeng, Z. T., et al., 2019. Assessing the human health risks of perfluorooctane sulfonate by in vivo and in vitro studies. Environment International. 126, 598-610.