Gut Physiological Dysregulation Induced by Microplastic Exposure

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ABSTRACT

Due to the staggering quantities of plastic production and disposal around the world, microplastic pollution is a growing environmental and public health concern. Microplastics refer to plastic materials that are less than 5 mm in diameter and are usually found in water, food, soil, and in the atmosphere. The human exposure is primarily by ingestion of contaminated water and food and inhalation of airborne particles. Recent research indicates that microplastics can negatively impact the gut physiology by causing oxidative stress, inflammation, microbial dysbiosis, intestinal barrier dysfunction, and a change in nutrient absorption. Such physiological disturbances can lead to gastrointestinal and systemic diseases. Besides this, microplastics can also potentially communicate with gut microbiota and affect the gut-brain axis, thus having an impact on metabolic and neurological health. This review explains the sources and routes of exposure to microplastic, the processes that lead to physiological changes in the gut, associated systemic health effects, and environmental management measures that can be taken to mitigate human exposure and contamination of the environment. The physiological impact of microplastic pollution should be understood to implement successful environmental policies and public health facilities.

Keywords: Microplastics, Gut physiology, Environmental pollution, Gut microbiota, Oxidative stress, Inflammation, Environmental management

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Introduction

Microplastic pollution has emerged as a worldwide environmental issue because of its ubiquity, persistence, and toxicity. Recent environmental reports state that millions of tons of plastic waste every year find their way into the aquatic and land ecosystems, where they break down into smaller fragments referred to as microplastics [1]. Microplastics are constantly entering the human body by way of contaminated seafood, processed food, bottled water, inhalation of particles in the air, consumption of personal care products, and dermal exposure. Ingestion is the major exposure route and gastrointestinal tract is the major site of exposure. The gut also has other important functions, such as digestion, absorption of nutrients, regulation of the immune system, and microbial balance.

After entering the body, microplastics could start disrupting the gut physiological functions locally which is an important barrier between the external and internal environments. Emerging scientific evidence suggests that microplastics interfere with normal gut functions and contribute to intestinal as well as systemic physiological disturbances. Microplastic exposure induces marked alterations in gut physiological features, supporting the concept of microplastic-induced gut physiological dysregulation. A causative link has recently been established between microplastic-induced gut dysbiosis, increased intestinal permeability, and systemic inflammation. Microplastics compromise epithelial barrier integrity by interfering with the formation and organization of tight junctions and increasing intestinal permeability, thereby facilitating the translocation of luminal microbiota and microbial-derived substances such as lipopolysaccharides into the circulation. Consequently, gut microbiota dysbiosis and elevated serological lipopolysaccharide levels have been observed following microplastic exposure, further supporting the development of bacterial translocation and systemic inflammation [2]. In recent years, increasing attention has been directed toward understanding the effects of microplastics on gut physiology and overall human health. This review aims to summarize current evidence regarding sources of microplastic exposure, mechanisms of gut physiological dysfunction, systemic health implications, and environmental management strategies to reduce plastic contamination and human exposure [3].

Background on Microplastics

Micro-plastics are small particles of plastics which are less than 5 mm and depending upon their source, they can be divided into primary and secondary microplastics. The primary micro plastics are produced for a specific use like cosmetics or industrial abrasives while the secondary ones are created from the breakdown of larger plastics. Microplastics are everywhere, in the air, soil, fresh water, and salt water and in food. There are many different possibilities for humans to be exposed to a variety of plastisols like through the intake of food and water and even through breathing in contaminated air. Many food products including beer, honey, fish, mollusks, salt, sugar and meat have been found to contain microplastics. Microplastics have become a pollutant of the environment and are found everywhere in fish tissues like their skin, muscles and even gut tissues. They are found in commercial fish species such as salmon, trout, perch, and sheephead. These microplastics containing fishes are commonly consumed by the human population [2].

Sources and Classification of Microplastics

Microplastics are the new class of environmental pollutants of which scientists have studied since they are persistent, pervasive and may significantly affect human health. They are defined as plastic pieces smaller than 5 mm in terms of diameter, produced in the industrial process or through the degradation of larger plastics and household waste. Since microplastics are not easily biodegraded, they collect in marine environments, freshwater, soil, food, and air [4].

The growing manufacture of plastics globally has been a major cause of environmental pollution. Polluted plastic materials are broken down by the ultra-violet radiation, mechanical abrasion, change in temperature, gradual oxidation, and finally, the materials break down into microscopic particles that can penetrate into biological systems [5].

Exposure to microplastics in humans is mainly caused by consuming contaminated food and water, inhaling airborne particles, and, to a smaller degree, dermal exposure. Of all these routes, ingestion is the most significant route that directly impacts the gastrointestinal tract [6].

Microplastics are generally classified into **two** major categories:

1. Primary Microplastics
2. Secondary Microplastics

Primary Microplastics

Primary microplastics are microscopic sized particles of plastic that are manufactured intentionally to be consumed in personal care items, cosmetics, detergents, pharmaceutical preparations and industrial abrasives. The particles are to be commercial in nature and upon usage, are directly discharged into wastewater systems. The main microplastics are microbeads in facial scrubs, toothpaste, and exfoliating products. These particles are very tiny and are not completely eliminated in the majority of the wastewater treatment systems and reach rivers and oceans. Another important source of primary microplastics is synthetic textile fibers and washing of synthetic fabrics such as polyester and nylon releases microscopic fibers into the water bodies and contaminate the environment [7].

Secondary Microplastics

Secondary microplastics are formed when larger plastic products, namely plastic bottles, bags, fishing nets, industrial waste, and food packages, are degraded. Through the exposure of environmental factors such as sunlight, wave action, heat and microbial activity, the polymer structures are eroded over time, creating smaller plastic fragments. The secondary microplastics contribute a significant percentage of the environmental plastic pollution due to the growing amount of plastic waste and poor waste management activities around the world [8].

Human Exposure Pathways

Human exposure to microplastics occurs through multiple pathways:

- Consumption of contaminated seafood and processed food
- Drinking bottled and tap water containing plastic particles
- Inhalation of airborne microplastics

- Use of plastic-containing consumer products
- Contact with synthetic textiles and packaging materials

Microplastic particles have been found in the stool samples of humans which signifies a serious gastrointestinal contamination. Constant environmental pollution increases the risk of a chronic build up in the biologic tissue [9-10].

Gut Physiology and Microplastic Interaction

The gastrointestinal tract forms an important physiological barrier between the external environment and internal circulation. The intestinal epithelial cells, mucus layers, immune cells, and tight junction proteins all work together in order to maintain intestinal homeostasis and protection against harmful substances. There are also trillions of microorganisms in the gut that are called the "gut microbiota." These microbes regulate digestion, nutrient metabolism, immunity, production of vitamins and resistance to pathogens. Gastrointestinal physiology disruption may negatively impact the health of the intestines and the entire system. Microplastic particles which get access to the gastrointestinal tract may also get in direct contact with intestinal epithelial cells and the gut microbiota, thus interfering with the normal physiological processes. However, a recent study showed that microplastics can induce alterations in epithelial signaling pathways and also disrupt mucosal immune regulation which would result in the disruption of intestinal homeostasis. In addition, pollutants or harmful environmental contaminants binding to the microplastic surface may increase their bioreactivity which would then exacerbate the toxicity of the intestinal cells. Mitochondrial dysfunction, changes in metabolic activity and pathological gut microbial composition have also been associated with repeated exposure affecting the systemic inflammatory response as well as metabolic disorders both. The recent studies also suggest that significant exposure to microplastics in the gastrointestinal tract could negatively impact the intestinal barrier function and also facilitate the transport of inflammatory molecules to the body's stream [11].

Mechanisms of Gut Physiological Dysfunction

Oxidative Stress

Oxidative stress is believed to be a major mechanism of toxicity because of microplastics in gastrointestinal tract. Excessive production of reactive oxygen species (ROS) can cause endogenous antioxidant defenses to be overstretched, resulting in oxidative imbalance and cell damage. Exposure to microplastic has been linked to lipid peroxidation, oxidative stress on proteins, mitochondrial dysfunction, and damage to DNA in intestinal epithelial cells. Moreover, oxidative stress can cause the activation of various inflammatory signaling pathways like nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) pathways thus worsening the inflammatory responses and intestinal tissue damage. Chronic oxidative stress may adversely affect epithelial barrier functions, cell metabolism, and also cause chronic gastrointestinal dysfunction as well as systemic inflammatory diseases (Figure 1) [12-13].

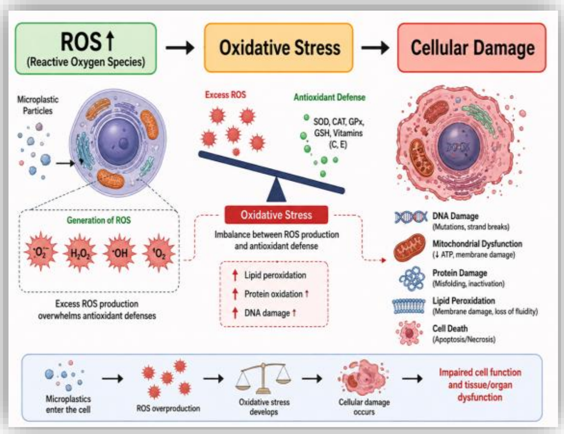

Fig. 1: Oxidative Stress vs Cellular Damage [14]

Inflammatory Responses

Microplastic can stimulate inflammatory signaling pathways and stimulate the production of pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-alpha (TNF-α). Chronic inflammation can cause damage to intestinal mucosa, decreased absorptive capacity, and lead to gastrointestinal conditions including inflammatory bowel diseases. Sustained inflammatory reactions can also predispose individuals to metabolic and immune-related disorders. In addition, inflammatory stress caused by microplastic can impair epithelial barrier integrity and change immune homeostasis in the gastrointestinal microenvironment. Evidence also pinpoints that over-exposure may induce significant oxidative harm and disturbed cellular interactions that are associated with chronic intestinal pathology [15].

Alteration of Gut Microbiota

The gut microbiota is important in terms of ensuring intestinal and systemic physiological homeostasis. Many studies have highlighted that exposure to microplastic changes the microbial diversity and composition leading to microbial dysbiosis.

Microbial imbalance may:

- Impair digestion
- Alter metabolic activity
- Weaken immune defense
- Increase inflammatory responses
- Disturb intestinal barrier function

Experimental animal models showed that there were significant changes in the populations of microbes after being exposed to polystyrene microplastics [8, 10].

Increased Intestinal Permeability

Tight junction proteins preserve the intestinal barrier by ensuring selective permeability. Microplastics may disrupt tight junction proteins, resulting in increased intestinal permeability commonly known as "leaky gut." Higher permeability allows toxins, pathogens, and inflammatory molecules to enter the systemic circulation and facilitate systemic inflammation.

Recent findings indicate that microplastic contamination can suppress the expression of essential tight junction-related proteins such as occludin, claudin-1, and zonula occludens-1 (ZO-1), all of which impairs the integrity of the epithelial barrier. In addition, microplastics may induce epithelial cytoskeletal remodeling and activate inflammatory signaling pathways such as NF-κB and NLRP3 inflammasome pathways which further exacerbate intestinal barrier dysfunction. Chronic disruption of barriers could cause endotoxin and microbial metabolite translocation into systemic circulation that then promotes chronic low-grade inflammation, immune dysregulation, and metabolic imbalances. New investigations also showcase that barrier impairment caused by microplastic can modify mucosal immune tolerance and lead to gut microbiota instability and intestinal epithelial apoptosis (Figure 2) [16].

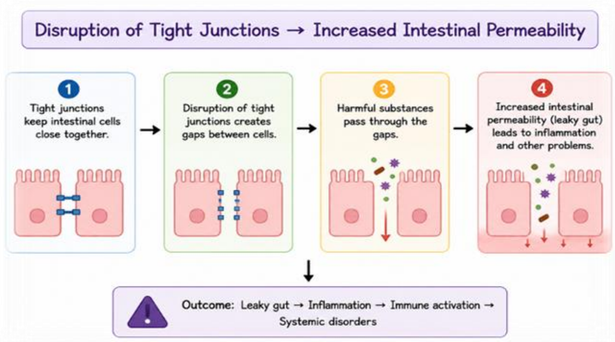

Fig. 2: Increased Intestinal Permeability [16]

Impaired Nutrient Absorption

The accumulation of microplastic can harm epithelial surfaces and disrupt the process of nutrient transportation. The prolonged impairment of absorptive processes can lead to metabolic imbalances as well as nutritional insufficiency. Moreover, new evidence appears to indicate that microplastics have the potential to disrupt intestinal enzyme functions and modify the expression of membrane transport proteins that mediate the uptake of glucose, lipid, and amino acid absorption. Chronic exposure has also been linked to mitochondrial bioenergetic dysfunction and derailment of epithelial metabolic homeostasis, which may undermine the efficiency of nutrient assimilation. Moreover, changes in villous architecture and mucosal integrity that occur due to microplastic impact can cause further decreased absorptive capacity and systemic metabolic dysregulation [17-18].

Microplastics and the Gut–Brain Axis

Recent discoveries have revealed that the gut microbiota forms a two-way neuroimmunological pathway with the central nervous system through the microbiota-gut-brain axis. Variations in microbial composition can end up causing significant impacts upon neurotransmitter production, vagal signaling, neuroendocrine regulation, and immune-mediated neural responses. Microplastic-induced dysbiosis has been linked to perturbation of serotonergic- and dopaminergic-related pathways resulting in neuroinflammation, oxidative neuronal injury, and impaired synaptic plasticity. In addition, the damage to the integrity of the intestinal barriers may predispose the systemic translocation of endotoxins and inflammatory mediators, which, in turn, are able to disrupt the blood-brain barrier activity and increase the inflammation of the central nervous system. Evidence also highlights that sustained exposure to microplastic can cause anxiety-like behavior, cognitive dysfunction, and neurodegenerative changes by disrupting the microbiota-gut-brain axis, but future longitudinal studies within humans are needed in order to confirm these mechanistic relationships [2, 19].

Microplastics versus Nanoplastics

Table 1: Microplastics versus Nanoplastics [20-21]

Feature	Microplastics	Nanoplastics
Size	1 µm – 5 mm	< 100 nm
Tissue Penetration Ability	Limited penetration	High penetration ability
Barrier Crossing	Less efficient crossing of biological barriers	Easily cross intestinal, blood–brain, and placental barriers
Cellular Interaction	Mostly extracellular interaction	Direct intracellular and organelle interaction
Oxidative Stress	Moderate ROS generation	Greater oxidative stress and ROS production
Inflammatory Potential	Induces local inflammation	Causes stronger inflammatory responses
Distribution in Body	Mostly localized accumulation	Rapid systemic distribution
Target Organs	Intestine, liver	Brain, liver, kidneys, reproductive organs
Toxicological Impact	Gastrointestinal dysfunction	Neurotoxicity, hepatotoxicity, reproductive toxicity
Bioaccumulation Risk	Moderate	High
Cellular Damage	Membrane and epithelial injury	DNA damage, mitochondrial dysfunction, apoptosis
Overall Health Risk	Significant environmental health concern	Higher systemic toxicity and long-term health risk

Human and Experimental Evidence

The majority of the existing evidence on microplastic toxicity is based on animal and experimental research. Oxidative stress, intestinal inflammation, microbial dysbiosis, and tissue accumulation have been seen in zebrafish and rodent models after chronic exposure. There is extremely limited human evidence but recent research that has identified microplastics in human stool samples and body tissues indicates that there is significant environmental exposure. Clinical and epidemiological studies are needed in order to establish the long-term physiological outcomes in humans [22-23].

Systemic Health Implications

The gastrointestinal tract is the main system into which microplastics enter but physiological disturbances because of them may also occur in various systems.

Potential systemic effects include:

- Immune dysfunction
- Hormonal imbalance
- Metabolic disorders
- Neuroinflammation
- Cardiovascular complications
- Reproductive toxicity

The possibility of nanoplastics entering systemic circulation into different tissues would expose them to the risks of developing chronic diseases [24].

Environmental Management Strategies

1. Reduction of Plastic Consumption

Single-use plastic products - when reduced - are one of the most effective responses to address environmental pollution. Adopting eco-friendly options and sustainable consumer behaviour can help to significantly minimise the amount of plastic waste generated [25].

2. Improved Waste Management Systems

Waste collection, recycling and disposal systems need to work properly in order to reduce environmental accumulation of plastic [26].

3. Wastewater Treatment Improvements

Advanced wastewater treatment options can minimize the release of microplastics into water bodies and into the food chain [27].

4. Promotion of Biodegradable Alternatives

Biodegradable and eco-friendly materials have to be developed since they would help to reduce the ecological persistence of synthetic plastics in the long-term [28].

5. Public Awareness and Education

Public education campaigns would prove to be helpful in terms of increasing the awareness towards the harmful effects of plastic pollution and also promote behaviors that are environmentally friendly [29].

6. Environmental Regulations

Production, use, recycling and disposal of plastic should be done as per the rules and regulations which would help to minimize contamination of the environment with microplastics everywhere [30].

Challenges and Limitations

Several limitations exist within the current research surrounding microplastic toxicity:

- Limited long-term human studies
- Particles vary in size and composition
- Absence of uniform exposure assessment methods
- Challenge in assessing level of environmental exposure
- Dose-dependent toxicity is not properly understood

Tackling these challenges is important for efficiently measuring risk and establishing evidence-based environmental policy measures.

Future Perspectives

Future research should put its focus upon:

- Long term human clinical trials
- Molecular mechanisms of intestinal injury
- Microplastic-gut microbiota interactions
- Nanoplastics and human physiology relation
- Prevention and therapeutic intervention development
- Improved systems for monitoring the environment

An interdisciplinary research effort among physiologists, toxicologists, environmental scientists and public health researchers is important to properly interpret the impacts of the microplastic pollution in human health.

Conclusion

Microplastic contamination, a new and emerging environmental problem, is associated with repercussion on gastrointestinal physiology and on the general health of humans. Available studies highlight that exposure to microplastics can cause oxidative stress, inflammation, intestinal dysbiosis, dysfunction of the intestinal barrier, and poor nutrient absorption and all these changes can cause gastrointestinal and systemic diseases. Minimisation of use of plastic, improvement of waste management, improvement of wastewater management, public awareness and good implementation of environmental policy measures are important to reduce environmental pollution and to protect health of individuals. More research is required to understand what the potential long-term health effects might be following exposure to microplastics and develop evidence-based prevention methods.

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