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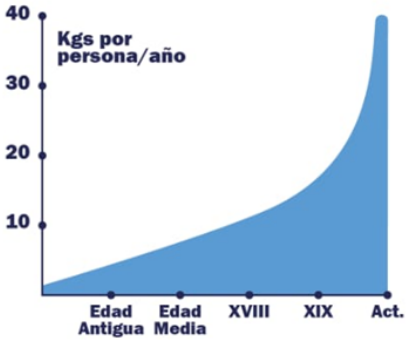
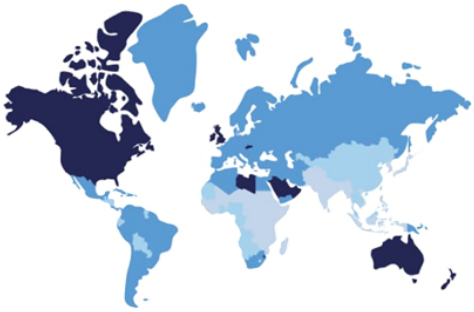
Historia del cultivo de azúcar y su impacto

Extensión histórica del cultivo de la caña de azúcar

- Cultivo en la antigüedad
- Cultivo desde el siglo VIII
- Cultivo tras 1492
- Regiones no aptas o sin cultivo de caña relevante



Evolución del consumo de azúcar per cápita (kg/año)



Prevalencia de obesidad y sobrepeso en adultos por país

- <10%
- 10–20%
- 20–30%
- >30%

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Sweet legacy, bitter outcomes: sugar, sweeteners, and the microbial origins of a modern syndrome. An evidence-based narrative review

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Abstract

The consumption of added sugars and artificial sweeteners has risen exponentially in recent decades, driven by industrial availability, food processing, and Western dietary patterns.

This narrative review, adopting a critical and multidisciplinary perspective, traces the history of sugar in the human diet, examines the evolution and safety of noncaloric sweeteners, and analyzes their impact on the gut microbiota. Drawing on experimental evidence and recent clinical studies, it explores how excessive intake of sugars and sweeteners can induce dysbiosis by reducing bacterial diversity, promoting the growth of proinflammatory microorganisms, altering short-chain fatty acid production, and compromising epithelial barrier integrity. The pathogenic role of these alterations is discussed in relation to digestive and metabolic disorders such as obesity, type 2 diabetes, metabolic dysfunction–associated steatotic liver disease, and inflammatory bowel disease.

The review also considers the social and commercial determinants that perpetuate population exposure to dysbiotic dietary patterns, particularly in contexts of socioeconomic vulnerability. It proposes an integrated approach to addressing the clinical impact of sugar and sweetener consumption—encompassing public health measures, real-food–based dietary interventions, structured nutritional education, and regulation of the food environment. Overall, it underscores the need to reconceptualize intestinal dysbiosis not merely as a biological phenomenon but as a deeply social one requiring coordinated strategies across primary care, digestive health, and nutrition policy.

Keywords: Diet. Sugar. Sweeteners. Microbiome. Inflammatory bowel disease. Pathogenesis. Environmental pollution.

1. Material and Methods

We performed an evidence-based narrative review focused on consumption of sugar, use of non-caloric sweeteners and gut dysbiosis, digestive and cardiometabolic diseases. We used reference books on all three topics and PubMed as the primary databases, including human observational and interventional studies, and reviews published mainly in the last five years in English, with justified inclusion of previous works when it was shown to be relevant to the conceptual or historical framework.

Key words used were (combined with booleans operators): “sugar”, “free sugars”, “fructose”, “non-nutritive sweeteners”, “artificial sweeteners”, “non-sugar sweeteners”, “microbiota”, “gut dysbiosis”, “inflammatory bowel disease”, “metabolic dysfunction–associated steatotic liver disease”, “MASLD”, “obesity”, and “type 2 diabetes”.

Inclusion criteria: human studies evaluating the history, epidemiology, and impact of sugar or sweetener consumption on microbiota, dysbiosis, and digestive and metabolic clinical outcomes; approval studies, systematic reviews and meta-analyses on sweeteners, microbiota and digestive or cardiometabolic disease.

Exclusion criteria: opinion articles not supported by original data, editorial comments without systematic synthesis of knowledge, very small case series without microbiological information and works without abstract or insufficient data on dietary exposure.

We have built a logical axis of the narrative that follows a clear sequence of clinical questions: history and expansion of sugar consumption; metabolic and digestive effects of excess sugars; emergence and safety of sweeteners; impact of sugars and sweeteners on microbiota/dysbiosis; structural and commercial determinants

2. The history of sugar consumption

Carbohydrates, including sugars, have always played a fundamental role in human nutrition (1). They were essential to our evolutionary development and to shifts in dietary patterns throughout history (2). It is undeniable that sugars have been, and will continue to be, key components of our diet, accounting for more than 50% of total daily energy intake. For this reason, particular attention must be given to their quality and origin to ensure the proper functioning of the body, which requires about 170 g of glucose per day (3).

The term *sugar* refers to monosaccharides such as glucose, galactose, and fructose, and to disaccharides such as sucrose, lactose, and maltose, found in fruits (fructose, glucose, sucrose), honey (fructose, glucose, sucrose), milk and dairy products (galactose, lactose), and table sugar (sucrose) (4). Sugars provide approximately 3.75 kcal per gram.

Although early humans likely discovered natural sweetness when tasting honey collected from wild bees, modern sucrose production derives primarily from sugarcane (around 80%) and sugar beet (about 20%). The history of sugarcane (*Saccharum officinarum*) spans thousands of years and has shaped human civilization through agriculture, trade, religion, and politics (5). Originally from New Guinea, sugarcane was cultivated more than 8,000 years ago. Capable of thriving in tropical climates—and, after hybridization with *Saccharum spontaneum*, also in subtropical regions—it spread to Southeast Asia and India, where refined sugar and crystallization of cane juice was discovered before 500 BCE (*sugar* itself can be traced to the Sanskrit *śarkarā*, meaning “granulated”). From India, it expanded westward into Persia and later into Mediterranean civilizations, although sugar remained an expensive luxury item.

With the expansion of Islam in the 7th century CE, Arab cultures became the principal promoters of the sugar industry, introducing its cultivation to new regions such as North Africa and the Iberian Peninsula, where climatic conditions were favorable.

After the discovery of the Americas, European colonial powers established sugar plantations in the tropical colonies of the Caribbean and Brazil. The expansion of the sugar industry in these territories was closely linked to the use of enslaved African

labor, creating a triangular system that allowed a large-scale sugar production.

During the 18th and 19th centuries, sugar ceased to be a luxury product and became a staple commodity in Europe and North America due to more efficient refining methods and steam-powered machinery (6), profoundly transforming diets and stimulating economic growth.

During the Napoleonic Wars (1803–1815), cane sugar became unavailable in continental Europe due to the British naval blockade. To meet demand, sugar began to be extracted from beet (*Beta vulgaris*). Later, the abolition of slavery in the British Empire caused cane sugar prices to rise sharply. By that time, beet varieties with sugar content comparable to sugarcane had been developed, and extraction costs had decreased substantially.

3. Impact of sugar consumption on health

According to the latest recommendations from the World Health Organization (WHO), free sugar intake should be limited to less than 10% of total caloric intake, with a further reduction to 5% suggested for additional health benefits. This corresponds to approximately 50 g or 25 g per day, respectively (3). However, it is estimated that the average person in Europe currently consumes about 100 g of sugar daily, whereas in the United States the figure can exceed 126 g per day. These levels are up to twenty times higher than sugar consumption in the eighteenth century and contribute substantially to the epidemic of metabolic syndrome and its associated diseases, particularly in countries following Western dietary patterns (7).

The term *sugar* encompasses a wide range of types and sources, underscoring the importance of public education in identifying risky consumption and promoting healthier lifestyle habits. Health education should aim to dispel misconceptions such as the belief that sugar is found only in foods considered sweet, overlooking the fact that most of the sugar consumed daily comes from processed and ultra-processed foods not perceived as sweet. These hidden sugars often appear under different names, including glucose, sucrose, fructose, honey, dextrose, and maltose, among others.

A further challenge is the growing prevalence of ultra-processed foods in industrialized countries, which has led to the excessive consumption of ingredients and

additives with little or no nutritional value. These products sacrifice the natural sensory qualities of food in favor of palatability and consumer appeal, often containing high concentrations —natural or artificial— of sugar, preservatives, sweeteners, salt, and saturated fats. As the food industry markets products labeled “light,” “zero,” or “sugar-free,” confusion has increased, and a growing number of artificial sweeteners such as saccharin, aspartame, acesulfame K, and sucralose have entered the market. Although their safety remains debated within the scientific community, they are still perceived by the general population as healthy and affordable alternatives.

These dietary shifts have resulted in lower fiber intake and decreased adherence to dietary models such as the Mediterranean diet. Consequently, the global prevalence of obesity, metabolic syndrome, and other chronic diseases —including type 2 diabetes mellitus and atherosclerotic cardiovascular disease, the leading preventable causes of death worldwide (3)— has risen. Metabolic-associated fatty liver disease, currently known as metabolic dysfunction–associated steatotic liver disease (MASLD), has also emerged as a strong predictor of cardiometabolic health (8). These diseases, rare in antiquity but increasingly prevalent in modern times, are largely behaviorally driven from early stages of life and have significant long-term effects on health and well-being.

There is growing interest in the relationship between diet and the gut microbiome and in its association with both gastrointestinal and systemic diseases. This complex community, composed of roughly 1,000 different species (9), has been identified as a key mediator of numerous physiological processes and communication pathways, including the gut–brain axis (10). Through its activity, enzymatic and metabolic capacity is expanded, enabling the degradation, absorption, and synthesis of micronutrients that would otherwise remain unavailable. Among these processes, bacterial fermentation of indigestible carbohydrates—such as dietary fiber—produces short-chain fatty acids (SCFAs), particularly butyrate, which play a central role in glucose metabolism and insulin sensitivity, lipid metabolism, appetite regulation, and immune system function (11).

4. The rise of artificial sweeteners as a sugar alternative

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Over the past 150 years, the use of sweeteners has evolved markedly from natural sources such as honey, fruit-derived fructose, and sugar obtained from cane and beet to the development of artificial and natural substitutes. The first artificial sweetener, saccharin, was discovered in 1879 by the German chemist Constantin Fahlberg. The discovery occurred by accident while he was experimenting with additives derived from anthranilic acid —a compound now used as an artificial flavoring for grape, jasmine, and orange, among others (12). Because it was inexpensive, calorie-free, and not associated with dental caries, saccharin quickly became the leading sugar substitute. During the widespread sugar shortages of both World Wars, its consumption rose sharply, consolidating its global use. In 1977, saccharin was banned because of its possible link with bladder cancer in rodent experiments. However, after a moratorium in 2001, "healthy" status was restored (13).

In 1937, Michael Sveda discovered cyclamate, again by accident. Approximately thirty times sweeter than sucrose, cyclamate was introduced to the U.S. market in 1950, initially as a means of helping to control insulin levels in diabetic patients. The Food and Drug Administration (FDA) deemed it safe in 1958 (12). However, its use was suspended in 1970 due to a possible link to cancer in animals (14). Subsequent analyses dismissed these concerns. Even so, cyclamate can be converted in the intestinal tract into compound which may be carcinogenic (15) (16). The World Health Organization currently classifies cyclamate as a "Group 3" substance, meaning it is not classifiable as to its carcinogenicity in humans.

In 1965, James M. Schlatter accidentally discovered aspartame while researching anti-ulcer drugs (12). Aspartame is 150 to 200 times sweeter than sucrose and, like other synthetic products, has been the subject of controversy. Regulatory agencies in more than ninety countries describe it as one of the most extensively studied additives in history and confirm safety (17).

Sucralose was discovered in 1976, also by accident, when Shashikant Phadnis, chlorinated sugar (12). It is approximately 600 times sweeter than sucrose. The safety of sucralose has been evaluated by major regulatory authorities, approved as a tabletop sweetener in 1998 and for general use in 1999. Before granting approval, the FDA reviewed more than one hundred safety studies, including cancer-risk

assessments, and found no evidence for cancer or other health hazards (18).

Neotame was developed in 2002 because competing industries deliberately sought the next major advance in sweetener technology. (13). Neotame is a dipeptide derivative of the amino acids aspartate and phenylalanine (19). It is between 8,000 and 13,000 times sweeter than sucrose. After reviewing more than one hundred scientific studies, regulatory bodies in several countries approved its general use as a sweetener and flavor enhancer in foods and beverages in 2002.

In recent decades, natural sweeteners such as stevia have gained popularity as alternatives to artificial compounds. Extracted from the South American plant *Stevia rebaudiana* Bertoni, stevia is an intensely sweet natural substitute for sugar, 200 to 300 times sweeter than sucrose.

In summary, over the past 150 years there has been a profound transformation in how humans consume sweetness, shifting from natural sources such as honey and sugarcane to calorie-free artificial sweeteners, as can be seen in Table 1. Although these products have provided options for individuals seeking to reduce sugar intake, concerns remain about their safety and long-term health effects.

Recent research suggests that excessive consumption of both sugars and substitutes may significantly reduce the concentration and diversity of the intestinal microbiota, a condition known as intestinal dysbiosis. These alterations may affect digestion and absorption processes, increasing susceptibility to unfavorable outcomes and even promoting the development of inflammatory bowel diseases (IBD) such as ulcerative colitis and Crohn's disease. This association is thought to involve chronic inflammation of the intestinal mucosa accompanied by the release of potentially carcinogenic compounds (11). Most available evidence comes from animal models, where significant effects have been observed, although extrapolation to humans remains difficult. A recent clinical trial conducted in Canada (20) explored this association further, particularly in relation to sucralose and aspartame, the most commonly used sweeteners in that country. Young adults (18–45 years) with a body-mass index between 20 and 25 and no comorbidities were randomized into two exposure groups for fourteen days, receiving acceptable daily doses in accordance with national guidelines. Pre- and post-exposure samples were collected and analyzed for

changes. The results differed from earlier experimental reviews, such as a 2020 Spanish study (21), although limitations —including the short exposure period and small, homogeneous population— were acknowledged. Nevertheless, it remains one of the most recent studies available and provides a valuable framework for future research.

5. The role of sugar and sweeteners in dysbiosis

Excessive sugar consumption can significantly affect the intestinal microbiota, altering both the composition and functionality of this complex ecosystem, which plays key roles in digestion, immunity, metabolism, and the production of vitamins and other energy compounds (22).

A balanced microbiota, or eubiosis, is characterized by a wide variety of microorganisms performing specific functions. The loss of this diversity —known as dysbiosis— has been linked to an increased risk of chronic diseases, inflammation, and metabolic dysfunction. An abundance of simple sugars in the intestinal lumen promotes the growth of pathogenic microorganisms and reduces beneficial bacteria, particularly *Bifidobacterium* and *Lactobacillus*.

Certain pathogenic bacteria release endotoxins and other compounds that activate the immune system, leading to chronic, low-grade inflammation. This process is associated with several metabolic disorders, including obesity and insulin resistance.

Symbiotic bacteria produce SCFAs, such as butyrate, which exert anti-inflammatory effects and help maintain intestinal mucosal integrity. A high-sugar diet can alter SCFA production by reducing the number of bacteria responsible for their synthesis. The resulting decrease in SCFA levels may compromise the intestinal barrier.

Excessive sugar intake not only impacts the microbiota but also disrupts overall metabolism. Dysbiosis induced by high sugar consumption can affect energy balance and fat storage, contributing to obesity, insulin resistance(23) and other metabolic complications such as type 2 diabetes mellitus (22). Moreover, an increase in bacteria that rapidly ferment sugar can cause gas accumulation, abdominal distension, and discomfort, contributing to nonspecific digestive symptoms.

The effects of artificial sweeteners on the intestinal microbiota have become a growing area of research. Initially regarded as safe and beneficial alternatives to sugar, recent studies indicate that they can affect gut health and microbiota composition.

Excessive consumption of both sugar and artificial sweeteners has been shown to reduce microbial diversity in the gut. These compounds, often combined with dietary emulsifiers typical of Western diets —such as carboxymethylcellulose and polysorbate 80— expose the microbiome and the epithelial mucus layer to cumulative stress, resulting in diminished diversity and heightened proinflammatory potential (24). The consequent overexpression of flagellin and lipopolysaccharides enhances bacterial motility and translocation through a degraded mucus layer. Ultimately, these alterations activate Toll-like receptor 4 and the nuclear factor κB (NF-κB) pathway, stimulating the secretion of proinflammatory cytokines as tumor necrosis factor-α (TNF-α) and interleukin 6 (IL-6).

Low-quality diets are also characterized by excessive salt intake and by additives commonly associated with emulsifiers, including colorants, preservatives, nanoparticles, and microplastics. Together, these factors have been shown to disrupt intestinal homeostasis (25). Experimental studies demonstrate that high-salt diets lead to a loss of *Lactobacillus* species and a reduced SCFA production (26). Likewise, exposure to microplastics —now widespread in bottled carbonated and sweetened beverages (27)— has been shown to decrease the transcription of genes involved in mucin production (28).

6. Sugar, dysbiosis, and structural determinants: a transdisciplinary threat to population health

Excessive consumption of sugar and noncaloric sweeteners, characteristic of Western diets, has been shown to profoundly alter the composition and functionality of the microbiota. As a result, intestinal permeability increases, activating the innate immune response which promotes low-grade systemic inflammation. This microbial imbalance is neither isolated nor purely experimental. It has been associated with a wide range of chronic disorders (obesity, insulin resistance, type 2 diabetes, atherosclerotic cardiovascular disease, neurocognitive impairment, depression, and

IBD, among others), constituting a transversal pathogenic axis capable of simultaneously compromising multiple organ systems.

However, exposure to dysbiosis-related risk is not evenly distributed. Low-income populations face material barriers to accessing fresh, unprocessed, and fiber-rich foods. In these contexts, food choices are often limited to inexpensive, calorie-dense, and nutrient-poor products. Diets based on refined sugars and trans fats reproduce the experimental profiles that induce dysbiosis and amplify underlying systemic inflammation. Poverty and food insecurity have been shown to double the risk of developing metabolic diseases and to worsen outcomes in preexisting conditions (29,30).

Furthermore, insufficient understanding of labeling, "hidden sugars", ingredients, and portion sizes reinforce long-term dysbiotic eating habits (31). Urban environments also shape risk: in so-called "food deserts" —where fresh foods are scarce— and in "food swamps" —where ultra-processed products abound— healthy diets are virtually inaccessible (32,33).

Moreover, the direct influence of the food industry on dietary choices has been recognized by international organizations as a structural driver of disease. Marketing campaigns have consolidated hyperglycemic consumption patterns from early childhood (34).

In addition, the role of stigma and barriers to healthcare access should not be underestimated. Socially marginalized groups, ethnic minorities, and individuals with chronic diseases often face systemic obstacles to obtaining nutritional education or personalized dietary guidance. The lack of early clinical intervention in these populations perpetuates exposure to pro-dysbiotic diets, reinforces disease chronicity, and deepens existing health inequalities (31).

Taken together, these findings indicate that sugar-induced intestinal dysbiosis is social phenomenon. The intestinal microbiota, as a sensitive ecosystem, responds to the environmental determinants —economic precariousness, obesogenic settings, commercial pressure, and educational inequality. This perspective requires reframing clinical and public health strategies not only along the diet–disease axis but within the broader social ecology of food.

Policies should reshape the food environment through systematic screening of social needs in primary care, subsidies for fruits and vegetables, taxation of sugary beverages with community reinvestment, prescription of whole-food diets under the *Food is Medicine* approach based on recommendations from gastroenterologists, and strict regulation of food marketing, particularly to children (35). Furthermore, translational research should integrate emerging technologies to design personalized interventions that take into account the sociocultural realities of vulnerable populations.

Sugar alters the microbiota, but society shapes its patterns of consumption —who consumes it, in what ways, and to what effect. Confronting the epidemic of dysbiosis requires coordinated action across every link in this causal chain, from gut health to food policy.

7. Limitations

Most of the data on dysbiosis induced by sugars and sweeteners comes from animal models or in vitro studies, with obvious limitations for extrapolation to humans. Human studies usually present: small samples, short intervention periods, exposure to doses that do not always reflect real long-term consumptions, and coexistence of other dietary factors that act as confounders. Definitions of dysbiosis and microbiota characterization techniques have evolved rapidly, making it difficult to compare between studies. Our review, being narrative and non-systematic, is subject to selection and publication biases, despite efforts to mitigate these risks through a structured search in PubMed and the inclusion of recent systematic reviews. We limited the bibliography to articles in English and relevant literature in Spanish, which may have excluded relevant studies in other languages.

8. Conclusions

Excessive sugar consumption —driven by the industrial production of cane and beet sugar and its widespread incorporation into Western diets— negatively affects not only cardiometabolic health but also the intestinal microbiota. It reduces microbial diversity, promotes the growth of pathogenic bacteria, increases inflammation, and

alters the production of beneficial metabolites such as SCFAs. Artificial sweeteners combined with other ingredients commonly found in processed and ultra-processed foods, including emulsifiers, likewise have deleterious effects on the microbiome.

These alterations can have far-reaching implications for human health, contributing to metabolic (like MASLD), inflammatory (like IBD), and other gastrointestinal diseases. Maintaining a balanced diet rich in fiber and low in refined sugars is essential for preserving intestinal health and overall well-being.

Health authorities should establish clear dietary guidelines to limit the consumption of low-quality foods, including a maximum sugar intake of less than 10% of total energy, as recommended in Scandinavian countries and the United States —or even less than 5%, according to the guidelines of the World Health Organization (36), the United Kingdom's Scientific Advisory Committee on Nutrition, and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

The promotion of healthy diets should be a cornerstone of public health strategies for the primary prevention of cardiometabolic disease, particularly among economically vulnerable populations. National health systems must shift from a reactive model —focused on treating disease after its onset— to one centered on prevention. This transition requires concrete measures to strengthen nutritional education and promote the consumption of unprocessed and minimally processed foods without added sugar.

Final statement

We support inclusive, diverse, and equitable research.

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Tables

Table 1: year of discovery and sweetening power of sucrose and sweeteners.

Name	Discovery	Year	Sweetening power
Sucrose	Agriculture in Indonesia	Ancient times (used in Eurasia from 3rd century BCE)	1 (gold-standard)

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Saccharin	Accidental chemical discovery	1879	300
Cyclamate	Accidental chemical discovery	1937	250
Aspartame	Accidental chemical discovery	1965	150-200
Stevia	Agriculture in South America	Ancient times (used in Western Countries from 1970)	150-300
Sucralose	Accidental chemical discovery	1976	600
Neotame	Intentional chemical discovery	2002	8.000-13.000

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Table 2: summary of the main works on diet, sugar and sweeteners and their impact on microbiota and cardiovascular health. SCFA: short-chain fatty acids; IBD: inflammatory bowel disease.

Auto, año	Diseño	Población	Exposición	Efectos microbiota/disbiosis	Resultado clínico principal	Limitaciones
Ceballos, 2021	Narrative Review	—	Diet quality (free sugars, fiber)	Declining diversity, changing SCFAs	Digestive/metabolic risk by diet	Heterogeneity, not systematic
Richardson, 2022	Narrative Review	—	Sweeteners	Changes in microbial composition	Composite-dependent impact	Small and heterogeneous studies
Quaglio, 2022	Review	—	Sweeteners	Alteration of permeability and microbiota	—	Preclinical predominance
Ahmad, 2020	Review	—	Sweeteners	Microbial variations according to sweetener	Modest metabolic benefit	Small Trials
Ruiz-Ojeda, 2019	Review	—	Sugars and Sweeteners	Bacterial Changes and SCFAs	Low-grade inflammation	Non-standardized techniques
Suez, 2014	Experimental + observational	Animal model; Human	Sweeteners	Microbiota changes associated with glucose intolerance	Microbiota-mediated glucose intolerance	Small sample
Kynde, 2010	Observational	Human	Sugars	Dysbiosis inferred by dietary pattern	Cardiometabolic risk	Does not analyse microbiota
Bancil, 2021	Review	—	Emulsifiers and additives	Alteration of barrier and mucous layer	IBD Risk	Animal model
Raoul, 2022	Review	—	Western diet	Inflammatory microbial remodeling	Intestinal inflammation	Narrative
Miranda, 2018	Experimental	Animal model	Western diet	Loss of barrier integrity, dysbiosis	Increased susceptibility to colitis	Animal model
Jin, 2019	Experimental	Animal model	Microplastics	Alteration of microbiota and barrier function	Pro-inflammatory phenotype	Uncertain human relevance
Hasjim, 2024	Observational	Human	Western diet	Indirect association with microbial changes	Digestive/metabolic risk	Observational
Ma, 2023	Observational	Human	Sweeteners	-	Cardiometabolic risk	Multiple diet analysis