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STUDYING THE EFFECTS OF FOOD ADDITIVES ON THE HUMAN MICROBIOME - A REVIEW

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Abstract: *The human microbiome is essential to maintaining health, influencing digestion, immunity, and even neurological functions. Modern diets increasingly include food additives—substances added to enhance flavor, texture, preservation, and appearance. This review explores how exposure to food additives may impact the human microbiome. It first outlines the importance of the microbiome, then discusses the nature and types of food additives, and finally presents current studies on the interactions between additives and microbial communities. Understanding these effects is crucial for public health and dietary recommendations.*

Keywords: *Microbiome, Food additive, Health*

INTRODUCTION

The human gut microbiome, composed of trillions of microorganisms, plays a critical role in sustaining physiological and metabolic balance (Valdes et al., 2018). In parallel with changes in diet patterns, the use of food additives has escalated over the past century. Although additives are regulated for safety, emerging evidence suggests that their impact on the gut microbiome warrants closer investigation (Chassaing et al., 2015). This review aims to summarize existing knowledge regarding food additives and their possible influence on the human microbiome, highlighting areas of concern and research gaps.

EXPOSURE

The Importance of the Human Microbiome for Health

The human microbiome, a complex ecosystem of trillions of microorganisms living in and on our bodies, plays an essential role in maintaining overall health and wellbeing. The composition and diversity of the microbiome are crucial in influencing various bodily functions, including metabolism, immune response, and gut health (Wang et al., 2024). Its importance goes beyond basic physiological functions, as disruptions to the microbiome have been linked to numerous chronic conditions, including inflammatory bowel disease (IBD), obesity, diabetes, and metabolic disorders (Zhou et al., 2023). Microbial communities, primarily composed of bacteria, fungi, viruses, and archaea, inhabit various body sites, such as the gut, skin, mouth, and respiratory tract, with the gut microbiome receiving the most research attention.

Research highlights that a balanced gut microbiome supports efficient digestion and nutrient absorption while also protecting the body from harmful pathogens. Beneficial bacteria, such as *Bifidobacterium spp.* and *Lactobacillus spp.*, produce short-chain fatty acids (SCFAs), which contribute to gut health by nourishing intestinal cells and regulating inflammation (Raoul et al., 2022). Additionally, the microbiome influences immune responses. It interacts with the host's immune cells, helping to develop immune tolerance and preventing overactive immune responses that may lead to autoimmune diseases (Round & Mazmanian, 2009).

Importantly, the microbiome also plays a crucial role in protecting against pathogens. Commensal bacteria in the gut and on the skin can outcompete harmful pathogens for resources and produce antimicrobial substances (Belkaid & Hand, 2014). Furthermore, the microbiome's ability to influence the body's metabolic processes is an area of intense study. Through interactions with the host's endocrine system, it can affect fat storage and energy expenditure (Ridaura et al., 2013).

However, modern lifestyle factors, such as the overuse of antibiotics, poor diet and exposure to environmental toxins, can disturb the microbiome, leading to dysbiosis - an imbalance in microbial populations. This imbalance can compromise gut barrier function and increase intestinal permeability, which in turn can contribute to the onset of diseases such as IBD and even affect mental health, a phenomenon referred to as the gut-brain axis (Ivanovic and Dimitrijevic Brankovic, 2024). Moreover, emerging studies indicate that food additives, such as emulsifiers and artificial sweeteners, may negatively affect microbial diversity, further exacerbating health conditions (Jarmakiewicz-Czaja et al., 2025).

Maintaining a healthy microbiome is essential for long-term health. Probiotics, prebiotics, and a diet rich in fiber and diverse nutrients can help sustain microbial balance and promote the beneficial actions of gut bacteria (Inan-Eroglu and Ayaz, 2019). As the scientific community continues to explore the intricate relationships between the microbiome and disease, it becomes increasingly clear that preserving microbiome health is a key strategy for preventing and managing chronic health conditions.

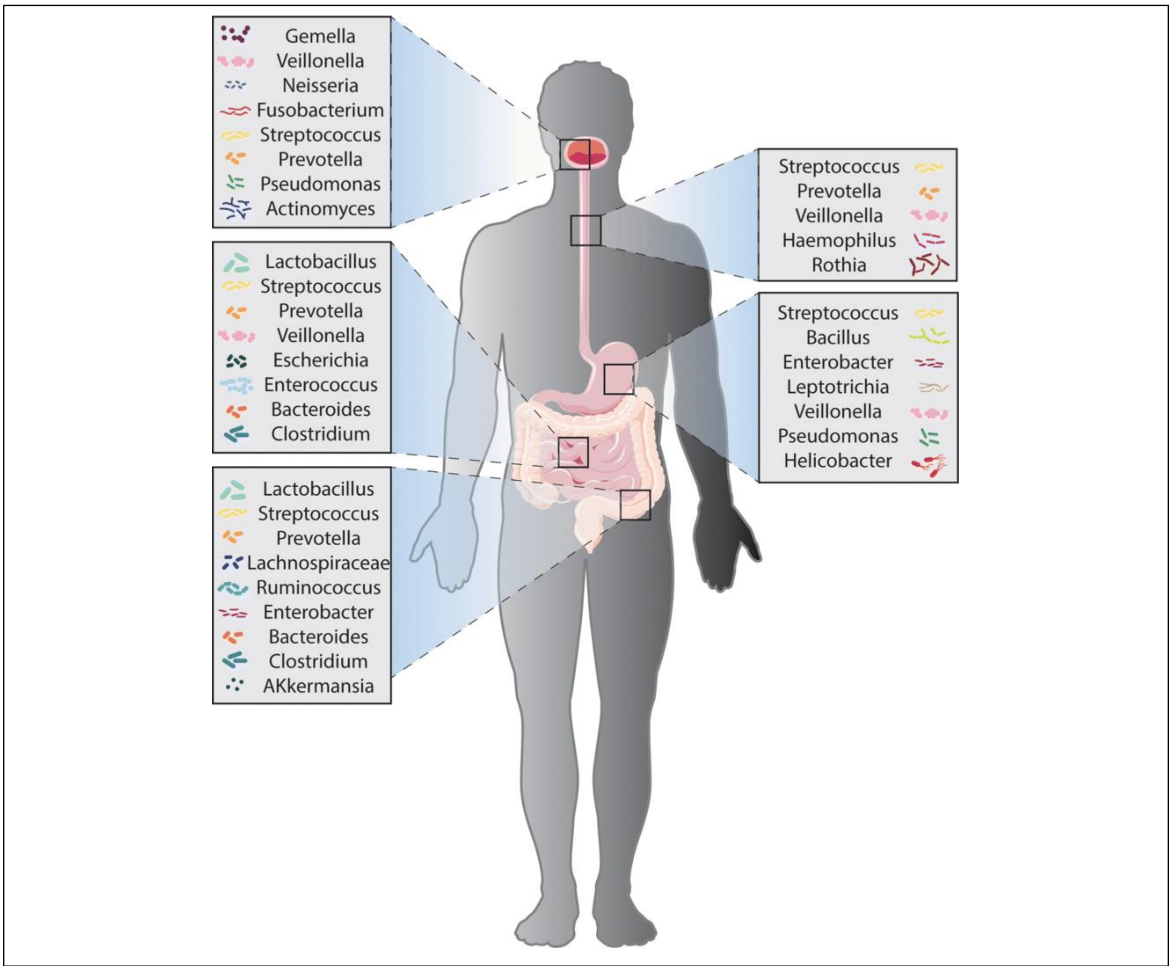

Fig. 1. Human microbiota composiotion in different locations of the body (Marques et al. 2020).

Essential Knowledge of Food Additives

A food additive is any substance that is not normally consumed as a food on its own, but is intentionally added to food in small quantities such that it does not define or constitute a major part of the food, regardless of whether it has nutritive value or not, to produce a specific desirable effect (Mwale, 2023).

Food additives encompass a wide range of substances and their primary functions are to improve shelf life, texture, taste or visual appeal (Sharma, Wadhwa and Thakur, 2021). There are four main categories of food additives based on their function – nutritive additives, preservatives, processing agents and sensory agents (Mwale, 2023) but frequently a single substance can exhibit multifunctionality.

Regulatory bodies such as the U.S. Food and Drug Administration (FDA) and European Food Safety Authority (EFSA) assess food additives for toxicity, but their effects on the gut microbiome have not historically been a focus of safety evaluations (Chassaing and Gewirtz, 2018).

Food labeling regulations are implied to ensure that contents of food products are known to customers to guide their choice. E-numbers are unique identifiers for specific food additives in the European Union. Regulations determine acceptable daily intake (ADI) expressed in mg/kg body weight. The list of all the food additives authorised in the EU, their E-numbers and conditions of use can be accessed through the European Commission's food additives database.

Table 1. E-numbers according to EFSA

E-Number Range	Function
E100–E199	Colorants
E200–E299	Preservatives
E300–E399	Antioxidants, acidity regulators
E400–E499	Thickeners, stabilizers, emulsifiers
E500–E599	Acidity regulators, anti-caking agents
E600–E699	Flavor enhancers
E900–E999	Sweeteners, glazing agents, gases
E1000+	Miscellaneous

Joint FAO/WHO Expert Committee on Food Additives (JECFA) globally evaluates over 500 food additives in all the categories. Approvals and restrictions on use differ by countries even though many additives are globally used.

Table 2. General categories of food additives and associated health risks (Mwale, 2023)

General category	Subcategory	Examples	Associated Health Risks
Nutritive Additives	Nutrient Restoration	Vitamin C (E300), Sodium ascorbate (E301), Iron (E175), Folic acid, Calcium carbonate, Vitamin D, Niacin	Generally safe; excessive intake can lead to vitamin toxicity (A, D), iron overload, or gastrointestinal issues.
Preservatives	Antimicrobials	Sodium benzoate (E211), Potassium sorbate (E202), Sodium nitrite (E250), Sodium sulfite (E221), Calcium propionate (E282)	Allergic reactions; nitrites can form carcinogenic nitrosamines; sulfites may trigger asthma or headaches.
	Antioxidants	Butylated hydroxyanisole/BHA (E320), Butylated hydroxytoluene/BHT (E321), Propyl gallate (E310), Ascorbyl palmitate (E304)	Potential carcinogenic or endocrine-disruptive effects with long-term exposure.

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Processing Agents	Emulsifiers	Lecithin (E322), Mono- and diglycerides of fatty acids (E471), Polysorbate 80 (E433), Sodium stearoyl lactylate (E481)	Possible gut inflammation; generally recognized as safe.
	Stabilizers/ Thickeners	Carrageenan (E407), Xanthan gum (E415), Guar gum (E412), Cellulose gum (E466), Pectin (E440), Agar (E406), Locust bean gum (E410)	Gastrointestinal discomfort in sensitive individuals; carrageenan linked to inflammation in animal studies.
	Humectants	Glycerol (E422), Sorbitol (E420), Propylene glycol (E1520)	Laxative effect or bloating in high amounts.
	pH-control Agents	Citric acid (E330), Lactic acid (E270), Malic acid (E296), Acetic acid (E260)	Tooth enamel erosion or mild gastric upset when overconsumed.
	Enzymes	Rennet, Bromelain, Papain, Amylase, Lipase (No E-numbers – typically not assigned)	Generally safe; some potential allergenicity or occupational sensitivity.
	Antimicrobials (Processing Aids)	Ozone, Chlorine dioxide, Ammonium hydroxide, Peracetic acid (No E-numbers)	Residual chemicals may form harmful byproducts; usage is tightly regulated.
Sensory Agents	Artificial Sweeteners	Aspartame (E951), Sucralose (E955), Acesulfame K (E950), Saccharin (E954)	Headaches, allergic reactions, neurological effects; aspartame is dangerous for individuals with PKU.
	Natural Sweeteners	Steviol glycosides (E960), Xylitol (E967), Erythritol (E968), Monk fruit (no E-number), Honey (no E-number)	Generally safe; sugar alcohols may cause bloating or diarrhea.
	Flavor Enhancers	Monosodium glutamate/MSG (E621), Disodium inosinate (E631), Disodium guanylate (E627)	Headaches, nausea, flushing in sensitive individuals ("MSG symptom complex").
	Natural Colorants	Caramel color (E150a–d), Beetroot red (E162), Annatto (E160b), Curcumin (E100), Paprika extract (E160c)	Generally safe; rare allergic reactions (e.g., annatto).
	Synthetic Colorants	Tartrazine (E102), Allura Red (E129), Sunset Yellow (E110), Brilliant Blue FCF (E133), Fast Green FCF (E143)	Hyperactivity in children, allergenic potential, some linked to tumors in animal studies; some are banned or restricted in the EU.

Correlation Between Food Additives and the Human Gut Microbiome

The modern diet, particularly in industrialized nations, is increasingly dominated by ultra-processed foods that contain a wide range of food additives. Although regulatory agencies have deemed most additives safe for human consumption, a growing body of evidence suggests that many of these compounds adversely affect the gut microbiome and thus human health.

Recent reviews have linked various additives to microbial alterations (Ivanovic, S. and Dimitrijevic Brankovic, S., 2024).

Emulsifiers and Gut Dysbiosis

Emulsifiers such as polysorbate 80 (P80) and carboxymethylcellulose (CMC) are among the most scrutinized additives. Ivanovic and Dimitrijevic Brankovic (2024) showed that these compounds reduce microbial diversity and increase mucolytic bacteria, thereby weakening the gut's protective mucus layer and promoting "leaky gut" and systemic inflammation. Chassaing et al. (2023) and Schrezenmeir and de Vrese (2020) confirmed these effects, observing increases in pro-inflammatory Proteobacteria and decreases in *Akkermansia muciniphila*. Further it is demonstrated that emulsifier exposure exacerbates colitis in genetically predisposed animals (Viennois et al.,2017 and Martinez-Medina et al.,2021). Similarly, significant reductions in

Faecalibacterium prausnitzii (duncaniae), a key anti-inflammatory microbe, is noted following long-term CMC exposure (Naimi et al., 2021).

Artificial Sweeteners and Functional Disruption

Artificial sweeteners such as saccharin, sucralose, aspartame, and acesulfame-K have been linked to profound shifts in gut microbiota composition. Suez et al. (2022) demonstrated that consumption of these sweeteners in human trials induced individualized changes in gut microbiota, leading to impaired glycemic control.A study showed that these additives reduce SCFA-producing bacteria like *Faecalibacterium prausnitzii*, thereby diminishing butyrate and acetate levels essential for colon health (Wang et al., 2024 and Zhao et al., 2023). Similar findings are reported in animal studies, noting reduced microbial diversity and increased inflammation-associated taxa (Palmnas et al., 2014 and Bian et al., 2017).

Preservatives and Pathogen Overgrowth

Preservatives such as sodium benzoate and potassium sorbate are frequently added to extend food shelf life. However, several studies suggest these compounds negatively impact the gut microbiota. Recent observation shows that these preservatives inhibit beneficial bacteria while promoting the growth of pathogenic species (Jarmakiewicz-Czaja et al., 2025). Miremadi et al. (2020) found that sodium benzoate drastically reduced *Bifidobacterium breve* while allowing *Klebsiella pneumoniae* to thrive. Narushima et al. (2021) reported that potassium sorbate inhibited biofilm formation by *Lactobacillus reuteri*, weakening its competitive fitness. High preservative intake is linked to reduced microbial diversity and unfavorable shifts in the Firmicutes/Bacteroidetes ratio (Rothschild et al., 2020 and Wang et al., 2020).

Depletion of Short-Chain Fatty Acids (SCFAs)

A recurring consequence of additive-induced dysbiosis is the reduction in SCFA production. These microbial metabolites, particularly butyrate, are crucial for immune regulation, epithelial integrity, and metabolic homeostasis. Trompette et al. (2020) reported a 50% drop in SCFA levels alongside increased colonic inflammation in emulsifier-fed mice. SCFA depletion has been linked to impaired regulatory T-cell (Treg) development and increased susceptibility to inflammatory diseases and insulin resistance (Zhao et al., 2023).

Antimicrobials and Selective Suppression

Food-grade antimicrobials can selectively inhibit beneficial microbes while sparing harmful strains. Additives like sodium nitrite selectively suppress Firmicutes, leading to a rise in Proteobacteria, a phylum associated with inflammation (Garcia-Gonzalez et al., 2019; Wu et al., 2021). Chronic antimicrobial ingestion impaires microbial xenobiotic metabolism, potentially compromising the host's detoxification processes (Bachmann et al., 2023).

Impact of Ultra-Processed Foods and Additive Synergy

Ultra-processed foods (UPFs) contain multiple additives that may synergistically disrupt gut microbial ecosystems. Raoul et al. (2022) and the NutriNet-Santé cohort (2023) found that high-UPF diets were associated with decreased microbial richness, increased inflammatory markers, and upregulation of lipopolysaccharide -producing genes. Such microbial shifts foster a pro-inflammatory state, implicated in the pathogenesis of obesity, metabolic syndrome, and gastrointestinal disorders (Raoul et al., 2022).

Colorants and Microbial Disruption

Food colorants, especially synthetic azo dyes like tartrazine, have also been shown to influence gut microbiota. Tartrazine exposure led to significant reductions in *Lactobacillus spp.*

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populations and disrupted SCFA biosynthesis in vitro (Khalaf et al., 2020; Chen et al., 2022). These changes may further compromise gut health and exacerbate additive-induced dysbiosis.

Despite widespread additive use, current regulatory frameworks often fail to assess their long-term microbiome effects. Inan-Eroglu and Ayaz (2019) called for reforms in food safety evaluation to include microbiota-centered risk assessments. As Zhou et al. (2023) emphasize, addressing this gap is essential for understanding the role of diet-induced dysbiosis in chronic disease etiology.

CONCLUSION

Food additives may impact the microbiota through several mechanisms: direct antimicrobial effects, alterations in mucus production and gut barrier function, induction of host immune responses that secondarily affect microbes as well as shifts in microbial metabolic activity.

A substantial and growing body of research suggests that food additives, though deemed safe under traditional toxicological evaluations, may have significant unintended effects on the gut microbiome. These changes can promote inflammation, metabolic dysfunction and chronic disease development. As dietary exposure to additives continues to rise, more comprehensive evaluations and policy revisions are urgently needed to protect long-term human health.

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