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END OF STUDY THESIS

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THEME

Gut microbiota dysbiosis and the therapeutic potential of dietary polysaccharides: A literature review

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(عمار ، سالم ، عبد الحفيظ) كنتم دائمًا اليد التي تمتد قبل أن أطلبها، والكتف الذي يحمل عني أثقال الطريق، فوجودكم نعمة عظيمة أعتز بها. لكم مني خالص المحبة وعظيم الامتنان، وأسأل الله أن يديمكم سندًا وفخرًا وأمانًا لا يميل أبداً.

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أستاذتي المشرفة الراقية محلو زينب ...

أتقدم إلي ,,ك بأسمى عبارات الشكر والتقدير والامتنان، عرفانًا بما بذل ,,ته من وقت وجهد، وما قدم ,,ته من علم و دعم واهتمام وعطاء وإخلاص نبيل ومرافقة طوال هذا المشوار العلمي. فقد كنت عقلًا حكيمًا يرشد الخطى كلما تاهت الطرق. أسأل الله أن يجعله في ميزان حسناتك وأن يديم عليك نعمة العلم والعطاء.

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بله باسي كريمة

الاهداء

بسم الله الرحمن الرحيم

" وقُل رَّبِ زِدنِي عِلمًا".

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وما وصلت إليه بعد فضل الله ، وتوفيقه بل كان حصيلة دعم وحب مساندة أشخاص كان لوجودهم أعظم الأثر في مسيرتي.

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هذه الحياة لا أملك إلا أن أقول: هذا أنت... وهذا جهدي بين يديك. (**أبي الغالي)**

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شيباني مفيدة

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الحمد لله أولاً وأخيرًا على نعمة التَّوفيق. وعلى القوة والصَبر اللَذين منحني إيَاهما لإتمام هذا العمل بعد سنوات من الاجتهاد والسَعي والتَعب. أحمد الله كثيرًا على كلّ خطوة وصَلتني إلى هذه اللَحظة الَتي طال انتظارها. وأسأله أن يبارك لي فيما هو قادم.

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أهدي ثمرة هذا التَخرج إلى أبي العزيز. الَذي كان دعمه وثقته بي دافعًا للاستمرار وتحقيق هذا الإنجاز. فله منّي كلّ الاحترام و التَقدير و إلى أمّي الغالية. مصدر الحنان والدَعاء والقوَة. الَتي كانت دائمًا بجانبي بكلماتهاودعمها وصبرها. فكان وجودها أكبر سند لي طوال هذا المشوار.

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إلى صديقات الرَوح: بوكة. فاطمة. خولة. وفاطمة. شكرًا لوجودكنّ الجميل ولكلّ لحظة دعم وصدق واهتمام.

وأخصّ بالشُكر مريم. مفيدة. وكريمة. اللَواتي شاركنني هذا المشوار بكلّ تفاصيله. وكان لوجودهُن ودعمهُن أثرجميل سيبقى دائمًا في قلبي.

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منار

ABSTRACTS

Gut microbiota dysbiosis and the therapeutic potential of dietary polysaccharides: A literature review

Abstract

The gut microbiota is a community of trillions of beneficial bacteria residing in the colon. Non digestible fibers are complex polysaccharides found in plants, fungi, and bacteria, and the human body cannot digest them on its own, so they reach the colon intact. The gut microbiota ferments these polysaccharides using their own enzymes, to produce short-chain fatty acids (SCFAs). The most important SCFAs is butyrate, which strengthens the intestinal barrier by increasing tight junction proteins, and alleviates inflammation by inhibiting the NF-κB pathway. Dysbiosis occurs due to antibiotics, environmental toxins, an unhealthy diet, or pathogenic organisms. Dysbiosis is characterized by loss of microbial diversity, a decrease in butyrate-producing bacteria, and an increase in pathogenic bacteria. These changes cause increased intestinal permeability through decreased tight junction proteins and a decreased mucin layer, allowing LPS, TMAO, and bacteria to translocate into the blood, activating NF-κB with elevated inflammatory cytokines (TNF-α, IL-6, and IL-1β). This leads to chronic diseases fatty liver disease, atherosclerosis, heart failure; and nervous system diseases such as Alzheimer's, Parkinson's and depression. In the dextran sodium sulfate model (DSS), an animal model of ulcerative colitis (UC), these same mechanisms cause colon shortening, bleeding, diarrhea, and an elevated disease activity index. Here comes the role of natural polysaccharides from various sources (plant; fungal-derived, bacterial-derived, and animal-derived,), which act as effective prebiotics that reprogram the microbiota toward a healthy state by increasing Akkermansia, Lactobacillus, and butyrate-producing bacteria and reducing pathogenic bacteria. Polysaccharides act through mechanisms including butyrate production, which fuels colonic cells and inhibits HDAC and NF-κB; strengthens the intestinal barrier by increasing ZO-1, occludin, claudin-1, and mucin 2 and increasing goblet cells; inhibits inflammation by reducing TNF-α, IL-6, IL-1β, and IL-17 and increasing IL-10 and TGF-β, and improves antioxidants while reducing oxidative stress. All 18 studies collected confirmed a uniform pattern of improvement, independent of the source of polysaccharides and instead dependent on structural features that enhance colonic delivery and slow fermentation for SCFA production, most notably low molecular weight (LMW), branched structure, and sulphated groups. Therefore, polysaccharides have been demonstrated to represent a promising multi-target strategy for managing DSS-induced UC and its associated liver, cardiovascular, and neurological diseases through restoring eubiosis, repairing the intestinal barrier, and modulating immunity, which is known as the microbiota-barrier-immunity axis.

Keywords: Gut microbiota, Dextran sodium sulfate (DSS), Dysbiosis, Polysaccharides, Short-chain fatty acids (SCFAs)

اختلال توازن الميكروبيوتا المعوية والإمكانات العلاجية للسكريات المتعددة الغذائية: مراجعة للأدبيات العلمية

الملخص

تمثل gut microbiota مجتمعًا من تريليونات البكتيريا النافعة المقيمة في القولون. الألياف غير القابلة للهضم هي متعددة سكريات معقدة توجد في النباتات والفطريات والبكتيريا، ولا يستطيع الجسم البشري هضمها بنفسه، لذا تصل إلى القولون سليمة. و تقوم microbiota gut بتخمير متعددة السكريات هذه باستخدام إنزيماتها الخاصة لإنتاج أحماض دهنية قصيرة السلسلة (SCFAs). أهم هذه الأحماض هو (butyrate)، الذي يقوي الحاجز المعوي عن طريق زيادة بروتينات الوصلات المحكمة، ويخفف الالتهاب من خلال تثبيط مسار NF-κB. يحدث اختلال التوازن الميكروبي (dysbiosis) نتيجة للمضادات الحيوية، أو السموم البيئية، أو النظام الغذائي غير الصحي، أو الكائنات الممرضة. يتسم هذا الاختلال بفقدان التنوع الميكروبي، وانخفاض في البكتيريا المنتجة للبيوتيرات، وزيادة في البكتيريا الممرضة. تسبب هذه التغيرات زيادة نفاذية الأمعاء من خلال انخفاض بروتينات الوصلات المحكمة وانخفاض طبقة الميوسين، مما يسمح بانتقال الـ LPS والـ TMAO والبكتيريا إلى الدم، مما ينشط مسار NF-κB مع ارتفاع السيتوكينات الالتهابية (TNF-α، IL-6، IL-1β). يؤدي هذا إلى أمراض مزمنة مثل مرض الكبد الدهني، وتصلب الشرايين، وفشل القلب، وكذلك أمراض الجهاز العصبي مثل الزهايمر، وباركنسون، والاكتئاب. في نموذج dextran sodium sulfate(dss) ، وهو نموذج حيواني لالتهاب القولون التقرحي (UC)، تؤدي هذه الآليات نفسها إلى تقصير القولون، والنزيف، والإسهال، وارتفاع مؤشر نشاط المرض. وهنا يأتي دور متعددة السكريات الطبيعية من مصادر مختلفة (نباتية، فطرية، بكتيرية، حيوانية)، والتي تعمل كمواد بريبايوتيك فعالة تعيد برمجة microbiota نحو حالة صحية عن طريق زيادة Akkermansia، Lactobacillus، والبكتيريا المنتجة للبيوتيرات، وتقليل البكتيريا الممرضة. تعمل متعددة السكريات عبر آليات تشمل: إنتاج البيوتيرات، الذي يغذي خلايا القولون ويثبط HDAC و NF-κB؛ تقوية الحاجز المعوي بزيادة ZO-1، occludin، claudin-1، و mucin 2 وزيادة الخلايا الكأسية؛ تثبيط الالتهاب بتقليل TNF-α، IL-6، IL-1β، IL-17 وزيادة IL-10 و TGF-β؛ وتحسين مضادات الأكسدة مع تقليل الإجهاد التأكسدي. جميع الدراسات الـ 18 التي تم جمعها أكدت نمطًا موحدًا من التحسن، بغض النظر عن مصدر عديدات السكريات ويعتمد بدلًا من ذلك على السمات البنيوية التي تعزز التوصيل إلى القولون والتباطؤ في التخمر لإنتاج SCFAs؛ وأبرزها الوزن الجزيئي المنخفض (LMW)، والبنية المتفرعة، والمجموعات الكبريتية. لذلك، ثبت أن عديدات السكريات تمثل استراتيجية متعددة الأهداف واعدة للسيطرة على التهاب القولون التقرحي المستحث بـ DSS وما يرتبط به من أمراض كبدية، قلبية وعائية، وعصبية من خلال استعادة الاتزان الميكروبي (eubiosis)، وإصلاح الحاجز المعوي، وتعديل المناعة،

وهو ما يُعرف بمحور microbiota-barrier-immunity axis.

الكلمات المفتاحية: الميكروبيوتا المعوية، ديكستران كبريتات الصوديوم(DSS)، اختلال التوازن الميكروبي، متعددة السكريات، أحماض دهنية قصيرة السلسلة(SCFAs).

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AD	Alzheimer's disease
ALS	Amyotrophic lateral sclerosis
BDNF	Brain-derived neurotrophic factor
BSH	Bile salt hydrolase
BSPs	Brown seaweed polysaccharides
CAT	Catalase
CAZymes	Carbohydrate-active enzymes
CFU/mL	Colony-forming units per milliliter
DSS	Dextran sodium sulfate
EPSs	Exopolysaccharides
FAS	Fatty acid synthase
FCS	Fucosylated chondroitin sulfate
GABA	Gamma-aminobutyric acid
GalNAc	N-acetylgalactosamine
GLA	Gut-liver axis
GSPs	Green seaweed polysaccharides
HFD	High-fat diet
IBD	Inflammatory bowel disease
IL	Interleukin
LAM	Lumen-associated microbiota
LPS	Lipopolysaccharide
MAM	Mucosa-associated microbiota
MDA	Malondialdehyde
MI	Myocardial infarction
NF-κB	Nuclear factor kappa B
PD	Parkinson's disease
PLs	Polysaccharide lyases
PS	Polysaccharides
ROS	Reactive oxygen species
RSPs	Red seaweed polysaccharides
SCFAs	Short-chain fatty acids
TCS	Triclosan
TMAO	Trimethylamine N-oxide
TNF-α	Tumor necrosis factor alpha
TPS	Tea polysaccharides
TPs	Tire particles
UC	Ulcerative colitis
VBNC	Viable but non-culturable

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INTRODUCTION

The intestine is defined as the part of the digestive tract extending from the gastric pylorus to the anus, and the average length of the small intestine alone is approximately 3 to 5 meters in healthy adults (Collins *et al*., 2025). Studies have shown that the human intestine represents a complex ecosystem supporting billions of living species, including bacteria, viruses, and fungi (Vos *et al*., 2022). The microbiota, defined as "the community of living microorganisms inhabiting a defined environment" (Chin *et al*., 2025), plays a pivotal role in maintaining host health, as it is essential for proper immune responses, aiding digestion, synthesizing essential nutrients, and protecting against pathogenic bacteria (Ananthakrishnan *et al*., 2025). However, any alteration in these bacterial communities may lead to a condition known as dysbiosis, which is characterized by microbial imbalance, loss of beneficial bacteria, and overgrowth of pathogenic bacteria (Rehman *et al*., 2025). It has been scientifically established that this microbial dysfunction contributes to the development of a wide range of non-communicable diseases, including obesity, diabetes, inflammatory bowel disease, and cancer (Asnicar *et al*., 2026). Therefore, distinguishing between the term "microbiota" (the microorganisms themselves) and "microbiome" (which includes, in addition to the microorganisms, their genes, gene products, and environmental activities) is essential for understanding the mechanisms by which these organisms influence health and disease (Sharma *et al*., 2025).

Carbohydrates are one of the three macronutrients in the human diet, along with protein and fat. These molecules contain carbon, hydrogen, and oxygen atoms and play an important role in the human body, acting as an energy source, helping control blood glucose and insulin metabolism, participating in cholesterol and triglyceride metabolism, and facilitating fermentation (Holesh *et al*., 2023). Dietary polysaccharides are complex bioactive macromolecules whose structural features—such as monosaccharide composition, glycosidic linkages, branching degree, and molecular weight—critically determine their interaction with the gut microbiota (Subhash *et al*., 2026). Under physiological conditions, these polymers act as prebiotic substrates, promoting beneficial bacteria (e.g., Lactobacillus and Bifidobacterium) and stimulating the production of short-chain fatty acids (SCFAs) and carbohydrate-active enzymes (CAZymes), thereby maintaining intestinal homeostasis (Subhash *et al*., 2026; Yang *et al*., 2025). However, when gut microbiota dysbiosis occurs—triggered by poor diet, oxidative stress, or genetic factors—the intestinal barrier is disrupted, leading to increased permeability, endotoxin translocation, and chronic low-grade inflammation. In this pathological context, natural polysaccharides exert a dual-effect therapeutic mechanism (Yang *et al*., 2025). First, they restore eubiosis by selectively enriching SCFA-producing bacteria and suppressing opportunistic pathogens, which reinforces the mucosal barrier through upregulation of tight junction proteins (e.g., claudin, occludin) and goblet cell proliferation. Second, they modulate immune and

metabolic pathways via the gut–organ axis, including the Th17/Treg balance, vagus nerve activation, and bile acid metabolism, thereby attenuating local intestinal inflammation and preventing systemic spread to distant organs such as the liver, lung, brain, kidney, and skin. These findings position dietary polysaccharides as promising therapeutic agents for treating inflammation driven by gut microbiota dysbiosis, acting not only as prebiotic regulators but also as multi-axis network modulators that bridge the gut to the whole body (Wei *et al*., 2026; Xue *et al.,* 2025).

This study aims to review the molecular mechanisms of the interaction between dietary polysaccharides and the gut microbiota in the healthy state, to identify external factors such as antibiotics, environmental toxicants, unbalanced dietary patterns, and pathogenic microorganisms that cause the intestine to shift from a state of balance (eubiosis) to a state of imbalance (dysbiosis). In addition, the present review stands to trace how this imbalance is transmitted across the biological axes to induce organic diseases of the liver (such as steatosis), of the heart (such as heart failure and atherosclerosis), and of the nervous system (such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis). The study also aims to highlight the opposing role of natural polysaccharides in restoring balance through reshaping the microbial composition toward an anti-inflammatory pattern and through the production of short-chain fatty acids (SCFAs), thereby confirming that the polysaccharide-microbiota axis determines the fate of healthy homeostasis or the transition toward organic diseases.

This document falls within the framework of two chapters. The first is dedicated to a general overview of the gut microbiota, its dysbiosis, and the extension of this imbalance to the liver, heart, and nervous system. The second chapter outlines several generalities about dietary polysaccharides and highlights their role in restoring gut microbiota balance namely via the production of short-chain fatty acids (SCFAs). A comprehensive conclusion, future perspectives and some recommendations complete the present work.

CHAPTER I

Gut microbiota dysbiosis

This chapter presents generalities about gut microbiota and its dysbiosis. It also highlights how the state of gut microbiota affect vital functions including the liver, the heart, and the nervous system.

I.1. Gut microbiota

I.1.1. Definition

Intestinal microbiota has been defined as a diverse and dynamic ecosystem consisting of trillions of microorganisms living inside the human body. These complex microbial communities are mainly settled in the colon (the large intestine). Microbes play a pivotal role in regulating the metabolic pathways of the host. They also transmit vital signals that directly affect the physiological functions of the body. Due to the lack of certain enzymes in the human body, it cannot digest complex carbohydrates alone. Hence the role of microbiota that break down these carbohydrates and use them as an energy source, resulting in important metabolic products such as short-chain fatty acids (SCFAs). Some studies have confirmed that diet and surrounding environment significantly affect the composition and diversity of microbiota. The occurrence of any imbalance in its balance (known as dysbiosis) is associated with many pathological conditions such as obesity, diabetes, inflammatory bowel disease (IBD), and ulcerative colitis (Wu *et al*., 2023).

A distinction between microbiota and microbiome has been made; microbiota basically refer to the same microorganisms that live in a specific environment together (such as the intestine). It is a diverse and dynamic biological community made up of trillions of microbes, including bacteria, viruses, and fungi. When studying the microbiota, scientists focus on the types of microbes present, their diversity, and their relative abundance in the colon. The microbiome is a more comprehensive term; it includes not only microorganisms but also their genetic material (genome) and surrounding environmental conditions. The microbiome is related to studies used in genomics and bioinformatics to understand the functional patterns of these organisms. The microbiome is analyzed through advanced techniques such as gene sequencing (16S rRNA) or metagenomic sequencing, which allows researchers not only to know "who lives there" but also to understand "what these microbes do" in metabolic and functional terms (Wang *et al*., 2025).

I.1.2. Classification of intestinal microbiota

Two basic divisions (Phyla), Firmicutes and Bacteroids, dominate the intestinal ecosystem, and form the most important indicator of biobalance. Other microbiota also includes phyla in lesser proport4ions such as Proteobacteria, which are often associated with increased inflammation when

their percentage is high. Verrucomicrobia like the genus Akkermansia, Actinobacteria like the genus Bifidobacterium, Deferribacteres and Tenericutes are types of less dominant phyla present in the intestinal ecosystem (Saurabh and Vineet, 2023).

Phyla branch out into diverse genera that play different functional roles. Lactobacillus are lactic acid bacteria and are considered an important biological sign of intestinal health. Bifidobacterium are associated with the strengthening of the immune system. Bacteroides and Prevotella have roles in the breakdown of polysaccharides and modification of the inflammatory response. Allobaculum and Turicibacter contribute to maintaining the integrity of the intestinal barrier (Wu *et al*., 2023).

Moreover, opportunistic and pathogenic genera can be present in the gut microbiota. Clostridium perfringens, Gram-positive bacteria, cause enteritis, necrotic enteritis, and secrete toxins that destroy the intestinal wall. Helicobacter, Escherichia and Shigella are associated with increased severity of inflammation in ulcerative colon cases (Blue *et al*., 2024; Huang *et al*., 2025).

Scientists also classify microbes based on what useful compounds they produce (such as short-chain fatty acids—SCFAs). Butyrate producers such as Roseburia and Faecalibacterium prausnitzii, are necessary to nourish intestinal cells and prevent inflammation. Acetate and propionate producers such as Bacteroides and Veillonella act as “chemical factories” within the colon, converting non-digestible polysaccharides into acetate and propionate. These metabolites subsequently provide energy to the host, protect the intestinal environment against pathogens, and regulate glucose and lipid metabolism through complex signaling pathways (Wu *et al*., 2023).

The gut microbiota exhibits a distinct spatial distribution along the gastrointestinal tract as a result of variations in physicochemical conditions among intestinal segments, including oxygen concentration, pH, intestinal motility, mucus content, and transit time. This spatial organization forms a gradual transition from the small intestine, which is predominantly colonized by aerobic and facultative anaerobic bacteria, to the large intestine, where obligate anaerobes become dominant. In the duodenum, where oxygen levels are relatively high and food transit is rapid, microbial density remains very low and generally does not exceed 10^3 colony-forming units/mL (CFU/mL), with Firmicutes, Proteobacteria, Streptococcus, and Prevotella being the predominant taxa. In the jejunum, microbial density increases to approximately 10^3-10^5 CFU/mL, and the microbiota is mainly composed of Firmicutes, Proteobacteria, Veillonella, and Escherichia, in addition to lipase-producing bacteria such as Lactobacillus and Enterococcus. In the ileum, microbial density further rises to about 10^7-10^8 CFU/mL. The proximal ileum resembles the upper gastrointestinal tract and is enriched with

Streptococcus, Haemophilus, and Escherichia, whereas the terminal ileum more closely resembles the large intestine, with increased abundances of Bacteroides and Enterobacteriaceae. In the cecum, microbial density reaches approximately 10^8 CFU/mL due to slower intestinal transit, and the dominant microorganisms include Escherichia, Lactobacillus, and Enterococcus. The colon harbors the highest microbial load within the gastrointestinal tract, reaching approximately 10^{11}-10^{12} CFU/mL as a consequence of low oxygen availability and prolonged transit time. Firmicutes and Bacteroidetes predominate in this region, together with important genera such as Bacteroides, Faecalibacterium, Akkermansia, and Prevotella. In the rectum, Firmicutes, Bacteroidetes, and Proteobacteria also predominate, along with families including Lachnospiraceae, Ruminococcaceae, and Bacteroidaceae. The study additionally described a horizontal gradient within the same intestinal segment between mucosa-associated microbiota (MAM), which are attached to the mucosal surface, and lumen-associated microbiota (LAM), which inhabit the intestinal lumen. This distinction is mainly driven by differences in oxygen tension, mucus concentration, and redox potential (Ohland and Jobin, 2015; Payling *et al*., 2020; Kumoro *et al*., 2025; Yang *et al*., 2025).

I.1.3. Functions of the gut microbiota

Gut microbiota play vital and crucial roles in maintaining homeostasis and human health. Functions vary to include nutritional, immune, and structural aspects (Zhengrui *et al*., 2026). Microbes ferment complex carbohydrates that the body cannot digest, producing short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate. Butyrates produced through fermentation are the primary fuel for colonic cells (colonocytes) and contribute to their protection against cancer. Species like Bifidobacteria contribute to the production of B vitamins and antioxidants. They play a significant role in the metabolism of certain food and drug components and enhance the absorption of minerals such as calcium by increasing the intestinal surface area (Payling *et al*., 2020).

These bacteria form the first line of defense against pathogens and toxins, producing antimicrobial compounds and competing with harmful bacteria for food and space. They play a pivotal role in shaping and modulating the immune response and contribute to regulating inflammatory processes. They break down carcinogens by converting proteins into sterols and bile acids, which helps eliminate potentially mutagenic bacteria in consumed food (Komori *et al*., 2025).

Gut microbiota help in supporting the mucosa, which is vital for maintaining the integrity of the intestinal barrier, preventing the penetration of harmful substances. They also regulate bowel

movements, as fatty acids produced by microbial activity directly affect the motility of the digestive tract (intestinal motility) (Stribling and Ibrahim, 2023).

Microbes in the large intestine convert excess cholesterol into a substance called cuprostanol, which is then eliminated. They also contribute to fluid and electrolyte balance in the body. They facilitate communication between cells by producing signaling molecules that enable interaction between microbes and body cells, influencing appetite regulation and blood sugar stability (Komori *et al.*, 2025). Furthermore, microbes support each other through cross-feedback; the digestive products of one species become fuel for another, ensuring the diversity and stability of the microbial community (Payling *et al.*, 2020).

I.2. Gut microbiota dysbiosis

The gut microbiota is a dynamic and complex ecosystem whose composition and function are significantly influenced by a wide range of external factors. The health of the microbiota depends not only on the host's genetic type but is also the result of continuous interaction with the surrounding environment, lifestyle, and diet. Therefore, any disruption to these factors can push the microbiota from a state of eubiosis (balance) to dysbiosis (imbalance), a condition associated with numerous chronic diseases (Obayomi *et al.*, 2025). This imbalance, or dysbiosis, is not merely shift but a functional disruption that directly impacts the intestinal barrier. Dysbiosis drives a loss of microbial diversity and an alteration in gut microbiota composition, which in turn leads to functional dysregulation of the microbial ecosystem. Consequently, these changes compromise the intestinal epithelial barrier, triggering inflammatory activation and perpetuating a vicious cycle of barrier dysfunction (Grover *et al.*, 2025).

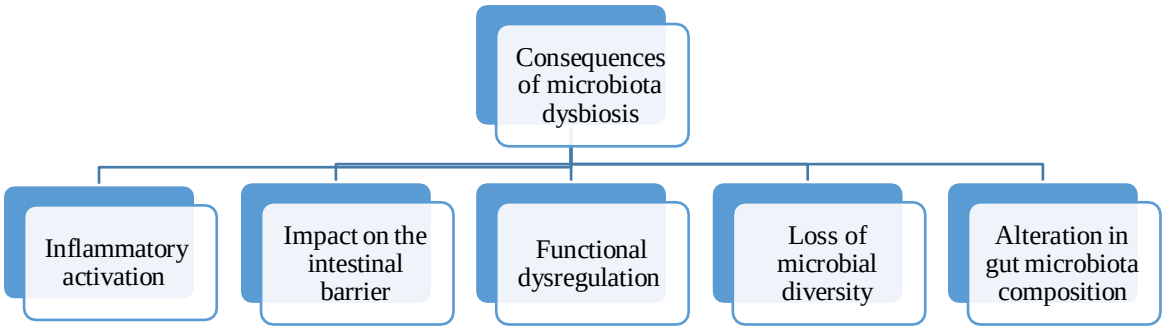

Figure 1 : Consequences of microbiota dysbiosis (Huang *et al.*, 2025)

I.2.1. Antibiotic effects on gut microbiota

Antibiotic treatment rapidly diminishes microbiome diversity (fig. 2), taking up to six months for partial recovery, leading to an imbalance favoring opportunistic pathogens (Babouce Flury *et al.*,

2024). Hence, antibiotic administration can profoundly alter the composition and diversity of the gut microbiota, disrupt homeostasis, and create selective pressure that promotes the proliferation of antibiotic-resistant bacteria (Shayista *et al.*, 2025)**.** Dysbiosis also impact the secretion of gut hormones crucial for metabolic regulation, appetite control, and immune homeostasis. One of the primary pathways through which antibiotics modulate hormonal dynamics is by impairing the microbial synthesis of SCFAs, notably acetate, propionate, and butyrate. SCFAs serve as potent inducers of gut hormone secretion by activating G-protein coupled receptors (e.g., GPR41, GPR43) on enteroendocrine cells. A reduction in SCFA-producing taxa, such as *Faecalibacterium prausnitzii* and *Roseburia spp*., following antibiotic exposure leads to attenuated glucagon-like peptide-1 (GLP-1) an incretin hormone , and peptide YY (PYY) an anorexigenic hormone , release, thereby impairing glucose tolerance and enhancing insulin resistance (Hareesha *et al*., 2025).

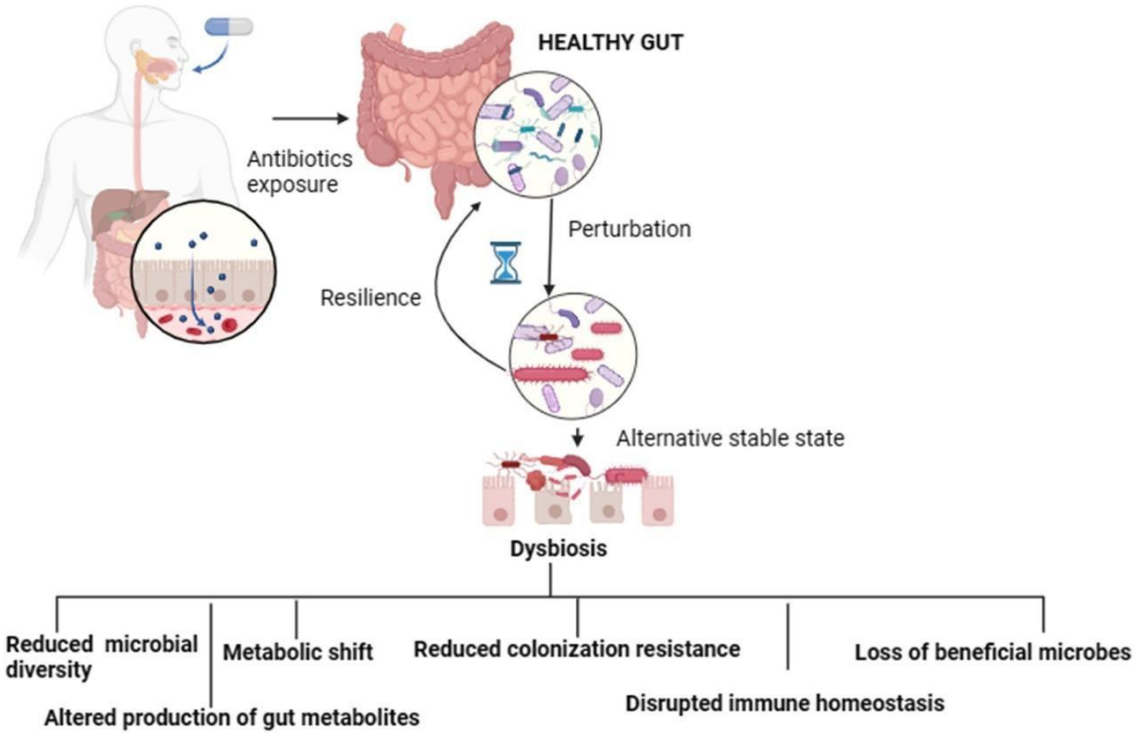

Figure 2 : Antibiotic-induced dysbiosis in the gut microbiota (Shayista *et al.*, 2025)

Doxycycline and tetracycline cause significant disruption of the gut microbiota with loss of beneficial taxa, lead to a decrease in 13 metabolites and an increase in 9 metabolites (notably a decrease in hippuric acid and indole-3-acetic acid), induce disruption in energy metabolism, increase pro-inflammatory cytokines (IL-1β, IL-6, IL-12, IL-17, TNF-α), and their microbial composition changes persist after withdrawal (Shayista *et al.*, 2025). Amoxicillin and cotrimoxazole induce

marked gut dysbiosis in young mice, characterized by a significant reduction in bacterial colony counts and disruption of the normal gut microbial balance (Cosmas *et al*., 2026).

I.2.2. Environmental toxicants

Environmental toxicants are among the major external factors capable of inducing acute disruption of the gut microbiota balance (dysbiosis) through direct mechanisms that include altering bacterial composition, inhibiting beneficial bacteria, and promoting the growth of pathogenic bacteria (Li *et al*.,2025; Gu *et al*., 2025; Keang *et al*., 2026) This microbial imbalance can negatively impact distant organs, particularly the liver, via the gut-liver axis (Li *et al*., 2025).

Triclosan (TCS), an antibacterial agent found in personal care products such as soaps and toothpastes, is strongly associated with a significant alteration in the composition of the gut microbiota in school-aged children. Using advanced statistical analyses, TCS exposure leads to a marked increase in the abundance of the bacterial genus Desulfovibrio, a genus known for its ability to produce hydrogen sulfide, which is linked to intestinal inflammation. Mechanistically, TCS acts as a broad-spectrum antibiotic, leading to the selective inhibition of sensitive bacteria while providing an opportunity for resistant bacteria such as Desulfovibrio to proliferate. This microbial imbalance (dysbiosis) causes increased intestinal permeability (leaky gut) by inhibiting the expression of tight junction proteins, allowing bacterial toxins (LPS) to translocate into the bloodstream and subsequently to the liver via the portal vein. Most importantly, mediation analysis revealed that the genus Desulfovibrio was responsible for explaining 48.5% of the total effect of TCS on liver function, confirming its role as a key microbial mediator in the toxic effects of this compound (Li *et al*., 2025).

Moreover, co-exposure to Microplastics (MPs) and Tire Particles (TPs) —two emerging environmental pollutants—leads to a synergistic and devastating effect on the gut microbiota, surpassing the effect of each substance alone. This effect was characterized by a sharp decrease in the abundance of the phylum Proteobacteria , which includes many bacterial genera important for gut health, alongside an increase in bacteria capable of resisting and tolerating these toxins, indicating a harsh bacterial selection that alters the natural balance of the microbiota. Mechanistically, once ingested, these particles accumulate in the gastrointestinal tract and cause localized oxidative stress through increased production of reactive oxygen species (ROS). This oxidative stress damages bacterial DNA, causing the death of sensitive bacteria while simultaneously promoting the growth of bacteria resistant to toxins and stress, explaining the observed shifts in microbial composition. Furthermore, these particles weaken the intestinal mucus layer, increasing the adhesion of plastic particles and preventing beneficial bacteria from establishing themselves. These changes in microbial

composition, accompanied by a marked increase in oxidative stress markers (MDA) and disruption of antioxidant enzymes (SOD/CAT), illustrate how plastic pollution disrupts the intestinal microbial ecosystem (Keang *et al.*, 2026).

Chronic exposure to low concentrations of Cadmium (Cd) —one of the most widespread toxic metals in the environment due to industrial and agricultural activities—leads to a clear disruption in the composition of the gut microbiota in mice, characterized by a marked increase in the abundance of the genus Prevotella and a significant decrease in the abundance of the genus Turicibacter. Mechanistically, cadmium acts through two integrated pathways. The first pathway involves direct oxidative stress on bacterial cells, where Cd enters bacterial cells through calcium and iron channels and generates reactive oxygen species (ROS), leading to damage of bacterial DNA and proteins, which explains the decrease in sensitive genera such as Turicibacter. The second pathway involves the inhibition of bacterial bile acid-metabolizing enzymes, where Cd inhibits the activity of the bacterial enzyme 7α dehydroxylase, responsible for converting primary bile acids into secondary bile acids, leading to the accumulation of bile acids toxic to the liver and disruption of lipid metabolism (Gu *et al.*, 2025).

I.2.3. Dietary factors

Consuming a consistently high-fat diet (HFD) leads to an imbalance in the gut microbiota, promoting the growth of harmful bacteria at the expense of beneficial ones. Studies indicate that this diet causes a decrease in anti-inflammatory microbes such as Ruminococcaceae and Coprococcus while increasing pro-inflammatory microbes such as Fusobacterium and Escherichia. High fats weaken the epithelial bonds in the intestinal wall, leading to a condition known as "leaky gut". This dysfunction allows bacterial components and toxins to pass from the intestinal lumen into the bloodstream. It has also been observed that the absence of certain bacteria, such as *Akkermansia muciniphila*, which play a role in maintaining the intestinal lining, contributes to the exacerbation of this permeability. As a result of this disorder and intestinal permeability, the levels of internal toxins increase, the most important of which is lipopolysaccharide (LPS) found in the cell wall of Gram-negative bacteria. LPS is transmitted thru the gut-liver axis (GLA), leading to the activation of pro-inflammatory cytokines. Additionally, a high-fat diet leads to an increase in bacteria that produce endogenous ethanol and alters the metabolism of choline and bile acids, resulting in toxic compounds such as trimethylamine N-oxide (TMAO) (Vachher *et al.*, 2025).

Adherence to a meat-based diet was a dominant independent factor in predicting microbial composition and its expected functions. Many low-abundance phyla, including Synergistetes and

Desulfobacterota, have been enriched by this diet. Functional characterization revealed significant metabolic differences, including those related to amino acid degradation, vitamin B synthesis, energy metabolism, intestinal barrier integrity, and protein fermentation. This type of diet is also associated with increased cellular toxicity, inflammation, and constipation. Long-term adherence to a meat-based diet leads to distinctive taxonomic changes and profound functional alterations in gut microbiota (Karačić *et al*., 2026).

I.2.4. Pathogenic microorganisms

Deoxynivalenol (DON) is a mycotoxin produced by certain species of Fusarium, such as *Fusarium graminearum*, *Fusarium oxysporum*, and *Fusarium culmorum*, common in cereals such as wheat, maize, and barley. The toxin is characterized by its high stability, as it remains stable and does not easily degrade during food processing or due to environmental conditions, which allows it to readily enter the human and animal food chain. It acts by destroying the intestinal barrier, as it reduces tight junction proteins (such as ZO-1 and occludin) that protect the intestine, thereby increasing its permeability and disrupting the intestinal structure. It also alters the microbial composition, where bacteria such as Alloprevotella increases; these bacteria are capable of degrading the mucosal layer lining the intestine. This is followed by a decrease in beneficial bacteria such as *Akkermansia muciniphila* (from the phylum Verrucomicrobiota) at high doses, which is an essential species for maintaining the integrity of the intestinal wall (Jin *et al.*, 2026).

Norovirus infection in children induces a clear imbalance in the gut microbiota, characterized by an abnormal increase in alpha diversity indices and a shift in beta diversity, reflecting a disruption in the ecological stability of the intestine. Quantitatively, the study showed a marked increase in certain bacterial taxa, most notably Bacteroides uniformis, which increased more than threefold and was considered the most discriminative marker of infection (LDA > 4), in addition to *Veillonella sp*., *Carjivirus communis*, *Veillonella nakazawae*, and *Limosilactobacillus mucosae*. In contrast, a decrease was recorded in other taxa such as Bacteroidetes (at the phylum, class, and order levels) and Eubacterium. Mechanistically, the study suggests that the virus induces a metabolic reprogramming of the microbiota, manifested by activation of carbohydrate and lipid metabolism pathways, thereby altering the nutritional environment available to bacteria, either as an adaptive response of the host or as a mechanism favoring the virus to enhance its replication. While emphasizing that the results

show a statistical association and not definitive causation, as these changes may be a secondary consequence of the infection or a contributing factor to it (Wang *et al*., 2025).

Some studies have shown the effect of some bacteria (like *Salmonella enteritidis*) when it is in a state known as "viable but non-culturable" (VBNC) on the balance of the gut microbiome and on a model of colitis. This is a state in which bacteria, such as Salmonella, enter as an adaptive strategy to harsh environmental conditions, such as exposure to chlorinated disinfectants; the bacteria do not grow in conventional laboratory culture media, yet they remain alive, metabolically active, and capable of resuscitation and causing infection again. Salmonella in the VBNC state increased the severity of colitis, as evidenced by shortening of the colon length and the presence of clear pathological histological changes. A significant increase in the levels of pro-inflammatory cytokines in the serum was observed, such as (LPS, TNF-α, IL-6). VBNC bacteria also severely impaired intestinal barrier function, as they reduced the density of goblet cells, decreased the thickness of the mucus layer, and reduced the expression of proteins responsible for maintaining intestinal cell integrity (such as MUC2 and occludin).They also increased the ratio of Firmicutes to Bacteroidota, a ratio considered a pathological indicator of ulcerative colitis. A notable increase was observed in the abundance of pathogenic bacteria such as *Escherichia flexneri* and *Klebsiella pneumoniae*. Genetic analysis showed that VBNC bacteria possess a high abundance of genes related to flagellar assembly and bacterial secretion systems, indicating that they are still capable of producing harmful substances despite their apparent "dormancy" (Xiao *et al*., 2025).

I.3. Effects of gut microbiota on vital functions

I.3.1. Liver metabolism

Given that the liver predominantly derives its blood supply from the portal vein, it is uniquely susceptible to gut-derived factors. Specifically, the gut microbiota and the byproducts resulting from the fermentation of food by these microbes can readily reach and impact (fig. 3) the liver (Yi *et al*., 2026). Disturbance of the gut microbiota caused by a high-fat diet leads to the absorption of lipopolysaccharide (LPS) into the intestinal capillaries, and LPS mediates the development of metabolic inflammatory responses in multiple tissues of the body (Chen *et al*., 2025). Spirochaetes and Collinsella bacteria are directly associated with LPS levels and the inflammatory protein NF-κB in the liver. The microbial community can modulate the farnesoid x receptor (FXR) signaling pathway by altering the composition of bile acids. In addition, SSD (Saikosaponin D) can significantly reduce the gut microbiota associated with bile salt hydrolase (BSH) expression, such as Clostridium (Li *et al*., 2024).

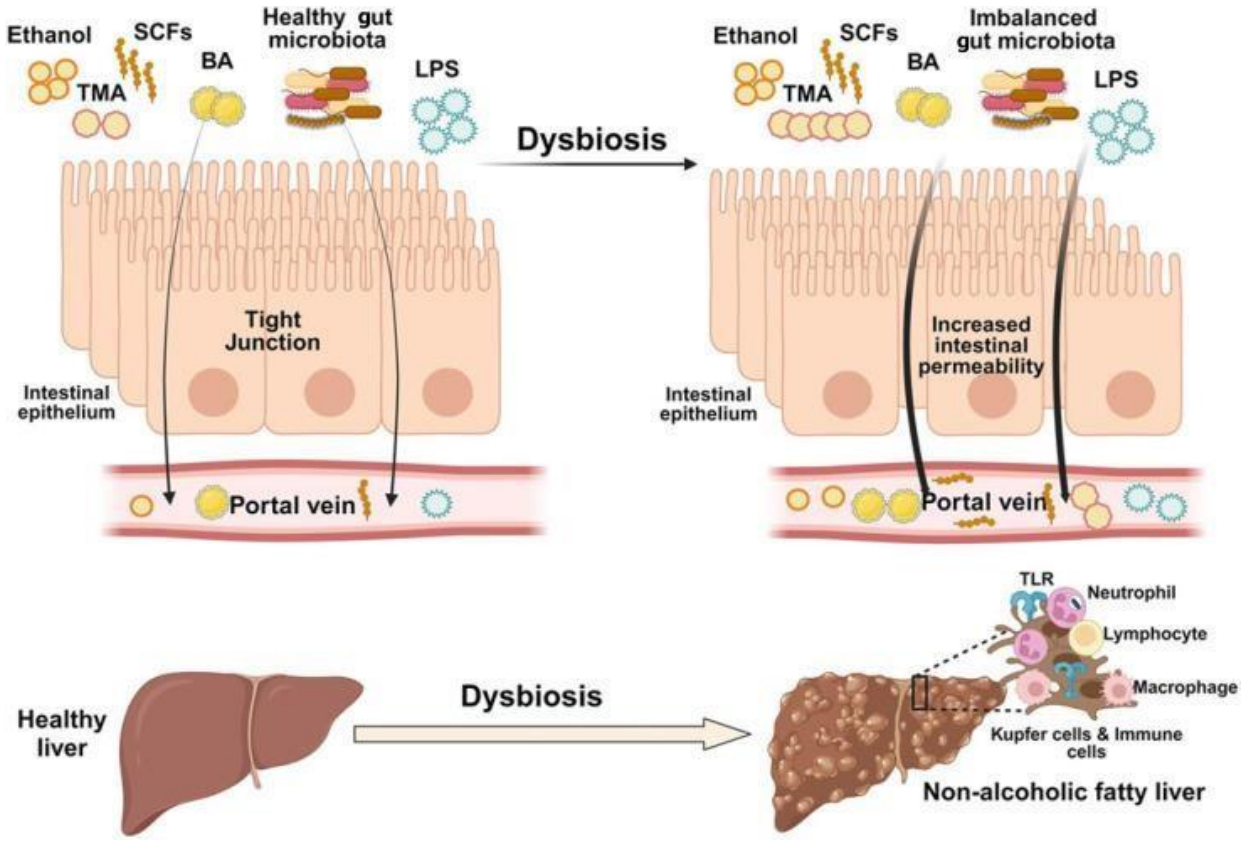

Figure 3 : Impact of gut microbiota dysbiosis on intestinal barrier dysfunction and non- alcoholic fatty liver disease (Yakut, 2025)

Moreover, Lachnospiraceae NK4A136 and Ruminococcaceae UCG-005 are among the bacteria associated with butyrate production, while sodium butyrate effectively alleviates hepatic steatosis by downregulating acetyl-COA carboxylase1 (ACC1), fatty acid synthase (FAS), and stearoyl-COA desaturase 1 (SCD1) and upregulating carnitine palmitoyltransferase 1A (CPT1A) *Limosilactobacillus reuteri* metabolizes tryptophan into indole-3-propionic acid (IPA), which activates aryl hedrocarbon receptor (AHR) receptors to protect the liver (Zhang *et al*., 2025; Chen *et al*., 2025). MAFLD mice gavaged with *Akkermansia muciniphila* exhibited reduced liver lipid accumulation and accelerated liver regeneration, possibly through the regulation of the tricarboxylic acid (TCA) cycle (Hu *et al*., 2024).

I.3.2. Cardiovascular system

Cardiovascular diseases (CVDs), including heart failure (HF), hypertension, myocardial infarction (MI), and atherosclerosis, are increasingly linked to gut microbiota dysbiosis and its metabolic byproducts (fig. 4). Dysbiosis contributes to systemic inflammation, vascular dysfunction, and disease progression through microbial-derived metabolites such as trimethylamine N-oxide (TMAO) and SCFAs. Certain bacteria such as Lachnoclostridium, Desulfovibrio, Clostridia, and Fusobacterium convert choline and carnitine (found in red meat and eggs) into a compound called

TMA, which is then converted in the liver into TMAO. There is growing evidence that gut dysbiosis is involved in HF progression through the disruption of homeostasis, increased intestinal permeability, and the induction of systemic inflammation. When there is an increase in bacteria such as Enterobacteriaceae, Proteobacteria, and Klebsiella, intestinal barrier permeability increases, allowing lipopolysaccharides (LPS) to enter the bloodstream. LPS binds to toll-like receptor 4 (TLR4) receptors, triggering a cascade of inflammatory cytokines (such as TNF-α and IL-6), which leads to endothelial dysfunction and increases the risk of myocardial infarction (MI) and heart failure. A marked reduction in beneficial short-chain fatty acid (SCFA)-producing bacteria, such as Roseburia, Faecalibacterium, and Akkermansia, leads to reduced SCFA production, resulting in loss of vascular protection and increased blood pressure due to impaired endothelial function (Trehan *et al*., 2024; Pfaffinger *et al*., 2025; Muttiah and Hanafiah, 2025; Epelde, 2025).

Recent research has shown that improving the balance of the gut microbiota plays a pivotal role in the prevention of heart and arterial diseases, as the microbiota affects heart health through multiple mechanisms including the production of beneficial metabolites and the modulation of the inflammatory response (Barathan and Hanafiah, 2025). A study has demonstrated that the bacterium *Bacteroides vulgatus* induces a significant improvement in cardiac function, as the researchers reported that administration of this bacterium to mice with heart failure improved their cardiac function and raised levels of short-chain fatty acids, particularly butyric acid. As for the molecular mechanism of this effect, the researchers clarified that *B. vulgatus* regulates the TGF-β1/MAPK pathway in the heart via butyric acid, thereby exerting anti-heart failure effects. Furthermore, the clinical importance of butyric acid was observed, as the same study reported that patients with lower levels of butyric acid had a marked increase in the occurrence of endpoint events (cardiac complications), compared to patients with higher levels (Zhang *et al*., 2025). A study also indicated that modulation of the microbiota through diet, probiotics, and pharmacological interventions holds potential therapeutic implications in the treatment of heart failure (Epelde, 2025). From a therapeutic perspective, a comprehensive review confirmed that dietary changes, probiotics, and prebiotics have shown promise in modulating the gut microbiota and reducing risk factors for cardiovascular disease (Trehan *et al*., 2024).

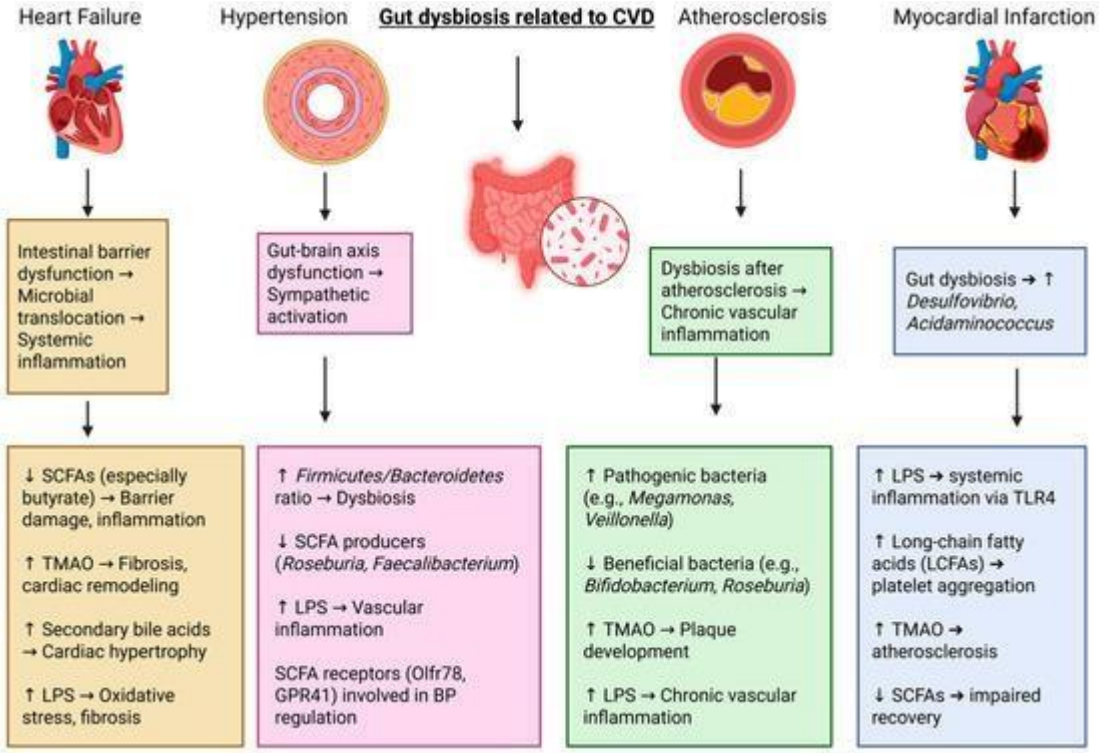

Figure 4 : Gut dysbiosis and cardiovascular diseases (Muttiah and Hanafiah, 2025)

I.3.3. Nervous system

Alzheimer's disease (AD) is strongly associated with gut microbiota dysbiosis, which leads to increased intestinal permeability and the translocation of bacterial toxins such as lipopolysaccharide (LPS) into the bloodstream. This process promotes neuroinflammation and enhances amyloid plaque deposition in the brain. Patients with AD commonly exhibit an increased abundance of pro-inflammatory bacteria such as Escherichia/Shigella and a reduced abundance of anti-inflammatory bacteria including Faecalibacterium and Eubacterium. In addition, elevated levels of trimethylamine N-oxide (TMAO) have been associated with disease progression and cognitive decline (Chen *et al.*, 2025; Carmazzo and Fanos, 2025; Li *et al.*, 2025).

Parkinson's disease (PD) is one of the neurological disorders most closely linked to the microbiota–gut–brain axis (fig. 5). Misfolded α-synuclein is believed to originate in the gut and subsequently spread to the brain through the vagus nerve. PD is characterized by a depletion of SCFA-producing bacteria such as Prevotellaceae and an increased abundance of Akkermansia and Enterobacteriaceae, which contribute to intestinal inflammation and impairment of the gut barrier. Moreover, certain bacteria such as *Enterococcus faecalis* can metabolize levodopa in the intestine, thereby reducing its therapeutic efficacy (Chen *et al.*, 2025; Radford-Smith *et al.*, 2025).

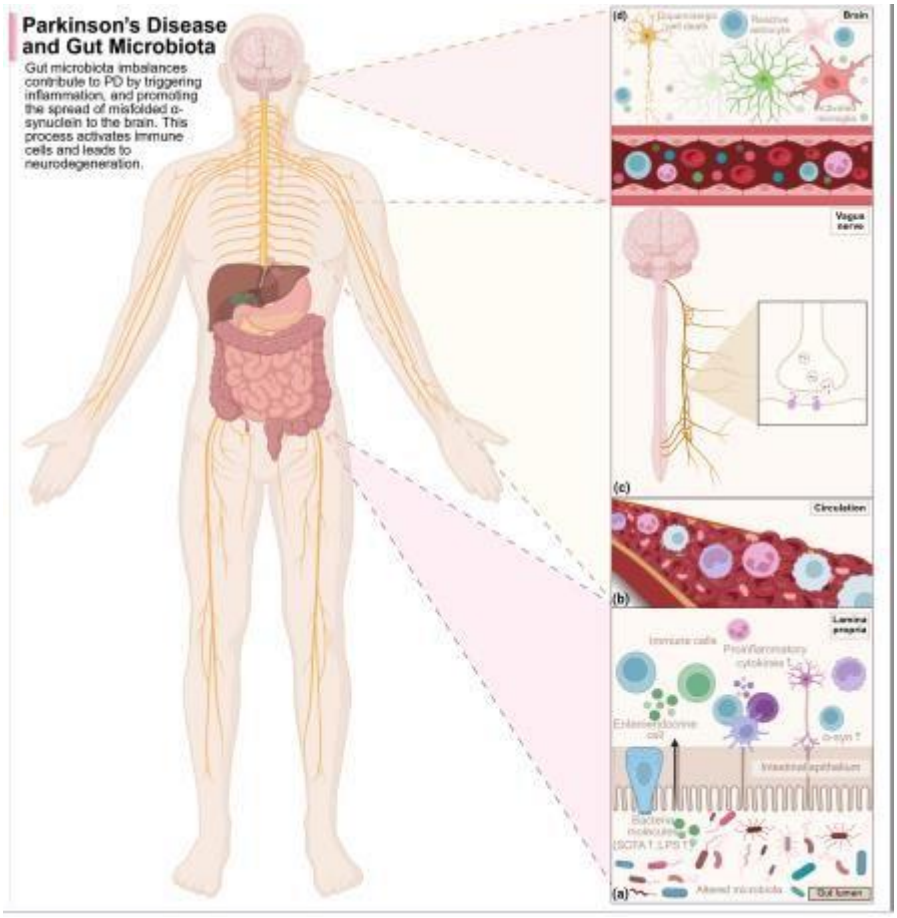

Figure 5 : Parkinson's disease and gut microbiota (Yassin *et al*., 2025)

Multiple sclerosis (MS) is associated with immune dysregulation induced by alterations in gut microbiota composition. Certain intestinal bacteria stimulate pro-inflammatory Th17 cells, which migrate to the central nervous system and attack the myelin sheath. Increased levels of Akkermansia and Methanobrevibacter alongside reduced butyrate-producing bacteria such as Faecalibacterium and Butyricimonas have been reported in MS patients, contributing to neuroinflammation and disease progression (Chen *et al*., 2025; Alshinawy *et al*., 2025; Doms *et al*., 2025; Mohsen *et al*., 2025).

Gut microbiota dysbiosis contributes to amyotrophic lateral sclerosis (ALS) a neurodegenerative disease ,through metabolic disturbances and reduced production of neuroprotective compounds. Decreased abundances of Roseburia and Faecalibacterium have been observed, whereas *Akkermansia muciniphila* appears to exert beneficial effects by producing nicotinamide (vitamin B3), which may protect neurons and slow disease progression (Wright *et al*., 2018; Chen *et al*., 2025; Chakraborty *et al*., 2026).

Major depressive disorder is linked to dysfunction of the gut–brain axis, leading to altered tryptophan metabolism and a shift toward the neurotoxic kynurenine pathway instead of serotonin synthesis. Reduced levels of SCFA-producing bacteria such as Faecalibacterium and Coprococcus

contribute to increased neuroinflammation and mood disturbances, while elevated levels of inflammatory bacteria such as Proteobacteria have also been reported (Halabitska *et al*., 2024; Nayak *et al*., 2025; Eskandar, 2025; Yu *et al*., 2026).

Schizophrenia is associated with significant alterations in gut microbiota composition that contribute to systemic inflammation and neurotransmitter imbalance. Increased abundances of Prevotella and Enterobacteriaceae have been documented, together with disruption of blood–brain barrier integrity and enhanced immune activation, which may contribute to the development of neurological and psychiatric symptoms (Wei *et al*., 2024; Li *et al*., 2024; Zajkowska *et al*., 2024; Eskandar, 2025).

Chronic fatigue syndrome is associated with increased intestinal permeability and reduced butyrate production, allowing bacterial endotoxins to enter the circulation and trigger systemic immune activation. Patients commonly exhibit increased levels of Enterobacteriaceae and Paraprevotella along with reduced abundances of Faecalibacterium and Ruminococcaceae, contributing to chronic fatigue and cognitive impairment (Wang *et al*., 2023; Yassin *et al*., 2025).

Stroke induces rapid alterations in gut microbiota composition, resulting in the migration of pro-inflammatory immune cells from the intestine to the brain, thereby exacerbating neurological injury. Gut-derived bacteria may also translocate to the lungs and contribute to post-stroke infections. Microbial changes associated with stroke include increased abundances of Enterobacter and Desulfovibrio and decreased levels of beneficial Bacteroides species (Yassin *et al*., 2025; Chen *et al*., 2025).

The gut microbiota plays a positive and pivotal role in improving nervous system functions through multiple mechanisms. It is essential for microglia maturation through the production of short-chain fatty acids (SCFAs), as its absence leads to developmental defects in these cells (Radford-Smith *et al*., 2025; Yu *et al*., 2026). SCFAs, particularly butyrate, enhance blood-brain barrier (BBB) integrity by increasing the expression of tight junction proteins, thereby preventing inflammatory molecules from entering the brain (Radford-Smith *et al*., 2025; Yu *et al*., 2026). Moreover, the microbiota contributes to the production and regulation of major neurotransmitters such as serotonin (via Clostridia) and GABA (via Bacteroides), positively affecting mood and cognitive function (Yu *et al*., 2026). By maintaining intestinal barrier integrity and reducing inflammation, healthy microbiota prevents excessive activation of the kynurenine pathway, shifting tryptophan metabolism toward serotonin production and protecting against neurotoxicity (Carmazzo and Fanos, 2024). SCFAs also cross the blood-brain barrier and stimulate the expression of BDNF, enhancing neuroplasticity, learning, and memory (Carmazzo and Fanos, 2024; Yu *et al*., 2026). In addition,

SCFA-producing microbiota (e.g., Akkermansia and Bifidobacterium) are associated with a reduced risk of neurodegenerative diseases such as Alzheimer's, while Parkinson's disease studies have shown that the presence of microbiota is necessary for disease development, and its modulation can improve outcomes (Carmazzo and Fanos, 2024; Li *et al*., 2025). Furthermore, SCFAs promote regulatory T cell (Treg) differentiation and inhibit the NF-κB pathway, reducing pro-inflammatory cytokine production and alleviating neuroinflammation. Finally, probiotics (e.g., *Lactobacillus rhamnosus*) have been shown to reduce depressive- and anxiety-like behaviors through regulation of GABA receptors in the brain and via the vagus nerve (Yu *et al*., 2026).

CHAPTER II

Polysaccharides' effects on gut microbiota

This chapter presents several generalities about polysaccharides and their effects on gut microbiota.

II.1. Polysaccharides

Sugars are the most stereochemically complex family of biomolecules and, as pyranose rings, have clear conformational preferences (Agirre *et al*., 2017; Dharanie, 2024).

II.1.1. Generalities about carbohydrates

Carbohydrates are chemically defined as polyhydroxy aldehyde or ketone molecules, or their derivatives. They are usually followed by the general chemical formula $(CH_2O)n$. They are the main source of energy in human diet, and one of the most abundant ingredients in cereals, fruits, vegetables and legumes (Stylianopoulos, 2013; Stribling and Ibrahim, 2023; Wang, *et al.*, 2025).

Carbohydrates are classified based on several criteria. According to the chemical composition, carbohydrates can be monosaccharides, disaccharides, oligosaccharides or polysaccharides. Monosaccharides are the simplest forms of carbohydrates that cannot be hydrolyzed into smaller units, the most important of which are "hexose" (such as glucose and fructose) and "pentose" (such as ribose). Disaccharides consist of two units of monosaccharides associated with glycosidic bonds, such as sucrose, lactose and maltose. Oligosaccharides are formed by chains consisting of 3 to 9 units of monosaccharides, widely found in plants. Polysaccharides are made of long chains consisting of 10 or more units (up to thousands), such as starch, glycogen and cellulose (Stylianopoulos, 2013; Liu et al., 2023).

According to molecular weight, carbohydrates have low molecular weight (LMW), such as low sugars and inulin, or high molecular weight (HMW), like non-starchy polysaccharides (NSP) and resistant starch. Furthermore, carbohydrates can be digestible such as starch and simple sugars absorbed by the body, or indigestible (dietary fiber). The indigestible carbohydrates are plant components that resist digestion in the small intestine and reach the colon to be fermented by intestinal microbiota (Stribling and Ibrahim, 2023).

Carbohydrates play vital and crucial roles in living organisms. They are the main source of energy; glucose is used as a primary cellular fuel, and the surplus is stored in the form of starch in plants or glycogen in animals. They intervene in the structure of cellular walls (such as cellulose, pectin and chitin) and form the backbone of nucleic acids (ribose and deoxyribose). In addition, they

are actively involved in the processes of immunological recognition and recognition between "self and non-self" cells, and proteins known as "lectins" act as readers of this "glycatic encryption" on cell surfaces. Moreover, they modify the structure and functions of biomolecules like proteins and lipids, affecting their folding, location and function within the cell. Furthermore, dietary fibers maintain the health and movement of the colon, and help reduce cholesterol and regulate sugar levels (Naithani *et al*., 2021).

II.1.2. General properties of polysaccharides

Some studies have defined polysaccharides as macromolecules with a high molecular weight, characterized by structural complexity and high flexibility, and are considered bioactive components in many natural sources such as plants and algae. Polysaccharides consist of a complex combination of sugar and non-sugar components. The sugar components are monosaccharidic units that consist of various types, the most abundant of which are glucose (Glc), rhamnose (Rha), arabinose (Ara), and galactose (Gal). They also contain uronic acids such as galactoronic acid and D-glucuronic acid. Polysaccharides can be linked to non-glycan components like proteins (up to 38%) via covalent bonds (N- or O-covalent bonds). They also include inorganic important elements such as iron, magnesium, zinc, and selenium (Blue *et al*., 2024; Huang *et al*., 2025).

The vital functions of polysaccharides depend heavily on the way their molecules are organized with types of covalent bonds. The sugar units are connected to each other via oxygen glycosidic bonds by multiple binding methods, such as (1 → 2), (1 → 3), (1 → 4), or (1 → 6). Moreover, branching is characterized by a structure consisting of a main chain (Backbone) connected to side chains or branches, which leads to a huge diversity in the forms of polysaccharides molecules. Also, polysaccharides have a broad molecular weight usually between 1.2 kD and 3900kD, which is affected by the source and the extraction method (Aiman *et al*., 2021; Huang *et al*, 2025).

Polysaccharides are among the most complex and diverse biomolecules in nature, as their functional identity is determined by a set of properties. In terms, monosaccharide units are associated with various glycosidic bonds; The determination of the geometric shape of chains, whether solid linear structures or flexible branching networks, is due to the different patterns of these bonds. This structural arrangement directly affects the molecular weight of these polymers. Solubility also plays a pivotal role in biological reactions, as it is strongly affected by the degree of structural branching and the presence of polar or charged functional groups, such as sulfate groups common in animal

sources, which increase the molecule's interaction with water and facilitate its interaction with the cellular environment (Tang *et al*., 2022).

II.1.3. Role of polysaccharides

Studies have shown that polysaccharides have an important role in reducing the inflammatory response. These compounds show remarkable abilities in modifying immune processes, acting as antioxidants by eliminating free radicals, and suppressing excessive inflammatory pathways. Thus, it contributes to enhancing the normal state of health and maintaining the dynamic balance of the body. They also work to repair and strengthen the intestinal barrier and maintain the integrity of the intestinal wall by relieving mucosal damage and promoting damaged tissue repair. They also stimulate the secretion of myosin from goblet cells, which protects the surface of the intestine, and increase the expression of tightly binding proteins, necessary to prevent harmful intestinal permeability. Polysaccharides also act as a catalyst for beneficial bacteria by increasing the abundance of beneficial bacteria such as Lactobacilli, Firmicutes, and Allobaculum. In addition, they help reduce harmful bacteria associated with digestive disorders, such as bacteroides. Polysaccharides also affect the chemical pathways in the body, especially in regulating the biosynthesis of primary bile acids, which contributes to the protection of the colon. Moreover, they help regulate the pathways of amino acid metabolism and protein absorption (Samee *et al*., 2019; Tang *et al*., 2022; Wang *et al*., 2025).

II.1.4. Classification of polysaccharides

From a functional standpoint, polysaccharides are classified based on their biological roles, which are intrinsically linked to the metabolic and structural needs of the organism. They are primarily divided into two major functional classes; storage polysaccharides and structural polysaccharides (Wang *et al*., 2026).

Starch is one of the most important types of stored polysaccharides (fig. 6). It is a natural polysaccharide and the primary source of energy in plants. Starch is widely recognized as an important biomolecule in numerous food and nutritional applications. It consists of two types of glucose polymers; amylose, which forms linear chains, and amylopectin, which has a branched structure. Its role is evident in encapsulating biologically active compounds, protecting them and

releasing them in a controlled manner. Starch nanoparticles can also stabilize emulsions for extended periods. Starch continues to be widely used in many food applications (Zhu, 2023; Wang *et al.*, 2026).

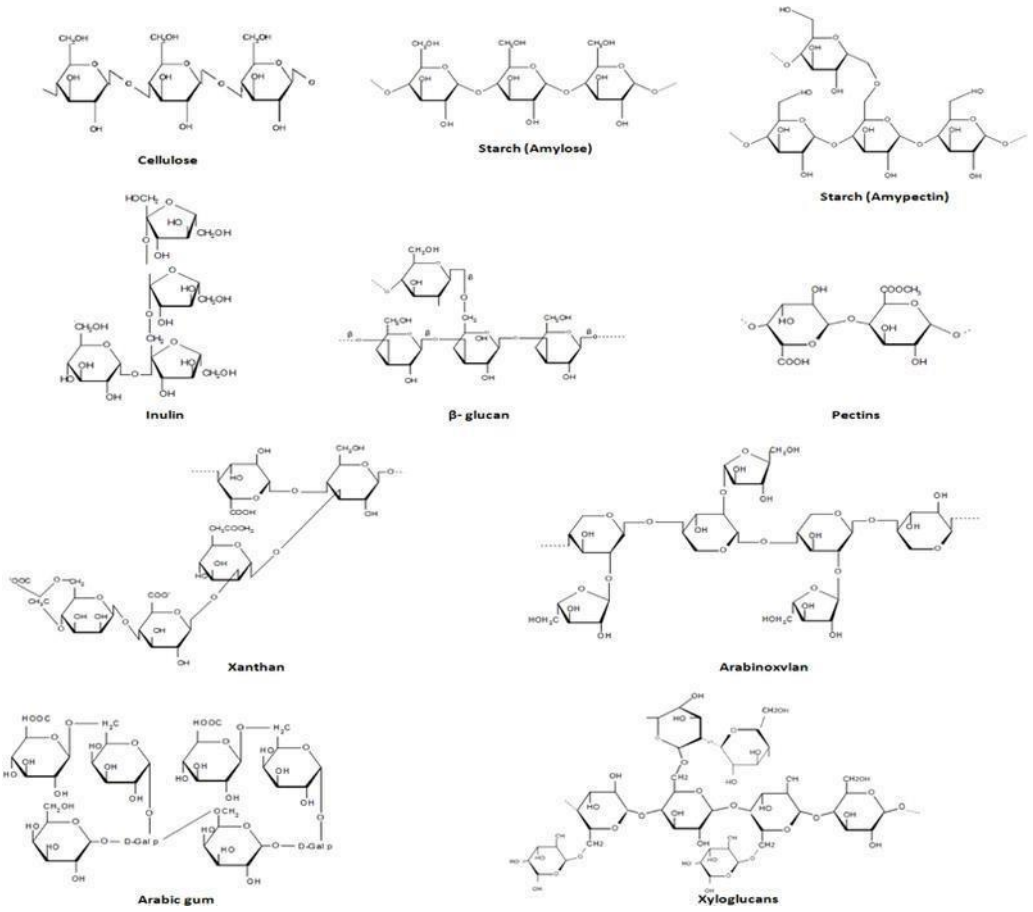

Figure 6: Chemical structures of major dietary polysaccharides (Ahmdi *et al*., 2018)

Cellulose forms the basic structural unit with which plants build their cell walls, giving them hardness and the ability to maintain their shape. Based on this role it plays in living organisms, cellulose is classified as a polysaccharide with a structural function. At the molecular level, cellulose consists of long, unbranched chains composed of glucose molecules linked to each other by special bonds called β (1→4) glycosidic bonds. This type of binding gives the chains a regular and solid arrangement, which explains the durability of the cellulose fibers and their resistance to decomposition (Pastrana-Alta *et al*., 2025). Its biological role is that it maintains the integrity of parenchyma cells and their survival intact even after cooking processes such as frying or boiling. It also supports the health of the digestive system; its presence prevents the occurrence of "dysbiosis" caused by poor fiber meals. Through its structural properties, it contributes to determining the

permeability of the cell wall, allowing the passage of certain molecules (such as small starch hydrolysis products like "maltose") and preventing other larger molecules. This helps in achieving a sustainable and moderate glucose profile in the blood (Gómez-Maqueo *et al.,* 2023).

Polysaccharides are classified by source into plant, animal, and microbial types.

II.1.4.1. Plant polysaccharides

This includes all sugars extracted from plants, such as *Gastrodia elata* polysaccharide (GEP), sesame seed polysaccharides (Ssps), and tea polysaccharides.

Gastrodia elata polysaccharide (GEP) is the main polysaccharide extracted from the tubers of the *Gastrodia elata* plant, a medicinal plant belonging to the orchidaceae family. It is considered one of the main bioactive components contributing to the plant's pharmacological activity, responsible for most of its pharmacological effects. It is characterized by a large molecular structure (macromolecule) that contributes to its biological activities, such as protection of nerve cells, reduction of oxidative stress and modulation of cellular signaling mechanism that helps regulate the body's antioxidant response (Wen *et al*., 2025).

Sesame seed polysaccharides are polysaccharides extracted from sesame seed pulp. After purification, five fractions can be obtained (fractions) named SMP-1, SMP-2, SMP-3, SMP-4, and SMP-5. The SMP-2 fraction was dominant in terms of yield at 2.12%, consisting mainly of arabinose, galactose, and rhamnose with the presence of uronic acids in different proportions, SMP-2 was the richest. FTIR, GC-MS, and NMR analysis showed that SMP-2 consists mainly of a linear chain of α-L-arabinofuranose units linked by (1→5) bonds with galactose-rich side chains. High antioxidant activity was confirmed by DPPH, •OH, and DMPD+ tests (Cai *et al*., 2025).

Tea polysaccharides (TPS) are an important bioactive component in the tea plant *Camellia sinensis*. Its percentage ranges, depending on the type of tea and the method of processing, between 0.14% and 10.73%. It consists of complex carbohydrate molecules with a high molecular weight ranging from 1.2KDa and 3900 KDa. It is characterized by neutral monosaccharides that include: glucose, galactose, arabinose, rhamnose, mannose, ribose, xylose rhamnose, and Fucose, in addition to uronic acids (galacturonic acid and glucuronic acid). The partial structure characterized by the presence of branched chains and contains multi-pattern glycoside bonds such as: (1→2), (1→3), (1→4), and (1→6). This diversity results in a wide range of structural variations. The structure has characteristic properties such as antioxidant, anti-inflammatory, immunomodulatory and

improvement of metabolic disorders. A large part of its effects is related to its ability to modify thestructure and functions of intestinal microbiota by stimulation of beneficial metabolites production (Wu *et al*., 2023).

II.1.4.2. Animal polysaccharides

These are all polysaccharides derived from animal sources; such as chitosan and fucosylated chondroitin sulfate (FCS).

Chitosan is an animal-derived polysaccharide, primarily extracted by the removal of the acetyl group from chitin. Chitin is a structural polymer found in the exoskeletons of marine crustaceans. Chitosan oligosaccharide (COS) has a lower molecular weight than conventional chitosan and is highly soluble in water. These properties enhance its bioavailability within the digestive tract. COS acts as a potent immunomodulator. This regulation is essential for maintaining the integrity of the intestinal mucosa barrier and preventing abnormal inflammatory responses. It also acts selectively as a prebiotic, promoting the growth of beneficial bacteria such as Lactobacillus. It contributes to the modulation of the gut microbiota (Wen *et al*., 2024; Pastrana-Alta *et al*., 2026).

Fucosylated chondroitin sulfate (FCS) is a polysulfur polysaccharide (sulfur aminoglycan polysaccharide). It is derived mainly from marine invertebrates such as *Holothuria tubulosa* and *Sarcotragus spinosulus*. The basic structure consists of repeated units of N-acetylgalactosamine (GalNAc) and glucuronic acid, characterized by the presence of different side branches and fucoses according to the source. It contains complex and branched glycoside bonds that determine their vital properties. Its biological role is manifested in promoting the growth of endothelial cells. It strengthens the intestinal barrier by increasing tight-binding proteins. It also regulates the immune response by stimulating pro-inflammatory cytokines (IL-10 and IL-12B). It reduces inflammatory factors such as calprotectin. Furthermore, it protects tissues and reduces intestinal lesions caused by harmful bacteria (Obino *et al*., 2025).

II.1.4.3. Microbial polysaccharides

Microorganisms are considered one of the most important modern natural sources for extracting polysaccharides; some examples include exopolysaccharides (EPSs) from *Enterococcus faecium* and *Streptococcus thermophilus,* and polysaccharides from *Ganoderma Parvulum*. Exopolysaccharides are carbohydrate polymers produced by microbes. They can be closely related to the cell surface or secreted in the surrounding environment. EPSs derived from *Enterococcus faecium*

(EPS-LB13) and *Streptococcus thermophilus* (EPS-MLB10) have been obtained from traditional dairy products. It consists of basic monosaccharides such as glucose, galactose, and mannose. The composition of EPS-LB13 and EPS-MLB10 varies depending on the source of the bacteria. They enhance cellular adhesion and act as prebiotics used selectively by beneficial microbes in the intestine, which supports its growth and reduce pathogenic bacteria. They contribute to the modification of the composition and function of the intestinal microbiota by stimulating the production of Short-Chain Fatty Acids (SCFAs), acetate, propionate, and butyrate (Tarique *et al*., 2024).

Ganoderma parvolum polysaccharides are potent biopolymers. They are classified as fungal polysaccharides, specifically within the β-glucan family. The biological activity of this purified compound is attributed to its sugar structure. It plays a key role in activating macrophages and converting them into the tumor-fighting type (M1). It stimulates the release of nitric oxide (NO) and tumor necrosis factor-alpha (TNF-α). It is readily absorbed into the bloodstream without any toxic effects on the intestines, liver, or kidneys. It enhances the overall immune response against health risks (Contreras-Ramirez *et al*., 2025).

II.2. Microbial fermentation of dietary polysaccharides

The human gastrointestinal tract hosts a complex community of over 10^{13} microorganisms, forming a symbiotic "superorganism" essential for health. In a normal physiological state, the gut microbiota (MB) is dominated by four primary phyla: Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria, which account for over 90% of the total population. Since the human host lacks the enzymes to degrade complex polysaccharides (PS), these compounds reach the colon to be selectively fermented by specialized anaerobic genera like Bacteroides and Bifidobacterium. This interaction (fig. 7) provides a vital energy source for beneficial bacteria, maintaining intestinal homeostasis and preventing the growth of pathogens. Scientific evidence indicates that a sophisticated enzymatic hierarchy mediates the interaction between dietary polysaccharides (PS) and the gut microbiota (MB). At the molecular level, data analysis reveals that the initial degradation of PS is strictly dependent on the expression of microbial Carbohydrate-Active Enzymes (CAZymes), specifically glycoside hydrolases (GHs) and polysaccharide lyases (PLs). These enzymes demonstrate high specificity for

glycosidic linkages within the PS structural backbone (Glowacki and Martens, 2021; Das *et al*., 2026).

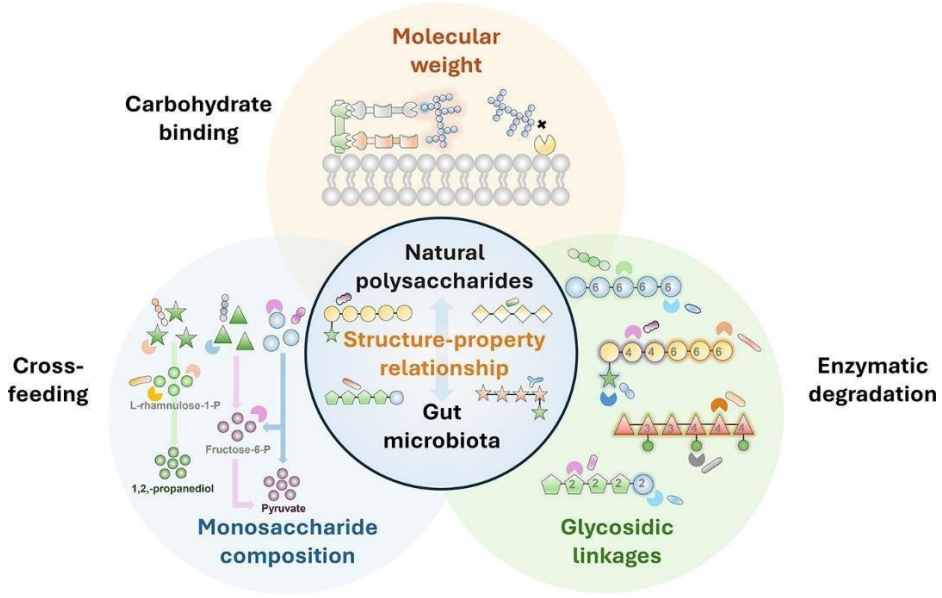

Figure 7 : Polysaccharides-gut microbiota interactions (Keung *et al.*, 2025)

Furthermore, studies outcomes highlight "metabolic cross-feeding" as a pivotal mechanism where primary degraders, such as Bacteroides, facilitate the breakdown of complex glycans into substrates for secondary fermenters. This metabolic flux converges through the glycolytic and pentose phosphate pathways, leading to a significant accumulation of short-chain fatty acids (SCFAs). Mechanistically, butyrate provides essential energy for colonocytes via β-oxidation, while propionate and acetate serve as systemic modulators of gluconeogenesis and lipogenesis through G-protein-coupled receptors (GPCRs). Additionally, PS structural analogs are shown to maintain intestinal homeostasis by competitively inhibiting pathogen adherence via receptor mimicry (Zhang *et al*., 2024).

Gut microbiota metabolites are primarily noted by Short-Chain Fatty Acids (SCFAs), with a notable emphasis on butyrate (fig. 8). Under normal physiological conditions, these metabolites function beyond mere energy substrates; they act as vital regulatory signaling molecules that maintain intestinal homeostasis and fortify the integrity of the mucosal barrier. Furthermore, empirical data demonstrate that these fermentation products modulate gene expression and metabolic enzyme activities, thereby regulating energy absorption, intestinal motility, and local immune responses,

which collectively safeguards the host against systemic metabolic dysregulation (Guan *et al*., 2024; Nambidi *et al*., 2025).

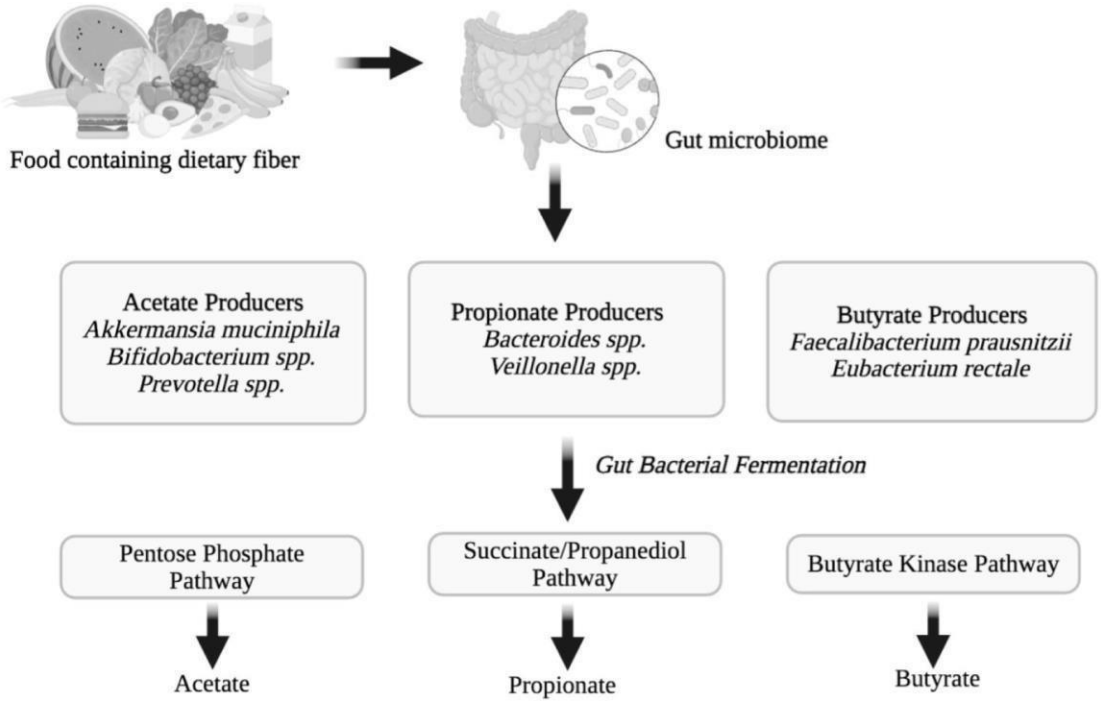

Figure 8 : Production of SCFA from dietary fiber (Nambidi *et al*., 2025)

Structural properties of seaweed polysaccharides highlight their role as essential carbon sources and metabolic substrates, such as red seaweed polysaccharides (RSPs), brown seaweed polysaccharides (BSPs) and green seaweed polysaccharides (GSPs). Due to their complex glycosidic linkages and high molecular weight, these polysaccharides remain recalcitrant to host digestive enzymes in the upper gastrointestinal tract. Consequently, they reach the large intestine intact, where they serve as a primary nutritional substrate for specific fermentative bacteria, functioning as non-digestible prebiotics. The pooled evidence indicates that these compounds induce fundamental changes in the microbial composition of the colon. The fermentation of these polysaccharides by the gut microbiota establishes a direct correlation with improved host physiological biomarkers (Deniz *et al*., 2025).

A significant increase in the production of short-chain fatty acids (SCFAs) was recorded following the administration of the RSP Agars, which effectively inhibited the growth of opportunistic pathogens such as Escherichia. Regarding metabolic management, the findings confirm

that Carrageenan (specifically kappa-type) contributes to reducing the Firmicutes/Bacteroidetes ratio—a key biomarker associated with obesity reduction—through the selective stimulation of Akkermansia. Furthermore, studies have validated the role of Porphyran in promoting butyrate-producing bacteria like Roseburia, thereby maintaining colonic mucosal integrity (Zang *et al*., 2023).

BSPs indicate high efficacy in modulating metabolic pathways. Studies investigating Fucoidan reported a significant rise in the abundance of *Akkermansia muciniphila* and Alloprevotella, which clinically correlated with reduced insulin resistance and hepatoprotection. In the context of intestinal barrier enhancement, Alginate Oligosaccharides (AOS) demonstrated the ability to stimulate Lactobacillus and Bifidobacterium, leading to an up-regulation of tight junction proteins. Additionally, Laminaran effectively reduces pathogenic load while improving the morphological structure of intestinal villi (Yang *et al*., 2022).

Moreover, ulvan (type of GSPs) possesses unique properties in supporting gut homeostasis. The results proved its capacity to enhance *Faecalibacterium prausnitzii*. This microbial modulation consistently led to increased activity of antioxidant enzymes (SOD and CAT) and a reduction in pro-inflammatory cytokines, providing systemic protection against oxidative stress and intestinal inflammation (Karagöz *et al*., 2025).

Plant fibers, particularly cellulose, act as major substrates for the growth of beneficial bacteria in the intestines of humans and animals. Certain bacterial genera, such as Ruminococcus and Fibrobacter, degrade cellulose through a fermentation process in the large intestine. These bacteria play pivotal roles beyond digestion, including the degradation of complex carbohydrates, as they secrete specialized enzymes such as cellulases or form complex enzymatic assemblies known as cellulosomes to break down the plant cell wall. Cellulose degradation results in the production of short-chain fatty acids, which represent an important source of energy and contribute directly to intestinal nutrition and health. These bacteria also play a major role in maintaining gut microbiota balance and the stability of the intestinal environment. They have been observed to be abundant in rural and hunter-gatherer populations, whereas they are scarce in industrialized societies due to differences in lifestyle and dietary patterns, which may reduce the ability of urban populations to digest dietary fibers (Froidurot and Julliand, 2022).

Pectin is a complex heteropolysaccharide found in plant cell walls and is rich in galacturonic acid. The importance of this compound lies in the inability of human enzymes to digest it, allowing it to reach the large intestine (colon) in a nearly intact form. A specific group of bacteria, known as

pectin-degrading microorganisms, possess the enzymes required to break down its complex structure, mainly genera from the phylum Bacteroidetes such as Bacteroides, and genera from the phylum Firmicutes such as Clostridium, Eubacterium, Faecalibacterium, and Monoglobus. Once bacteria degrade pectin into monosaccharides, the anaerobic fermentation process begins, leading to the production of short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate. Pectin acts as a selective modulator of the gut microbiota, promoting the growth of beneficial bacteria and contributing to the balance of microbial communities, including Lactobacillus and Bifidobacterium. The gut microbiota does not interact with all types of pectin in the same manner; this relationship is influenced by the structural characteristics of pectin. Low-molecular-weight pectin produces higher levels of short-chain fatty acids compared to high-molecular-weight forms. In addition, the degree of methyl esterification and the presence of sugar side chains affect the anti-inflammatory activity and the manner in which bacteria utilize these fibers (Elshahed *et al*., 2021).

β-glucans are glucose polymers found in the cell walls of yeast, fungi, and cereals such as oats and barley. These polysaccharides reach the colon in a largely intact form, as they are classified as non-digestible carbohydrates by the human body. The gut microbiota enzymatically degrades these sugars to obtain energy, while these compounds also function as prebiotics by modulating the composition of the microbiota in favor of the growth of beneficial bacteria, such as members of the phyla Bacteroidetes and Firmicutes. They also help maintain microbial balance through the selective enrichment of commensal microorganisms and the inhibition of pathogens such as *Enterococcus spp.* and *Escherichia coli*. Through the fermentation process carried out by bacteria such as Bacteroidetes and Firmicutes, important metabolic products such as short-chain fatty acids are produced, which play a crucial role in regulating metabolic pathways and systemic inflammation. These metabolites contribute to supporting intestinal barrier function, thereby helping to exclude pathogens. They also contribute to obesity management through appetite regulation and exert hypoglycemic effects, making them beneficial in the management of type 2 diabetes (Jayachandran *et al*., 2018; Edo *et al*., 2025).

II.3. Relationship between gut microbiota dysbiosis and polysaccharides

In recent years, it has become evident that the relationship between polysaccharides and the gut microbiota is a complex, interactive one that directly affects human health. Polysaccharides that are indigestible by human enzymes reach the colon, where they serve as a nutritional substrate for the microbiota, thereby altering its composition and functions (Porter *et al*., 2017). These molecules stimulate the growth of beneficial bacteria and contribute to increased production of short-chain fatty

acids (SCFAs), which play an important role in regulating inflammation and energy metabolism (Xue *et al*., 2025). Furthermore, the effects of polysaccharides depend on their chemical structure, including molecular weight, the type of glycosidic linkages, and monosaccharide composition, which determines the specific types of microbiota capable of breaking down and utilizing them (Zhang *et al*., 2026). Conversely, microbial dysbiosis resulting from dietary changes or environmental factors disrupts these interactions, which is associated with diseases such as obesity, diabetes, and inflammatory bowel diseases (Xue *et al*., 2025). Additionally, some polysaccharides act as prebiotics and contribute to reshaping the microbiota toward a healthy state, whereas their disruption may lead to an increase in harmful products such as lipopolysaccharides (LPS), which promote chronic inflammation (Zhang *et al.,* 2022). Thus, the polysaccharide–microbiota axis represents a sensitive biological system, where its balance leads to the maintenance of healthy homeostasis, while its disruption causes multiple pathological effects involving the gastrointestinal, metabolic, and immune systems (Huang *et al*., 2025).

18 studies were collected as examples of the effect of natural polysaccharides in dextran sodium sulfate (DSS)-induced ulcerative colitis (UC) models (tab.1).

The study no.1 by Sun et al. (2026) used the red rice seed coat extract, which is characterized by its richness in insoluble fibers (cellulose and hemicellulose) and structurally associated phenolic compounds. This extract reduced the Disease Activity Index (DAI) and increased colon length, with a marked decrease in inflammatory cytokines (TNF-α, IL-6, and IL-1β) and myeloperoxidase (MPO) enzyme and improved intestinal barrier function through regulation of tight junction proteins and reduction of MMP9. It also reduced oxidative stress marker MDA and increased SOD. At the microbiota level, the researchers observed an increase in the Shannon index (microbial diversity), an increase in Enterorhabdus, and a decrease in Staphylococcus.

The study no.2 by Yang et al. (2026) focused on polysaccharides derived from the red seaweed Bangia fusco-purpurea (BFP). BFP is characterized by its presence in the algal cell wall, consisting primarily of galactose (Gal) and 3,6-anhydrogalactose with a certain proportion of sulfate groups (sulfated groups). This sulfated structure makes it similar to agar. BFP demonstrated an ability to reduce inflammation by lowering TNF-α and IL-22, with a unique modulation of the microbiota characterized by a decrease in Bacteroides and Prevotella and an increase in Lachnoclostridium and Staphylococcus, indicating a selective effect on specific bacterial strains.

Table 1: Examples of polysaccharides Effects from different sources on DSS -induced ulcerative colitis models

No.	Reference	Animal	Intervention	Outcomes
1	Sun *et al.*, 2026	mice C57BL/6J	Red Rice Seed Coat Extract	Physical and Clinical :Body weight ↑, Colonic length ↑ , DAI ↓ Oxidative Stress : MDA ↓ , SOD ↑ Intestinal Barrier : D-Lactate ↓, Mucin and Goblet cells ↑, MMP9 ↓ Inflammatory Cytokines and Proteins: TNF-α ↓ ,IL-6↓ , IL-1β↓ ,MPO↓ CCR5 ↓, NFκB↓ , PTGS2↓ , NO↓, NOS2 ↓ Gut Microbiota : Shannon index↑ , Enterorhabdus↑ Staphylococcus↓
2	Yang *et al.*, 2026	mice BALB/c	*Bangnia Fusco-purpurea* polysaccharide (BFP)	Physical and Clinical :DAI ↓ , Colon length ↑ Inflammatory Cytokines and Proteins: TNF- α ↓,IL-22 ↓ Gut Microbiota : Arachidonic acid ↓ , Bacteroides ↓ Prevotella ↓ , Staphylococcus ↑ , Lachnoclostridium↑
3	Li *et al.*, 2026	mice C57BL/6J	A polysaccharide derived from *Gastrodia elata* (GEP-2)	Physical and Clinical :Colon length ↑ , Body weight ↑ DAI ↓ Inflammatory Cytokines and Proteins: TNF-α↓, IL-1β↓ , IL-6↓ , IL-10 ↑ , ZO-1 ↑ Intestinal Barrier : Occludin ↑ , Claudin-1 ↑, LPS ↓ ,D-lactate↓
4	Huang *et al.*, 2025	mice C57BL/6J	•*Passiflora edulis* Leaves polysaccharides	Physical and Clinical : DAI ↓ ,Colon length ↑ Inflammatory Cytokines and Proteins : TNF-α ↓ , IL-6 ↓ , IL-1β ↓ CRP ↓ Intestinal Barrier : SOD ↓ , T-AOC ↓,GSH-Px ↓ ,CAT ↓ Gut Microbiota :Lactobacillus ↑

5	Ye *et al*., 2025	mice BALB/c	PTPs – polysaccharides from *Phaeodactylum tricornutum* (marine diatom); Mw 12.56 kDa; main monosaccharides: Rib, Rha, Gal, Glu	Physical and Clinical : DAI ↓ ,Colon length ↑ Inflammatory Cytokines and Proteins :IL-1β ↓ ,IL-6 ↓ ,TNF-α ↓,MPO ↑ Intestinal Barrier : Mucin2↑ ,Claudin3↑,Occludin ↑ ,ZO-1 ↑ ,Bacterial translocation reduced↓ , Butyrate-producing genes expression ↑ Oxidative Stress : CAT ↑ ,SOD ↑ Gut Microbiota : Akkermansiaceae↑, Lactobacillaceae ↑ Muribaculum ↑, Erysipelotrichaceae ↓, Prevotellaceae ↓
6	Li *et al*., 2024	mice C57BL/6J	Polysaccharide from *Armillarilla tabescens* (ATP).	Physical and Clinical : DAI ↓ ,Colon length ↑ Inflammatory Cytokines and Proteins :IL-1β ↓ ,IL-6 ↓ Intestinal Barrier :ZO-1 ↑ ,Occludin ↑ ,Claudin-1 ↑, Mucin2↑, Immunoglobulins ↑ , SCFAs ↑ Gut Microbiota : Muribaculaceae↑ , Alistipes↑
7	Cui *et al*., 2025	mice C57BL/6J	Persimmon peel polysaccharide (PPP) – composed of Gal A, Ara, Gal, Xyl, Glu, Man	Physical and clinical : DAI ↓ ,Colon length ↑ Inflammatory Cytokines and Proteins : TNF-α ↓ , IL-6 ↓ , IL-1β ↓, MPO↓ Oxidative Stress: MDA ↓ , SOD ↑ Intestinal Barrier : Occludin ↑, Claudin-1↑, LPS ↓ ,D-lactate↓ Gut Microbiota : Parabacteroides ↑ ; Ligilactobacillus ↑ Akkermansia ↑ ; Lactobacillus↑ ; Alistipes↓ ; Escherichia_Shigella ↓ Dubosiella↓ ; Odoribacter↓ ;Parasutterella↓ ; Turicibacter ↓

8	Na *et al*., 2025	mice C57BL/6J	HLP-4-2 (pectic polysaccharide from *Hypecoum leptocarpum*, 19.7 kDa	Physical and clinical : DAI ↓ ,Colon length ↑ Inflammatory Cytokines and Proteins : TNF-α ↓ , IL-6 ↓ , IL-1β ↓ Intestinal Barrier : Mucin and Goblet cells ↑ Gut Microbiota : SCFA-producing bacteria ↑ ,Klebsiella ↓
9	Wan *et al*., 2024	mice C57BL/6J	*Poria cocos* polysaccharide (PCP) – composed mainly of Glu, Gal, and Man	Physical and Clinical :Body weight ↑, Colonic length ↑ , DAI ↓ Inflammatory Cytokines and Proteins : NF-κB ↓ Intestinal Barrier : ZO-1 ↑ ,Occludin ↑ ,Claudin-1 ↑ Gut Microbiota : Akkermansiaceae ↑
10	Ding *et al*.,2026	mice C57BL/6J	Peach Gum Polysaccharide (PGP)	Physical and Clinical :Body weight ↑, Colonic length ↑ Inflammatory Cytokines and Proteins : TNF-α ↓ , IL-6 ↓ , IL-1β ↓ Oxidative Stress : MDA ↓ , MPO ↓ , SOD ↑ ,GSH ↑ Intestinal Barrier : ZO-1 ↑ ,Occludin ↑ ,Claudin-1 ↑ Gut Microbiota : Butyrate ↑ , Propionate ↑
11	Li *et al*., 2025	mice C57BL/6J	HSWP-1a – a starch-like polysaccharide isolated from *Hirsutella sinensis mycelia*	Physical and Clinical :Body weight ↑, Colonic length ↑ Inflammatory Cytokines and Proteins : Anti-inflammatory cytokines ↑ , proinflammatory cytokines ↓ Gut microbiota: Lachnospiraceae↑, Proteobacteria and Cyanobacteria ↓
12	Zhou *et al*., 2026	mice C57BL/6J	*Cordyceps cicadae* polysaccharides (CCP) –	Physical and Clinical :Body weight ↑, Colonic length ↑ Inflammatory cytokines: TNF-α ↓, IL-1β ↓, IL-6 ↓ ,ZO-1 ↑, Intestinal Barrier : Occludin ↑, Claudin-1 ↑

			primarily composed of Glu, Man, and Gal	Gut microbiota: Lachnospiraceae ↑ ,Proteobacteria ↓ , Cyanobacteria ↓
13	Chen *et al*., 2025	mice C57BL/6J	NCSP-50 – a homogeneous α-(1→4)-D-glucan (976 kDa) from *Ophiocordyceps sinensis*	Physical and Clinical : Colonic length ↑, DAI ↓ Inflammatory cytokines: TNF-α↓ , IL-10↑ , IL-17↓ , IL-13↑ Oxidative Stress : iNOS↑ Gut microbiota: Bacteroides acidifaciens↑ , Lachnospiraceae bacterium↑ Blautia ↑ , overall beneficial microbiota balance↑ .
14	Sui *et al*., 2025	mice C57BL/6J	*Larimichthys crocea Isinglass* polysaccharide (CIP)	Physical and Clinical : Weight loss ↓ , Colon length ↑ Histopathological damage ↓ Inflammatory cytokines: TNF-α ↓, IL-1β ↓, IL-6 ↓ , IL-10↑ Intestinal Barrier : Tight junction proteins (TJs) ↑ , Mucin2 ↑ Oxidative Stress : iNOS ↓ Gut microbiota: Bacteroidota↓ , Campylobacter ↓
15	Wang *et al*., 2025	mice C57BL/6J	FAP1a – polysaccharide from fresh *Areca catechu* L.; MW ~65 kDa;	Physical and Clinical : Weight loss ↓ , Colonic tissue damage ↓ Oxidative Stress : ROS↓ , MDA↓ , SOD↑ , CAT ↑ , GSH ↑ Intestinal Barrier : Bacterial translocation ↓ , Intestinal permeability↓ ZO-1↑ , Occludin↑ , Claudin ↑ Inflammatory cytokines: TNF-α↓ , IL-6↓ , IL-1β↓ , NF-κB↓, IL-10↑ Gut microbiota: Muribaculaceae↑ , Alistipes ↑ , Butyrate and SCFAs production↑
16	Hu *et al*., 2026	mice C57BL/6J	AHP – *Agrimoniae Herba* Polysaccharides;	Physical and Clinical : Colonic length ↑, DAI ↓, Spleen index↓ Inflammatory Cytokines: ↓ TNF-α, ↓ IL-6, ↓ IL-1β –

				Oxidative Stress: MDA↓, SOD↑, GSH↑, MPO↓ Intestinal Barrier: ZO-1↑, Occludin↑, Mucin2↑ GutMicrobiota: *F. rodentium*↑
17	Xiong *et al.*, 2026	mice C57BL/6J	ALP – a sulfated polysaccharide extracted from *Laminaria japonica* .	Physical and Clinical : Colonic length ↑, DAI ↓ Intestinal barrier: ZO-1↑, Occludin↑, Mucin-2 ↑ Inflammatory cytokines: TNF-α↓, IL-6↓, IL-1β ↓ Gut microbiota: Muribaculaceae↑, Clostridia↑, Enterobacteriaceae↓.
18	Tian *et al*., 2025	mice C57BL/6J	Pomelo peel polysaccharide (PP).	Physical and Clinical : DAI↓, Colon length↑ , Weight loss↓ Intestinal barrier: ZO-1↑ , Occludin↑ , Claudin↑ Mucus layer integrity ↑ Oxidative Stress: MDA↓ , ROS↓ , SOD↑ , CAT↑ , GSH↑ Inflammatory cytokines: TNF-α ↓, IL-6 ↓, IL-1β↓ , IL-10↑ Pro-inflammatory cytokines overall↓ Gut microbiota: Bacteroides ↑, Lachnospiraceae ↑, Ruminococcaceae↑

DAI : Disease Activity Index (DAI) score ; MDA :Malondialdehyde ; SOD :Superoxide Dismutase ;MMP9 :Matrix Metalloproteinase 9 ; Myeloperoxidase :MPO ; CCR5 : C-C Chemokine Receptor Type 5 ; NFkB : Nuclear Factor kappa-light-chain-enhancer of activated B cells ; PTG S2: Prostaglandin-Endoperoxide Synthase 2 ; NO : Nitric Oxide ; NOS 2 : Nitric Oxide Synthase 2 ; UCG-010 : Uncultured Clostridiales Group-010 ; ZO-1 : Zonula Occludens-1 ; T-AOC : Total Antioxidant Capacity ; GSH-Px : Glutathione Peroxidase ; iNOS : inducible Nitric Oxide Synthase ; ROS : Reactive Oxygen Species

The study no.3 by Li *et al*. (2026) aimed to isolate a specific fraction from Gastrodia elata tubers (GEP-2). GEP-2 is characterized by a low molecular weight ranging between 2.54 and 9.24 kDa and a branched structure consisting primarily of α-D-glucose with (1→4) linkages in the main chain and (1→6) linkages in the side chains. This low molecular weight gives it higher solubility and stronger biological activity. GEP-2 successfully enhanced the intestinal barrier by increasing tight junction proteins (ZO-1, occludin, and claudin-1) and reducing D-lactate and LPS in the blood and inhibited the NF-κB p65/STAT3 pathway, leading to a strong reduction in inflammatory cytokines (TNF-α, IL-1β, and IL-6) and an increase in anti-inflammatory IL-10.

The study no.4 by Huang *et al*. (2025) used Passiflora edulis leaf extract, which contains a complex mixture of pectin, cellulose, and hemicellulose. The results showed a significant protective effect represented by reducing systemic inflammation (reducing TNF-α, IL-6, IL-1β, and CRP) and improving antioxidant defenses (increasing SOD, T-AOC, GSH-Px, and CAT). This effect was associated with a clear increase in Lactobacillus counts, confirming the role of these bacteria as a primary target of prebiotics.

The study no.5 by Ye *et al*. (2025) was distinguished by its use of polysaccharides (PTPs) from the marine diatom Phaeodactylum tricornutum with a specific molecular weight of 12.56 kDa, composed of ribose (Rib), rhamnose (Rha), galactose (Gal), and glucose (Glc). A high proportion of sulfate groups characterizes this marine biopolymer. PTPs showed an exceptional ability to repair the intestinal barrier by enhancing butyrate-producing gene expression (increasing genes responsible for SCFA production) and increasing goblet cells and mucin 2. The effect on the microbiota was very clear, with a significant increase in the numbers of Akkermansiaceae, Muribaculum, and Lactobacillaceae and a decrease in Prevotellaceae and Erysipelotrichaceae.

The study no.6 by Li *et al*. (2024) examined polysaccharides from the fungus Armillaria tabescens (ATP). ATP is a complex β-glucan with the ability to stimulate innate immunity via activation of Dectin-1 receptors. ATP demonstrated the ability to inhibit the NF-κB pathway and reduce inflammatory cytokines (IL-1β and IL-6), enhance the intestinal barrier (increase ZO-1, occludin, claudin-1, and mucin2), and increase immunoglobulins and short-chain fatty acids (SCFAs). At the microbiota level, the researchers observed an increase in Muribaculaceae and Alistipes, both of which are butyrate-producing bacteria.

The study no.7 by Cui *et al*. (2025) treated colitis using persimmon peel polysaccharide (PPP), which is rich in galacturonic acid (GalA), arabinose (Ara), and galactose (Gal) with the presence of xylose (Xyl), glucose (Glc), and mannose (Man). PPP is characterized by a complex

pectic structure with side chains. PPP showed excellent results in reducing oxidative stress (MDA), increasing antioxidant enzymes (SOD) and reducing D-lactate and LPS in the blood. At the microbiota level, PPP induced a radical shift by increasing beneficial butyrate-producing bacteria such as Parabacteroides, Ligilactobacillus, Akkermansia, and Lactobacillus while strongly suppressing pathogenic and harmful bacteria such as Escherichia/Shigella, Dubosiella, Odoribacter, Parasutterella, Turicibacter, and Alistipes, demonstrating a dual effect pattern (enhancing beneficial and inhibiting harmful).

The study no.8 by Na *et al*. (2025) used, a pectic polysaccharide (HLP-4-2) extracted from the Mongolian medicinal plant Hypecoum leptocarpum, with an average molecular weight of 19.7 kDa, composed primarily of galacturonic acid (GalA), galactose (Gal), and arabinose (Ara). HLP-4-2 is characterized by a complex pectic structure with side chains and a specific degree of esterification. This polysaccharide showed high selective ability to enhance short-chain fatty acid (SCFA)-producing bacteria and reduce opportunistic bacteria such as Klebsiella. This effect was associated with a clear decrease in inflammatory cytokines (TNF-α, IL-6, and IL-1β) and an increase in goblet cells and mucin production, confirming that the average molecular weight and pectic structure play a key role in the selectivity of the biological effect.

The study no.9 by Wan *et al*. (2024) examined Poria cocos fungus polysaccharide (PCP), which is a complex β-glucan composed primarily of glucose (Glc), with galactose (Gal) and mannose (Man) in lower proportions. PCP is characterized by its ability to modulate innate immunity through activation of phagocytes and macrophages via Dectin-1 receptors. PCP treatment led to strong enhancement of the intestinal barrier through increased expression of tight junction proteins (ZO-1, occludin, and claudin-1) and inhibition of the NF-κB pathway. At the microbiota level, the researchers observed a marked increase in the Akkermansiaceae family, which are vital bacteria for maintaining the integrity of the colonic mucus layer.

The study no.10 by Ding *et al*. (2026) used peach gum polysaccharide (PGP), which is a highly branched arabinogalactan characterized by a high degree of branching and the presence of galacturonic acid and rhamnose (Rha) units. PGP demonstrated a superior ability to enhance the production of short-chain fatty acids (SCFAs), particularly butyrate and propionate, which are the primary energy source for colonocytes. This effect was associated with a marked decrease in oxidative stress markers (MDA, MPO), an increase in antioxidant molecules (SOD, GSH), improvement of the intestinal barrier (ZO-1, occludin, and claudin-1), and reduction of inflammatory cytokines (TNF-α, IL-6, and IL-1β). This confirms that the branched structure of this polysaccharide facilitates its delivery to the colon and its slow fermentation for SCFA production.

The study no.11 by Li *et al*. (2025) used a starch-like polysaccharide (HSWP-1a) isolated from Hirsutella sinensis mycelia (the anamorph of Cordyceps sinensis). Glucose units linked by (1→4) and (1→6) bonds similar to amylopectin, with a high molecular weight, characterize this polysaccharide. Despite being a relatively simple storage polymer, it demonstrated the ability to enhance the intestinal barrier and increase anti-inflammatory cytokines while reducing pro-inflammatory cytokines. At the microbiota level, HSWP-1a led to a marked increase in the Lachnospiraceae family (butyrate producers) and a significant decrease in Proteobacteria (which includes many pathogenic bacteria) and Cyanobacteria.

The study no.12 by Zhou *et al*. (2026) examined polysaccharides from the fungus Cordyceps cicadae (CCP), which is composed primarily of glucose (Glc), mannose (Man), and galactose (Gal) in specific ratios (4.58:2.25:1.00). CCP is characterized as a glycoprotein with strong immunological properties. CCP demonstrated an excellent ability to enhance the intestinal barrier by increasing tight junction proteins (ZO-1, Occludin, and Claudin-1), inhibiting inflammatory cytokines (TNF-α, IL-1β, and IL-6), and regulating the bile acid/FXR/NF-κB pathway. At the microbiota level, CCP increased butyrate-producing Lachnospiraceae bacteria and decreased Proteobacteria and Cyanobacteria, the same patterns observed in the HSWP-1a study, confirming a common mechanism of action among Cordyceps fungus polysaccharides.

The study no.13 by Chen *et al*. (2025) used NCSP-50 polysaccharide from Ophiocordyceps sinensis (the same fungus as in Studies 11 and 12), which is a homogeneous α-(1→4)-D-glucan with a very high molecular weight of 976 kDa. It is characterized by a very long linear structure of glucose units with negligible branching. Despite its very high molecular weight, it demonstrated the ability to modulate cellular immunity by increasing secretory IgA (sIgA) and improving the Th17/Treg balance (decreasing IL-17 and increasing IL-10 and IL-13). At the microbiota level, NCSP-50 increased Bacteroides acidifaciens (an immune-regulating bacterium), Lachnospiraceae, and Blautia (butyrate producers). This confirms that a very high molecular weight does not necessarily prevent efficacy if the polysaccharide has good solubility and the ability to interact with immune receptors on intestinal cells.

The study no.14 by Sui *et al*. (2025) examined a polysaccharide extracted from Larimichthys crocea isinglass (CIP), which is chondroitin sulfate composed of repeating units of glucuronic acid (GlcA) and N-acetylgalactosamine (GalNAc) with sulfate groups at different positions. These sulfated groups are among the most important structural factors that give polysaccharides the ability to inhibit inflammation through interaction with immune molecules and inhibition of adhesion proteins. CIP demonstrated the ability to inhibit the NF-κB pathway, reduce inflammatory cytokines

(TNF-α, IL-1β, IL-6), increase IL-10, and inhibit iNOS. It also enhanced the intestinal barrier (TJs and mucin2). At the microbiota level, it led to a decrease in Bacteroidota (phylum) and Campylobacter (a pathogenic bacterium associated with intestinal inflammation).

The study no.15 by Wang *et al*. (2025) used FAP1a polysaccharide from fresh Areca catechu L. with a molecular weight of approximately 65 kDa. This polysaccharide is characterized by the presence of mannose (Man), galactose (Gal), and glucose (Glc) units in a molar ratio of (1.00 : 0.60 : 0.31) in addition to the presence of glucuronic acid (GlcA). FAP1a demonstrated exceptional ability to repair the intestinal barrier by increasing tight junction proteins (ZO-1, occludin, and claudin), reducing intestinal permeability, and preventing bacterial translocation to the liver, spleen, and blood. It also succeeded in reducing oxidative stress (MDA, ROS), increasing antioxidants (SOD, CAT, and GSH), reducing inflammatory cytokines (TNF-α, IL-6, IL-1β), inhibiting NF-κB, and increasing IL-10. At the microbiota level, it increased Muribaculaceae, Alistipes (SCFA producers), the production of butyrate, and other short-chain fatty acids.

The study no.16 by Hu *et al*. (2026) examined AHP polysaccharide from Agrimoniae Herba (agrimony). AHP is characterized by its ability to promote the growth of Faecalibaculum rodentium bacteria, which in turn produce quinic acid, a natural bioactive metabolite that inhibits inflammation by promoting regulatory T cell (Treg) differentiation (increasing the proportion of Treg among $CD4^+$ T cells). This discovery highlights a novel and important mechanism where the polysaccharide acts indirectly by promoting specific bacteria that produce active metabolites. AHP also showed improvement in the intestinal barrier (ZO-1, occludin, and mucin2), combating oxidative stress (reducing MDA and MPO and increasing SOD and GSH), and reducing inflammatory cytokines (TNF-α, IL-6, and IL-1β).

The study no.17 by Xiong *et al*. (2026) used a sulfated polysaccharide (ALP) extracted from the seaweed Laminaria japonica, which is fucoidan, characterized by a high proportion of sulfate groups (sulfated fucose) reaching approximately 30% and a complex structure of (1→3) and (1→4) linkages with the presence of galactose (Gal), mannose (Man), and glucuronic acid (GlcA) units. The sulfated groups in this marine polysaccharide give it a high ability to inhibit inflammation through inhibition of adhesion proteins (selectins) and inhibition of the TLR4/NF-κB pathway. ALP demonstrated superior ability to repair the intestinal barrier (increasing ZO-1, occludin, and mucin-2) and inhibit inflammatory cytokines (TNF-α, IL-6, and IL-1β). At the microbiota level, it increased Muribaculaceae and Clostridia (butyrate producers) and caused a sharp decrease in Enterobacteriaceae (pathogenic intestinal bacteria such as E. coli and Shigella).

The study no.18 by Tian *et al*. (2025) concluded this series with a study of pomelo peel polysaccharide (PP), which is a complex pectin mixture rich in galacturonic acid (GalA) at up to 74.5%, in addition to arabinose (Ara), galactose (Gal), and rhamnose (Rha) in specific proportions, with the presence of methyl ester groups affecting the degree of esterification ranging between 35% and 40%. PP showed excellent results in improving the intestinal barrier (increasing ZO-1, occludin, and claudin) and strengthening the mucus layer; combating oxidative stress (reducing MDA and ROS and increasing SOD, CAT, and GSH); modulating the inflammatory response (reducing TNF-α, IL-6, and IL-1β and increasing IL-10); and improving clinical symptoms (reducing DAI, body weight loss, and colon length shortening). At the microbiota level, PP led to a marked increase in Bacteroides, Lachnospiraceae, and Ruminococcaceae, three core bacterial families essential for butyrate production and maintaining colon health.

The collective findings of studies investigating the effects of natural polysaccharides in dextran sodium sulfate (DSS)-induced ulcerative colitis (UC) models (tab.1) indicate a consistent pattern of beneficial effects on the colonic microbiota, regardless of the chemical, plant, fungal, or animal origin of the polysaccharide. These polysaccharides restore microbial diversity to levels close to the normal state, increasing richness and evenness indices (such as Chao1 and Shannon) that were reduced by inflammation. They induce a qualitative shift in microbial composition characterized by a marked increase in the abundance and activity of beneficial bacteria, particularly short-chain fatty acid (SCFA)-producing bacteria such as Lachnospiraceae, Ruminococcaceae, Muribaculaceae, and Clostridia, in addition to classical probiotics such as Lactobacillus, Bifidobacterium, and Akkermansia. These polysaccharides exert selective inhibition against harmful and pro-inflammatory bacteria, most notably Proteobacteria (especially Enterobacteriaceae and Escherichia-Shigella), Desulfovibrio, and certain species of Bacteroides, Prevotella, Klebsiella, and Campylobacter. This microbial shift leads to a significant enhancement in the production of short-chain fatty acids, particularly butyrate, which is the primary energy source for colonocytes and a potent enhancer of intestinal barrier integrity. This restored microbial balance is reflected in improved intestinal barrier function and mucosal immunity, as tight junction proteins (ZO-1, Occludin, and Claudin) are upregulated and the mucin layer is improved, thereby reducing intestinal permeability and preventing the translocation of bacteria and toxins. Altogether, this translates into an anti-inflammatory immunomodulatory effect manifested by the restoration of the Th17/Treg axis balance toward an anti-inflammatory profile, increased intestinal sIgA secretion, reduced inflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-17) and oxidative stress markers (MDA and MPO), along with elevated antioxidant defenses (SOD, CAT, and GSH). In conclusion, converging evidence demonstrates that natural polysaccharides possess an intrinsic ability to reshape the colonic microbiota toward a healthy

and anti-inflammatory profile, regardless of their chemical origin, making them promising functional strategies for the management of ulcerative colitis through targeting the microbiota–barrier–immunity axis ((Huang et al., 2025; Sui et al., 2025; Chen et al., 2025; Ye et al., 2025; Xiong et al., 2026; Hu et al., 2026; Sun et al., 2026; Yang et al., 2026; Li et al., 2026).

CONCLUSION, PERSPECTIVES AND RECOMMENDATIONS

Conclusion

Exposure to external factors such as antibiotics, environmental toxicants (triclosan, microplastics, and cadmium), unhealthy diets (high-fat or meat-based), and pathogenic factors (DON mycotoxin and Salmonella) leads to dysbiosis through specific mechanisms including inhibition of tight junction proteins, generation of oxidative stress, and inhibition of bacterial enzymes. The imbalance (dysbiosis) is not limited to the intestine but extends to affect the liver via LPS translocation and NF-κB activation, and the heart via TMAO and LPS. The nervous system is also affected via LPS, neuroinflammation, and disruption of the tryptophan/kynurenine pathway, causing Alzheimer's disease, Parkinson's disease, multiple sclerosis, and depression.

The present work highlights the role of natural polysaccharides from plant, animal, and microbial origin in possessing an intrinsic ability to reshape the microbiota toward a healthy state. These polysaccharides, which reach the colon intact after resisting human digestive enzymes, act as fermentable substrates that selectively recruit beneficial bacteria through precise molecular mechanisms dependent on CAZyme enzymes (GHs and PLs) and metabolic cross-feeding. This fermentation leads to a marked increase in SCFA-producing bacteria such as Lachnospiraceae, Ruminococcaceae, Faecalibacterium prausnitzii, and Roseburia, in addition to classical probiotics such as Lactobacillus, Bifidobacterium, and Akkermansia. At the same time, these polysaccharides exert selective inhibition against harmful and pro-inflammatory bacteria, particularly Proteobacteria (Enterobacteriaceae and Escherichia-Shigella) and Desulfovibrio.

At the functional level, this microbial shift translates into marked enhancement of the intestinal barrier through increased expression of tight junction proteins (ZO-1, occludin, and claudin) and improvement of the mucin layer, thereby reducing intestinal permeability and preventing the translocation of bacteria and toxins. Furthermore, the production of SCFAs, particularly butyrate, leads to an anti-inflammatory effect through inhibition of the NF-κB pathway, reduction of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-17), increase of antioxidant defences (SOD, CAT, and GSH), and reduction of oxidative stress markers (MDA and MPO). Taken together, these findings confirm that dietary polysaccharides represent a promising strategy for restoring microbial balance and combating organic diseases associated with gut dysbiosis.

Perspectives

Further research is needed to investigate the role of different species of the gut microbiota for strengthening the study of the gut-organizational axis.

The study of the simultaneous exposure to multiple factors leading to dysbiosis, and the poor translation of animal study findings to humans are also necessary to confirm the existing data.

Developing treatment protocols aimed at reversing microbial imbalances and restoring microbial equilibrium is also recommended.

Further research is needed to investigate the effects of polysaccharides on the gut microbiota, both positive and negative, and to gain a thorough understanding of their mechanisms of action on gut health.

Recommendations

1. Limit the prescription of broad-spectrum antibiotics (such as doxycycline, tetracycline, amoxicillin, and cotrimoxazole) except when absolutely necessary.
2. Accompany antibiotic therapy with the administration of probiotics and prebiotics (such as polysaccharides) to reduce dysbiosis.
3. Monitor microbiota restoration for up to 6 months following antibiotic treatment.
4. Raise awareness about the risks of triclosan found in toothpaste and personal care products, and ensure utensils are washed with plain water to avoid soap residues.
5. Reduce exposure to microplastics (MPs) by limiting the use of plastic containers for hot foods and beverages.
6. Raise awareness about the risks of high-fat diets, which reduce SCFA-producing bacteria.
7. Raise awareness about the risks of meat-based diets, which increase TMAO-producing bacteria and cause inflammation and constipation.
8. Encourage dietary patterns rich in fibre and natural polysaccharides (found in fruits, vegetables, whole grains, legumes, and seaweeds).
9. Daily consumption of dietary fibre and polysaccharides at a rate of 25-30 grams for adults.
10. Improve the storage of grains and cereals to limit contamination with Fusarium fungi producing the mycotoxin DON.
11. Monitor drinking water quality to limit exposure to bacteria in the VBNC state (such as Salmonella).

REFERENCES

1. Agirre, J., Davies, G. J., Wilson, K. S., & Cowtan, K. D. (2017). Carbohydrate structure: the rocky road to automation. Current Opinion in Structural Biology, 44, 39-47. https://doi.org/10.1016/j.sbi.2016.11.011 .

2. Ahmadi, S., Mainali, R., Nagpal, R., Sheikh-Zeinoddin, M., Soleimanian-Zad, S., Wang, S., Deep, G., Mishra, S. K., & Yadav, H. (2017). Dietary polysaccharides in the amelioration of gut microbiome dysbiosis and metabolic diseases. Obesity Control and Therapy, 4(3), 1–15. https://doi.org/10.15226/2374-8354/4/2/00140 .

3. Aiman, R., et al. (2021). Polysaccharides; Classification, Chemical Properties, and Future Perspective Applications. Journal of Polymers and the Environment. https://pubmed.ncbi.nlm.nih.gov/33526994/ .

4. Alshinawy, A. S., Badeia, E. A., Swelam, M. S., Sayed, A. A., & Mohamed, M. R. (2025). Decoding the Gut Microbiota in Multiple Sclerosis Using Nanopore Long-Read Sequencing: Insights into Disease Severity and Subtypes. Molecular Neurobiology, 62, 14245–14260. https://doi.org/10.1007/s12035-025-05194-9

5. Ananthakrishnan, A. N. (2025). The gut microbiome connects nutrition and human health. Nature Reviews Gastroenterology & Hepatology, 22(4), 234–248. https://doi.org/10.1038/s41575-024-00945-6 .

6. Asnicar, F., Manghi, P., Fackelmann, G., Baldanzi, G., Bakker, E., Ricci, L., Piccinno, G., Piperni, E., Mladenovic, K., Amati, F., Segata, N., & Huttenhower, C. (2026). Gut micro-organisms associated with health, nutrition and dietary interventions. Nature, 650(8101). https://doi.org/10.1038/s41586-025-09854-7 .

7. Babouee Flury, B., Andrey, D., & Kohler, P. (2024). Antibiotics' collateral effects on the gut microbiota in the selection of ESKAPE pathogens. CMI Communications, 1(2), 100012. https://doi.org/10.1016/j.cmicom.2024.100012 .

8. Barathan M, Hanafiah A. Gut Microbiota and Cardiovascular Diseases: Unraveling the Role of Dysbiosis and Microbial Metabolites. International Journal of Molecular Sciences. 2025; 26(9):4264.

9. Blue, C. E. C., García Suarez, M., Nacer-Khodja, E., Rodriguez, M. A., & Dalloul, R. A. (2024). Positive impact of dietary marine sulfated polysaccharides derived from macroalgae during a necrotic enteritis challenge. Poultry Science, 103(12), 104502.

10. Cai, D.-J., Liu, H.-M., Zhang, R.-Y., & Luo, Y.-Q. (2025). Polysaccharides from defatted sesame seed kernel: Structural characterization and potential applications. Food Chemistry Advances, 9, 101150. https://doi.org/10.1016/j.focha.2025.101150 .

11. Carmazzo, S. M., & Fanos, V. (2025). The Microbiota-Gut-Brain Axis: A Lifespan Perspective. Manuscript under review / Preprint. https://doi.org/10.3390/jcm15083065

12. Carnazzo, S. M., & Fanos, V. (2026). The microbiota–gut–brain axis across the lifespan: From neurodevelopment to neurodegeneration. Journal of Clinical Medicine, 15(8), 3065. https://doi.org/10.3390/jcm15083065 .

13. Chakraborty, D. K., Roy, T., Ngo, S. T., Al-Chalabi, A., & Al Khleifat, A. (2026). Gut microbiota and ALS: Cause, consequence or correlation? A systematic review. Frontiers in Neuroscience, 20, Article 1774417. https://doi.org/10.1378/fnins.2026.1774417 .

14. Chen, C., Wang, G. Q., Li, D. D., & Zhang, F. (2025). Microbiota–gut–brain axis in neurodegenerative diseases: molecular mechanisms and therapeutic targets. Molecular Biomedicine, 6, 64. https://doi.org/10.1186/s43556-025-00254-x

15. Chen, C., Wang, G., Li, D., & Zhang, F. (2025). Microbiota–gut–brain axis in neurodegenerative diseases: molecular mechanisms and therapeutic targets. Molecular Biomedicine, 6, 31. https://doi.org/10.1186/s43556-025-00307-1 .

16. Chen, L., Pu, X., Li, L., Zhang, M., Liu, Y., Hu, K., Wang, J., Zhang, F., & Yu, J. (2025). Shenling Jianpiwei formula ameliorates metabolic associated fatty liver disease through modulation of the gut microbiota and attenuation of LPS-mediated inflammation. Fitoterapia, 186, 106862. https://doi.org/10.1016/j.fitote.2025.106862 .

17. Chen, R., Qian, J., Wang, Q., Li, Y., Xu, Z., Zhang, M., Wang, M., Nie, H., Yang, W., Tong, X., & Yan, F. (2025). Periodontitis exacerbates metabolic dysfunction-associated steatotic liver disease via the gut microbiota-derived tryptophan metabolism-AHR axis in obesity. eBioMedicine, 122, 106037. https://doi.org/10.1016/j.ebiom.2025.10603.

18. Chen, S., Wang, J., Fang, Q., Dong, N., Cui, S. W., & Nie, S. (2025). Polysaccharide from natural Ophiocordyceps sinensis alleviated dextran sulfate sodium-induced colitis through modulating sIgA formation and gut microbiota. Journal of Functional Foods, 131, 106921. https://doi.org/10.1016/j.jff.2025.106921 .

19. Chin, V. K., Lee, K. Q., Ruslan, N. A., & Seow, H. F. (2025). Microbiota-host interactions: Exploring their dynamics and contributions to human diseases. MicrobiologyOpen, 14(3), e70012. https://doi.org/10.1002/mbo3.70012 .

20. Collins, J. T., Nguyen, A., Omole, A. E., & Badireddy, M. (2025). Anatomy, abdomen and pelvis, small intestine. In StatPearls. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK459366/ .

21. Contreras-Ramírez, K., López-Legarda, X., Tabares-Guervía, J. H., Hernández, J. C., Segura-Sánchez, F., & Villa-Pulgarín, J. A. (2025). Anti-tumor and immunomodulatory activity of Ganoderma parvulum-derived polysaccharides. Research Article. https://doi.org/10.1042/BSR20240113 .

22. Cosmas, K. K., Kiruki, S., Njiri, O. A., Nyambati, G. K., Mose, J. M., Omwenga, I., Isaac, A. O., & Nyariki, J. N. (2026). Amoxicillin and cotrimoxazole-driven dysbiosis disrupted blood cell levels, cytokine balance and induced oxido-nitrosative stress in young mice. Advances in Biomarker Sciences and Technology, 8, 1–18 https://doi.org/10.1016/j.abst.2025.11.002 .

23. Cui, Y., Zhang, S., Wang, X., Kang, W., & Lü, X. (2025). Persimmon peel polysaccharides alleviated colitis via regulating gut microbiota and protecting intestinal barrier integrity. Food Bioscience, 65, 106123. https://doi.org/10.1016/j.fbio.2025.106123 .

24. Das, S., Fletcher, C. J., & Wu, Y. (2026). The role of different dietary fibers in modulating human gut microbiota. Nutraceuticals, 6(1), 18.

25. Deniz, N., Sarıtaş, S., Bechelany, M., & Karav, S. (2025). Prebiotic and functional fibers from micro- and macroalgae: Gut microbiota modulation, health benefits, and food applications. International Journal of Molecular Sciences, 26(22), 11082.

26. Dharanie, S., Meghana, C. H., Lavanya, M., Baskaran, N., Elumalai, A., & Vignesh, S. (2024). Bioactive food polysaccharides: A review on sources, classification, and its potential health benefits in humans. Food and Humanity, 3, Article 100451. https://doi.org/10.1016/j.foohum.2024.100451 .

27. Ding R, Wang W, Zhu Y, Cao Y, Fang M, Yang Q, Gong Z. Protective effect of peach gum polysaccharides on dextran sulfate sodium-induced ulcerative colitis in mice. Int J Biol Macromol. 2023. https://doi.org/10.1016/j.ijbiomac.2022.11.183 .

28. Doms, S., Baines, J. F., & Hendriks, J. (2025). Gut Microbiome Structure and Progression in Multiple Sclerosis: A Meta-Analysis Across 14 Cohorts. medRxiv. https://doi.org/10.1101/2025.09.08.25335213 .

29. Edo, G. I., Mafe, A. N., Ali, A. B. M., Akpoghelie, P. O., Yousif, E., Isoje, E. F., Igbuku, U. A., Zainulabdeen, K., Owheruo, J. O., Essaghah, A. E. A., Umar, H., Ahmed, D. S., & Alamiery, A. A. (2025). A critical review on the impacts of β-glucans on gut microbiota and human health. The Microbe, 7, 100394. https://doi.org/10.1016/j.microb.2025.100394 .

30. Elshahed, M. S., Miron, A., Aprotosoaie, A. C., & Farag, M. A. (2021). Pectin in diet: Interactions with the human microbiome, role in gut homeostasis, and nutrient-drug

interactions. Carbohydrate Polymers, 255, 117388. https://doi.org/10.1016/j.carbpol.2020.117388 .

31. Epelde, F. (2025). The Role of the Gut Microbiota in Heart Failure: Pathophysiological Insights and Future Perspectives. Medicina (Kaunas, Lithuania), 61(4), 720. https://doi.org/10.3390/medicina61040720 .

32. Eskandar, K. (2025). The gut–brain axis in depression, anxiety, and schizophrenia: a scoping review of mechanisms, biomarkers, and therapeutic implications. Middle East Current Psychiatry, 32, 87. https://doi.org/10.1186/s43045-025-00585-z .

33. Froidurot, A., & Julliand, V. (2022). Cellulolytic bacteria in the large intestine of mammals. Gut Microbes, 14(1), 2031694. https://doi.org/10.1080/19490976.2022.2031694 .

34. Glowacki, R. W. P., & Martens, E. C. (2021).If you eat it or secrete it, they will grow: the expanding list of nutrients utilized by human gut bacteria.Journal of Bacteriology, 203(9), e00481-20. https://pmc.ncbi.nlm.nih.gov/articles/PMC8092160 .

35. Gómez-Maqueo, A., Ferreira-Lazarte, A., Amirruddin, N. S., & Lin, A. H.-M. (2023). Generating slow digestibility in cooked potatoes by modulating starch accessibility to α-amylase and mucosal α-glucosidase to different levels. Food Hydrocolloids, 141, 108718. https://doi.org/10.1016/j.foodhyd.2023.108718 .

36. Grover, M., Vanuytsel, T., & Chang, L. (2025). Intestinal Permeability in Disorders of Gut–Brain Interaction: From Bench to Bedside. Gastroenterology, 168(3), 480–495. https://doi.org/10.1053/j.gastro.2024.09.001 .

37. Gu, P., Xu, Y., & Li, X. (2025). Chronic low-dose cadmium exposure disrupts gut microbiota and lipid metabolism to induce liver injury. Food and Chemical Toxicology, 115603. https://doi.org/10.1016/j.fct.2025.115603 .

38. Guan, F., Fu, G., Ma, Y., Zhou, L., Li, G., Sun, C., & Zhang, T. (2024). Spirulina polysaccharide-based prebiotic foods preparations-a promising approach for modulating gut microbiota and improving health. Journal of Functional Foods, 116, 106158. https://doi.org/10.1016/j.jff.2024.106158

39. Halabitska, I., Petakh, P., Kamyshna, I., Oksenych, V., Kainov, D. E., & Kamyshnyi, O. (2024). The interplay of gut microbiota, obesity, and depression: Insights and interventions. Discover Mental Health, 4, Article 48. https://doi.org/10.1007/s44192-024-00123-7 .

40. Hareesha, P., Terepogu, D., Pitchika, G. K., & Buddolla, V. (2025). Probiotic regulation of gut hormones following antibiotic-induced dysbiosis: Insights into host-microbiota-endocrine interactions. Medicine in Microecology, 26, 100158. https://doi.org/10.1016/j.medmic.2025.100158 .

41. Holesh, J. E., Aslam, S., & Martin, A. (2023). Physiology, Carbohydrates. In StatPearls [Internet]. StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459280/ .

42. Hu, J., Yu, Y., Wang, Z., Wang, M., Wang, Y., Chen, X., Liu, Y., Zheng, M., Liang, C., Lv, C., Yang, A., Lin, Z., Jiao, Y., Li, Y., Huang, H., Li, J., & Mao, T. (2026). Faecalibaculum rodentium-derived quinic acid-mediated Treg differentiation drives the attenuation of intestinal inflammation by Agrimoniae Herba polysaccharides. Carbohydrate Polymers, 385, 125373. https://doi.org/10.1016/j.carbpol.2026.125373 .

43. Hu, Y., Hu, X., Jiang, L., Luo, J., Huang, J., Sun, Y., Qiao, Y., Wu, H., Zhou, S., Li, H., Li, J., Zhou, L., & Zheng, S. (2025). Microbiome and metabolomics reveal the effect of gut microbiota on liver regeneration of fatty liver disease. eBioMedicine, 111, 105482. https://doi.org/10.1016/j.ebiom.2024.105482 .

44. Huang, R., Cai, Y., Wang, X., Jiang, T., Khoo, H. E., Li, J., Dong, X., Guan, Y., & Li, X. (2025). Passiflora edulis leaves polysaccharides mitigate DSS-induced ulcerative

colitis in mice via inflammation inhibition and gut microbiota modulation. Journal of Functional Foods, 129, 106891.

45. Huang, Y., Chen, Y., He, J., Shi, X., He, Y., Sun, W., Wu, C., Zhao, K., & Xu, D. (2025). Polysaccharide from Ziziphus jujuba cv. Changzao prevented colitis in mice by regulating the inflammation-gut microbiota-metabolite axis. Journal of Functional Foods, 127, 107098.

46. Huang, Y., Chen, Y., He, J., Shi, X., He, Y., Sun, W., Wu, C., Zhao, K., & Xu, D. (2025). Polysaccharide from Ziziphus jujuba cv. Changzao prevented colitis in mice by regulating the inflammation-gut microbiota-metabolite axis. Journal of Functional Foods , 135, 107098 [7, 8].

47. Huang, Y., Guo, H., Liu, Y., Jin, W., Palanisamy, C. P., Pei, J., Oz, F., & Abd El-Atty, A. M. (2025). Effects of natural polysaccharides on the gut microbiota related to human metabolic health. Molecular Nutrition & Food Research, 69(11), e202400792. https://doi.org/10.1002/mnfr.202400792 .

48. j D, Liu Y, Li S, et al. Bacteroides vulgatus ameliorates heart failure by targeting the TGF-β1/MAPK signaling pathway. Journal of Translational Medicine. 2025; 23(1):456.

49. Jagtap, A. S., Vijay Sankar, N. P., Ghori, R. I., & Manohar, C. S. (2022). Marine microbial enzymes for the production of algal oligosaccharides and its bioactive potential for application as nutritional supplements. Folia Microbiologica, 67(2), 175–191. https://doi.org/10.1007/s12223-021-00943-4 .

50. Jayachandran, M., Chen, J., Chung, S. S. M., & Xu, B. (2018). A critical review on the impacts of β-glucans on gut microbiota and human health. Journal of Nutritional Biochemistry, 61, 101–110. https://doi.org/10.1016/j.jnutbio.2018.06.010 .

51. Jin, J., Li, F., Hu, Y., Zhang, Z., Zhang, R., & Xing, F. (2026). Gut microbiota dysbiosis transmits deoxynivalenol toxicity and triggers liver inflammation. Journal of Advanced Research. https://doi.org/10.1016/j.jare.2026.01.011 .

52. Karačić A, Gregorovic R, Hammer P, Liberati-Prso AM, Krumbiegel C, Moskalenko O, Kralj S, Zeman K, Kspan E, Kamel A, Yoshida M. Long-term adherence to the carnivore diet and its impact on the gut microbiota: a cross-sectional study. Microbiota and Host. 2026. https://doi.org/10.1530/MAH-25-0015 .

53. Karagöz, M. F., Ünaldı, B. Ö., Buhurcu, C. A., Şen, N., Aydoğdu, G. S., Demirci, K. Ş., Gündüz, Z. G., Güler, M. S., Ağagündüz, D., & Coreta-Gomes, F. (2025). Seaweed polysaccharides and their potential health effects via gut microbiota modulation. Carbohydrate Polymers, 347, 122731. https://doi.org/10.1016/j.carbpol.2024.122731 .

54. Karagöz, M. F., Ünaldı, B. Ö., Buhurcu, C. A., Şen, N., Aydoğdu, G. S., Demirci, K. Ş., Gündüz, Z. G., Güler, M. S., Ağagündüz, D., & Coreta-Gomes, F. (2025). Seaweed polysaccharides and their potential health effects via gut microbiota modulation. Carbohydrate Polymers, 124621. https://doi.org/10.1016/j.carbpol.2025.124621 .

55. Keang, K., Cheng, S., Zhao, X., Wasnik, S., Zhang, H., & Cross, J. S. (2026). Co-exposure to microplastics and tire particles exacerbates oxidative stress and gut microbiome dysbiosis in zebrafish (Danio rerio). Environmental Research, 124069. https://doi.org/10.1016/j.envres.2026.124069 .

56. Kedia, S., & Ahuja, V. (2023). Human gut microbiome: A primer for the clinician. JGH Open, 7(5), 337–350. **https://doi.org/10.1002/jgh3.12902** .

57. Keung, W. S., Zhang, W. H., Luo, H. Y., Chan, K. C., Chan, Y. M., & Xu, J. (2025). Correlation between the structures of natural polysaccharides and their properties in regulating gut microbiota: Current understanding and beyond. Carbohydrate Polymers, 352, 123209. https://doi.org/10.1016/j.carbpol.2024.123209 .

58. Komori, E., Kato-Kogoe, N., Imai, Y., Sakaguchi, S., Taniguchi, K., Omori, M., Ohmichi, M., Hamada, W., Nakamura, S., Nakano, T., Lee, S. W., & Ueno, T. (2025). Gastrectomy-induced alterations in gut microbiota linked to changes in oral and gastric microbiota. Frontiers in Microbiology, 16, Article 1599503. **https://doi.org/10.3389/fmicb.2025.1599503** .

59. Kumoro, A. C., Wardhani, D. H., Kusworo, T. J., Azis, Y. M. F., Alhanif, M., & Ping, T. C. (2025). Unlocking the prebiotic carbohydrates: Insights into Indonesian exotic fruit seeds. Food Chemistry: X, 26, 102471. https://doi.org/10.1016/j.fochx.2025.102471 .

60. Li, A., Li, M., Xu, W., Zhang, Y., Yin, S., Yu, Y., Zheng, S., Hu, Y., & Song, M. (2025). Association between gut microbiota composition and liver dysfunction in school-aged children exposed to triclosan. Journal of Environmental Sciences. https://doi.org/10.1016/j.jes.2025.10.026 .

61. Li, J., Yuan, Z., Li, J., Liu, Z., Wang, Y., Cui, M., Suo, C., Jin, L., Ding, D., Chen, X., & Jiang, Y. (2025). Immune, blood-brain barrier, and metabolic biomarkers mediate gut-brain axis crosstalk in Alzheimer's disease. Biomarker Research, 13, 137. https://doi.org/10.1186/s40364-025-00851-6 .

62. Li, L., Yang, S., Liang, X., Liu, Y., Xu, H., Guo, X., Xie, C., & Xu, X. (2024). Saikosaponin D improves non-alcoholic fatty liver disease via gut microbiota-bile acid metabolism pathway. Food Science and Human Wellness, 13(5), 2703-2717. https://doi.org/10.26599/FSHW.2022.9250218 .

63. Li, N., Wen, X., He, X., Liang, R., Fan, J., Liao, D., Li, M., Wang, Y., & Luo, Y. (2026). Low molecular weight water-soluble Gastrodia elata polysaccharide GEP-2 alleviates DSS-induced ulcerative colitis by enhancing the intestinal barrier, modulating gut microbiota, and suppressing inflammation. International Journal of Biological Macromolecules, 343(Pt 2), 150385. https://doi.org/10.1016/j.ijbiomac.2026.150385 .

64. Li, Y., Wang, H., Bi, H., Feng, J., Gao, T., Dong, D., Li, G., Liu, B., Yuan, H., & Ni, W. (2025). A starch-like polysaccharide isolated from Hirsutella sinensis mycelia alleviates DSS-induced colitis in mice by strengthening the intestinal barrier, maintaining immune homeostasis, and modulating the gut microbiota and SCFA metabolism. Food Bioscience, 68, 106698. https://doi.org/10.1016/j.fbio.2025.106698.

65. Li, Z., Tao, X., Wang, D., Pu, J., Liu, Y., Gui, S., Zhong, X., Yang, D., Zhou, H., Tao, W., Chen, W., Chen, X., Chen, Y., Chen, X., & Xie, P. (2024). Alterations of the gut microbiota in patients with schizophrenia. Frontiers in Psychiatry, 15, 1366311. https://doi.org/10.3389/fpsyt.2024.1366311 .

66. Liu, J., Li, Z., Samui, S., Liu, X., & Yang, Y. (2025). Gut microbiome and metabolic health: mechanisms and precision interventions. Gut Microbes, 17(1), 2644677. https://doi.org/10.1080/19490976.2025.2644677 .

67. Liu, Y., Huang, Y., Zhu, R., Farag, M. A., Capanoglu, E., & Zhao, C. (2023). Structural elucidation approaches in carbohydrates: A comprehensive review on techniques and future trends. Food Chemistry .

68. Ma, Z., Zuo, T., Frey, N., & Rangrez, A. Y. (2024). A systematic framework for understanding the microbiome in human health and disease: from basic principles to clinical translation. Signal Transduction and Targeted Therapy, 9(23). https://doi.org/10.1038/s41392-024-01946-6 .

69. Martinez-Guryn, K., Hubert, N., Frazier, K., Urlass, S., Musch, M. W., Ojeda, P., Pierre, J. F., Miyoshi, J., Sontag, T. J., Cham, C. M., Reardon, C. A., Leone, V., & Chang, E. B. (2018). Small Intestine Microbiota Regulate Host Digestive and Absorptive Adaptive Responses to Dietary Lipids. Cell Host & Microbe, 23(4), 458–469.e5. https://doi.org/10.1016/j.chom.2018.03.011 .

70. Mohammed, A. S. A., Naveed, M., & Jost, N. (2021). Polysaccharides; Classification, Chemical Properties, and Future Perspective Applications in Fields of Pharmacology and Biological Medicine (A Review of Current Applications and Upcoming Potentialities). Journal of Polymers and the Environment, 29(8), 2359–2371. https://doi.org/10.1007/s10924-021-02052-2 .

71. Mohsen, E., Haffez, H., Ahmed, S., Hamed, S., & El-Mahdy, T. S. (2025). Multiple Sclerosis: A Story of the Interaction Between Gut Microbiome and Components of the

Immune System. Molecular Neurobiology. https://doi.org/10.1007/s12035-025-05194-9 .

72. Moraïs, S., Winkler, S., Zorea, A., Levin, L., Nagies, F. S. P., Kapust, N., Lamed, E., Artan-Furman, A., Bolam, D. N., Yadav, M. P., Bayer, E. A., Martin, W. F., & Mizrahi, I. (2024). Cryptic diversity of cellulose-degrading gut bacteria in industrialized humans. Science, 383(6688). https://doi.org/10.1126/science.adj9223 .

73. Muttiah, B., & Hanafiah, A. (2025). Gut microbiota and cardiovascular diseases: Unraveling the role of dysbiosis and microbial metabolites. International Journal of Molecular Sciences, 26(9), 4264. https://doi.org/10.3390/ijms26094264 .

74. Na, C., Shi, X., Fu, J., Li, J., Jiang, H., Guo, Z., Lai, H., Zhang, Z., Zhao, L., Yuan, Q., & Zhang, B. (2025). Pectic polysaccharides from Mongolian medicinal Hypecoum leptocarpum: Structure and ulcerative colitis amelioration via gut microbiota and intestinal inflammation regulation. Carbohydrate Polymers, 124717. https://doi.org/10.1016/j.carbpol.2025.124717 .

75. Naithani, S., Komath, S. S., Nonomura, A., & Govindjee, G. (2021). Plant lectins and their many roles: Carbohydrate-binding and beyond. Journal of Plant Physiology, 266, 153531 https://doi.org/10.1016/j.jplph.2021.153531 .

76. Nambidi, S., Sennie, N. S., Kondaveeti, S. B., Banerjee, A., & Duttaroy, A. K. (2025). A review of short-chain fatty acids in gut and skin: Possible implications in skin aging. Elsevier Journal of Functional Foods, 133, 107010. https://doi.org/10.1016/j.jff.2025.107010 .

77. Nayak, A., Bera, S., Purohit, S., & Jain, C. K. (2026). Gut microbiota mediated neuroinflammation in psychiatric disorders: Current perspectives and challenges. Behavioural Brain Research, 466, 116019. https://doi.org/10.1016/j.bbr.2025.116019 .

78. Obayomi, O. V., Olaniran, A. F., Malomo, A. A., Agaja, F. O., Olojede, A. O., & Osemwegie, O. O. (2025). Gut dysbiosis and chronic diseases: Unraveling contributing

factors, health implications, and therapeutic interventions. Food and Humanity, 5, Article 100892. https://doi.org/10.1016/j.foohum.2025.100892 .

79. Obino, G., Nieddu, G., Nagy, M., Formato, M., Lapedda, A. J., & Moroni, L. (2025). Marine-derived sulfated polysaccharides enhance hemocompatibility and endothelialization of nanofibrous PCL for vascular graft applications. Cell Biomaterials, 1, 100155. https://doi.org/10.1016/j.cellbi.2025.100155 .

80. Ohland, C. L., & Jobin, C. (2015). Microbial activities and intestinal homeostasis: A delicate balance between health and disease. Cellular and Molecular Gastroenterology and Hepatology, 1(1), 28–40. https://doi.org/10.1016/j.jcmgh.2014.11.004 .

81. Pastrana-Alta, R.Y., Huarote-Garcia, E., Egusquiza-Huamaní, M.A., & Baena-Moncada, A.M. (2025). Antimicrobial activity of chitosan, alginate, pectin, and cellulose-based biopolymer composites with silver, copper oxide, and zinc oxide nanoparticles. RSC Advances, 15, 35807-35843. https://doi.org/10.1039/d5ra01892g .

82. Payling, L., Fraser, K., Loveday, S. M., Sims, I., Roy, N., & McNabb, W. (2020). The effects of carbohydrate structure on the composition and functionality of the human gut microbiota. Trends in Food Science & Technology, 97, 233–244. https://doi.org/10.1016/j.tifs.2020.01.009 .

83. Pfaffinger, J. M., Hays, K. E., Seeley, J., Ramesh Babu, P., & Ryznar, R. (2025). Gut dysbiosis as a potential driver of Parkinson's and Alzheimer's disease pathogenesis. Frontiers in Neuroscience, 19, 1600148. https://doi.org/10.3389/fnins.2025.1600148 .

84. Porter, N. T., & Martens, E. C. (2017). The critical roles of polysaccharides in gut microbial ecology and physiology. Annual Review of Microbiology, 71, 349–369. https://doi.org/10.1146/annurev-micro-102215-095316 .

85. Radford-Smith, D. E., Oke, K., Costa, C. F. F. A., & Anthony, D. C. (2025). Systematic review and meta-analysis of microbiota-gut-astrocyte axis perturbation in

neurodegeneration, brain injury, and mood disorders. Brain, Behavior, & Immunity - Health, 46, 101013. https://doi.org/10.1016/j.bbih.2025.101013 .

86. Rehman, S. S. U., Nasar, M. I., Mesquita, C. S., Al Khodor, S., Notebaart, R. A., Ott, S., Mundra, S., Arasardanam, R. P., Muhammad, K., & Alam, M. T. (2025). Integrative systems biology approaches for analyzing microbiome dysbiosis and species interactions. Briefings in Bioinformatics, 26(4), bbaf323. https://doi.org/10.1093/bib/bbaf323 .

87. Samee Ullah, Khalil A.A., Shaukat F., Song Y. (2019). Sources, Extraction and Biomedical Properties of Polysaccharides. Foods, 8(8), 304. https://doi.org/10.3390/foods8080304 .

88. Sharma, A., Andreani, N. A., Keller, L., Herpertz-Dahlmann, B., Seitz, J., Baines, J. F., & Dempfle, A. (2025). Comparison of 16S ribosomal RNA hypervariable regions in microbiome studies of anorexia nervosa. Frontiers in Microbiology, 16, 1665847. https://doi.org/10.3389/fmicb.2025.1665847 .

89. Shayista, H., Nagendra Prasad, M. N. N., Niranjan Raj, S., Prasad, A., Lakshmi, S., Ranjini, H. K., ... & Baker, S. (2025). Complexity of antibiotic resistance and its impact on gut microbiota dynamics. Engineering Microbiology, 5, 100187. https://doi.org/10.1016/j.engmic.2024.100187 .

90. Stribling, P., & Ibrahim, F. (2023). Dietary fibre definition revisited - The case of low molecular weight carbohydrates. Clinical Nutrition ESPEN, 55, 340–356. https://doi.org/10.1016/j.clnesp.2023.04.012 .

91. Stylianopoulos, C. (2013). Carbohydrates: Chemistry and Classification. In Encyclopedia of Human Nutrition (3rd ed., pp. 265–271). Elsevier. https://doi.org/10.1016/B978-0-12-375083-9.00041-6 .

92. Subhash, A. J., Abdin, M., Bamigbade, G. B., Arachchi, M. P., Ullah, N., & Ayyash, M. (2026). A comprehensive review on structural, chemical, and functional perspectives

of dietary polysaccharide-driven gut microbiota modulation: Mechanisms and challenges. Biochemistry and Biophysics Reports, 46, 102575. https://doi.org/10.1016/j.bbrep.2026.102575 .

93. Sui, D., Li, M., Ai, C., Li, S., Chang, H., Li, Y., Zhao, S., Li, H., & Ren, X. (2025). Larimichthys crocea isinglass polysaccharide attenuates DSS-induced colitis via gut microbiota regulation and NF-κB signaling inhibition. International Journal of Biological Macromolecules, 307(Pt 3), 142263. https://doi.org/10.1016/j.ijbiomac.2025.142263 .

94. Sun, J., Chen, Y., Li, X., Feng, Y., Sun, R., Li, Z., Yu, D., Lu, L., Tian, L., & Li, Y. (2026). Red rice seed coat maintained intestinal homeostasis in mice by alleviating inflammation, improving barrier function and modulating gut microbiota dysbiosis. Journal of Future Foods. https://doi.org/10.1016/j.jfutfo.2025.12.046 .

95. Tang M., Cheng L., Liu Y., Wu Z., Zhang X., Luo S. (2022). Plant Polysaccharides Modulate Immune Function via the Gut Microbiome and May Have Potential in COVID-19 Therapy. Molecules, 27(9), 2773. https://doi.org/10.3390/molecules27092773 .

96. Tarique, M., Ali, A. H., Kizhakkayil, J., Liu, S. Q., Oz, F., Dertli, E., Kamal-Eldin, A., & Ayyash, M. (2024). Exopolysaccharides from Enterococcus faecium and Streptococcus thermophilus: Bioactivities, gut microbiome effects, and fermented milk rheology. Food Chemistry: X, 21, 101073. https://doi.org/10.1016/j.fochx.2023.101073

97. Tian, H., Wen, Z., Chen, J., Zhao, C., Yang, C., Guo, Y., & Sun, B. (2025). Alleviation of DSS-induced ulcerative colitis by pomelo peel polysaccharides: Exploration for the potential mechanism from comprehensive analysis of multi-omics. Food Bioscience, 105955. https://doi.org/10.1016/j.fbio.2025.1059 .

98. Trehan, S., Singh, G., Bector, G., Jain, P., Mehta, T., Goswami, K., Chawla, A., Jain, A., Puri, P., & Garg, N. (2024). Gut Dysbiosis and Cardiovascular Health: A

Comprehensive Review of Mechanisms and Therapeutic Potential. Cureus, 16(8) , e67010. https://doi.org/10.7759/cureus.67010 .

99. Ullah, S., Khalil, A. A., Shaukat, F., & Song, Y. (2019). Sources, extraction and biomedical properties of polysaccharides. Foods, 8(8), 304.

100. Vachher, M., Kaur, K., Marothia, M., Burman, A., Deepanjana, & Bansal, S. (2025). Deciphering the role of dietary modifications and gut dysbiosis in Non-Alcoholic Fatty Liver Disease. Human Nutrition & Metabolism, 40, 200305. https://ouci.dntb.gov.ua/en/works/7qEmWLpe/.

101. Vos, W. M., Tilg, H., Van Hul, M., & Cani, P. D. (2022). Gut microbiome and health: mechanistic insights. Gut, 71(5), 1020–1032. https://doi.org/10.1136/gutjnl-2021-326789 .

102. Wan, J., Wang, F., Xiao, Y., Cheng, Y., Zheng, S., Jiang, Q., Tan, B., Li, X., Chen, J., & Liao, S. (2024). Poria cocos polysaccharide alleviates dextran sulphate sodium-induced ulcerative colitis in mice by modulating intestinal inflammatory responses and microbial dysbiosis. International Journal of Biological Macromolecules, 137450. https://doi.org/10.1016/j.ijbiomac.2024.137450 .

103. Wang Z, Wei X, Piao L, Zhang X and Wang H (2025) Gut microbiota dysbiosis and metabolic shifts in pediatric norovirus infection: a metagenomic study in Northeast China. Frontiers in Cellular and Infection Microbiology. 15:1600470. 10.3389/fcimb.2025.1600470 .

104. Wang, J. H., Choi, Y., Lee, J. S., Hwang, S. J., Gu, J., & Son, C. G. (2023). Clinical evidence of the link between gut microbiome and myalgic encephalomyelitis/chronic fatigue syndrome: a retrospective review. Journal of Translational Medicine, 21(1), 610. https://doi.org/10.1186/s12967-023-04565-1

105. Wang, J., Wang, J., Kang, Z., Pei, J., Xia, G., He, R., & Chen, H. (2025). Structural elucidation of polysaccharide from fresh Areca catechu L. and its mitigation effect on

DSS-induced colitis in mice. International Journal of Biological Macromolecules, 318(Pt 1), 145074. https://doi.org/10.1016/j.ijbiomac.2025.145074 .

106. Wang, X., Yu, C., Li, Y., Zhang, M., Zhang, J., & Wang, H. (2025). Dietary polysaccharides as gut health regulators: Structural characteristics and regulatory mechanism. Trends in Food Science & Technology, 161, 105074. https://doi.org/10.1016/j.tifs.2025.105074 .

107. Wang, Y., Li, J., Hou, Y., Wang, J., & Lu, J. (2026). Structural characteristics of Ficus carica L. dietary fibers and their in vitro fermentation properties in modulating gut microbiota and metabolites. Food Chemistry: X, 34, 103588. https://doi.org/10.1016/j.fochx.2026.103588 .

108. Wang, Z., Gao, C., Chen, Q., Wang, K., & Fan, B. (2023). A comprehensive perspective on melanoidins: definitions, polymerization, chromogenic mechanism, cross-linking, and bioactivity. Food Chemistry Advances, 9, 101181. https://doi.org/10.1016/j.foodchem.2024.108181 .

109. Wei, N., Ju, M., Su, X., Zhang, Y., Huang, Y., Rao, X., Cai, L., Lin, Z., & Dong, Y. (2024). Transplantation of gut microbiota derived from patients with schizophrenia induces schizophrenia-like behaviors and dysregulated brain transcript response in mice. Schizophrenia, 10(1), 14. https://doi.org/10.1038/s41537-024-00460-6 .

110. Wei, S., Sun, Y., Li, X., & Xue, J. (2026). From gut to whole body: Natural polysaccharide-based multi-axis network strategies for systemic disease adjuvant therapy. Trends in Food Science & Technology, 168, 105481.https://doi.org/10.1016/j.tifs.2025.105481 .

111. Wei, S., Sun, Y., Li, X., & Xue, J. (2026). From gut to whole body: Natural polysaccharide-based multi-axis network strategies for systemic disease adjuvant therapy. Trends in Food Science & Technology, 168, 105481.

112. Wen, M., Liu, M., Zhang, Y., Qiao, B., Luo, T., Liu, G., Li, D., & Zhou, B. (2025). Gastrodia elata polysaccharide alleviates depression via gut microbiota modulation and Keap1-Nrf2/BDNF-TrkB pathway activation. International Journal of Biological Macromolecules, 317, 144630. https://doi.org/10.1016/j.ijbiomac.2025.144630 .

113. Wright, M. L., Fournier, C., & Hertzberg, V. S. (2018). Potential role of the gut microbiome in ALS: A systematic review. Biological Research for Nursing, 20(5), 513–521. https://doi.org/10.1177/1099800418784202 .

114. Wu, G., Gu, W., Chen, G., Cheng, H., Li, D., & Xie, Z. (2023). Interactions of tea polysaccharides with gut microbiota and their health-promoting effects to host: Advances and perspectives. Food Hydrocolloids. https://doi.org/10.1016/j.jff.2023.105468 .

115. Xiao, X., Wang, W., Liu, F., Dong, Q., Maffei, D. F., Xiao, Y., Yang, H., & Wang, W. (2025). Exploring the effect of viable but non-culturable (VBNC) state Salmonella Enteritidis on gut microbiome imbalance in an infectious colitis model. Journal of Future Foods. (Journal Pre-proof). https://doi.org/10.1016/j.jfutfo.2025.05.016 .

116. Xiong, Y., Qiu, H., Chen, Y., Yong, J., Mueed, A., & You, L. (2026). Sulfated polysaccharide from Laminaria japonica alleviated colitis via remodeling gut microbiota and promoting butyrate-mediated barrier repair. International Journal of Biological Macromolecules, 151462. https://doi.org/10.1016/j.ijbiomac.2026.151462 .

117. Xue, H., Tang, Y., Zha, M., Xie, K., & Tan, J. (2025). The structure-function relationships and interaction between polysaccharides and intestinal microbiota: A review. International Journal of Biological Macromolecules, 291, 139063. https://doi.org/10.1016/j.ijbiomac.2024.139063 .

118. Yakut, A. (2025). Gut microbiota in the development and progression of chronic liver diseases: Gut microbiota-liver axis. World Journal of Hepatology, 17(3), 104167. https://doi.org/10.4254/wjh.v17.i3.104167 .

119. Yang, J., Huang, Q., Long, J., & Li, J. (2025). Microbiota and inflammatory bowel disease: the dual effect mechanism of polysaccharide therapy. Frontiers in Immunology, 16, 1666866.https://doi.org/10.3389/fimmu.2025.1666866 .

120. Yang, K., Li, G., Li, Q., Wang, W., Zhao, X., Shao, N., Qiu, H., Liu, J., Xu, L., & Zhao, J. (2025.). Distribution of gut microbiota across intestinal segments and their impact on human physiological and pathological processes. Journal name not specified. https://doi.org/10.1186/s13578-025-01385-y .

121. Yang, W., Yang, Y., Wu, W., Ou, Y., Hong, T., Li, Z., Zhu, Y., Ni, H., Jiang, Z., & Zheng, M. (2026). Bangia fusco-purpurea polysaccharides attenuate DSS-induced colitis in mice through gut microbiota and its metabolism modulation. Journal of Future Foods. Advance online publication. https://doi.org/10.1016/j.jfutfo.2026.03.017 .

122. Yang, Y., Liang, M., Ouyang, D., Tong, H., Wu, M., & Su, L. (2022). Research Progress on the Protective Effect of Brown Algae-Derived Polysaccharides on Metabolic Diseases and Intestinal Barrier Injury. International Journal of Molecular Sciences, 23(18), 10784. https://doi.org/10.3390/ijms231810784 .

123. Yassin, L. K., Skrabulyte-Barbulescu, J., Alshamsi, S. H., Saeed, S., Alkuwaiti, S. H., Almazrouei, S., Alnuaimi, A., BaniYas, S., Aldhaheri, D., Alderei, M., Shehab, S., & Hamad, M. I. K. (2025). The microbiota–gut–brain axis in mental and neurodegenerative disorders: opportunities for prevention and intervention. Frontiers in Aging Neuroscience, 17, 1667448. https://doi.org/10.3389/fnagi.2025.16674 .

124. Yassin, L. K., Skrabulyte-Barbulescu, J., Alshamsi, S. H., Saeed, S., Alkuwaiti, S. H., Almazrouei, S., Alnuaimi, A., BaniYas, S., Aldhaheri, D., Alderei, M., Shehab, S., & Hamad, M. I. K. (2025). The microbiota–gut–brain axis in mental and neurodegenerative disorders: opportunities for prevention and intervention. Frontiers in Aging Neuroscience,17, 1667448. https://doi.org/10.3389/fnagi.2025.1667448 .

125. Ye, Y., Deng, X., Yang, L., Cai, K., Xu, Y., Chen, K., Luo, X., Liang, W., Cheng, P., & Jia, L. (2025). Structural characteristics of Phaeodactylum tricornutum

polysaccharides and the effects on DSS-induced colitis via improving the intestinal barrier and modulating the gut microbiota. International Journal of Biological Macromolecules, 144685. https://doi.org/10.1016/j.ijbiomac.2025.144685 .

126. Yi, X., Zhu, H., He, M., Gao, S., & Li, M. (2026). Decoding Links between Gut Microbiota and Metabolic-associated Fatty Liver Disease: Meta-analysis and Mediation Study Uncover Species-specific Taxa and a Novel Bile Acid Mediator. Biomedical and Environmental Sciences, 39(2), 202-214. https://doi.org/10.3967/bes2025.162

127. Yu, B., Zhao, W. W., Tao, L., & Li, K. (2026). The microbiota-gut-brain axis perspective: mechanisms and intervention strategies for the comorbidity of chronic constipation and depression. Frontiers in Microbiology, 17, 1800520.

128. Zajkowska, I., Niczyporuk, P., Urbaniak, A., Tomaszek, N., Modzelewski, S., & Waszkiewicz, N. (2024). Investigating the Impacts of Diet, Supplementation, Microbiota, Gut-Brain Axis on Schizophrenia: A Narrative Review. Nutrients, 16(14), 2228. https://doi.org/10.3390/nu16142228 .

129. Zang, L., Baharlooeian, M., Terasawa, M., Shimada, Y., & Nishimura, N. (2023). Beneficial effects of seaweed-derived components on metabolic syndrome via gut microbiota modulation. Frontiers in Nutrition, 10, 1173225. https://doi.org/10.3389/fnut.2023.1173225 .

130. Zhang, D., Liu, J., Cheng, H., Wang, H., Tan, Y., Feng, W., & Peng, C. (2022). Interactions between polysaccharides and gut microbiota: A metabolomic and microbial review. Food Research International, 160, 111653. https://doi.org/10.1016/j.foodres.2022.111653 .

131. Zhang, H., Koshani, R., Pitcher, M. L., Yu, J., Mahajan, C. L., Kim, S. H., & Sheikhi, A. (2025). Plant Cell Wall-Like Soft Materials: Micro- and Nanoengineering, Properties, and Applications. Nano-Micro Letters, 17, 103. https://doi.org/10.1007/s40820-024-01569-0 .

132. Zhang, H., Tang, Y., Ge, H., Tong, H., Yang, L., Zhang, T., Han, C., & Liu, C. (2025). Sodium alginate supplementation can alleviate non-alcoholic fatty liver disease in rats by restoring hepatic lipid metabolism and gut microbiota. Current Research in Food Science, 11, 101199. https://doi.org/10.1016/j.crfs.2025.101199 .

133. Zhang, J., Ma, Y., Chang, R., Wang, R., & Zhang, J. (2026). The interplay of plant polysaccharide structure, gut microbiota metabolism, and host health: Mechanisms and perspectives. Life Sciences, 124383. https://doi.org/10.1016/j.lfs.2026.124383 .

134. Zhang, Q., Liu, Y., Tang, R., Kong, S., Lv, D., Li, H., Yang, H., & Lin, L. (2024). Gut microbiota and its metabolites: A potential approach for traditional Chinese medicine-derived non-starch polysaccharides to delay aging and prevent age-related diseases—A review. Carbohydrate Polymer Technologies and Applications, 8, 100567. https://doi.org/10.1016/j.carpta.2024.100567 .

135. Zhou, S., Su, F., Gao, Q., Wang, M., Duan, J., & Li, J. (2026). Cordyceps cicadae polysaccharides ameliorate ulcerative colitis by modulating the gut microbiota and regulating the bile acid/FXR/NF-κB signaling pathway. Phytomedicine, 153, 158007. https://doi.org/10.1016/j.phymed.2026.158007 .

136. Zhu, D., Li, R., Sun, Y., Li, Y., Ruan, J., & Wang, J. (2026). Coreopsis tinctoria buds polysaccharides boost metformin's antihyperglycemic effect in diabetic mice via gut microbiota and metabolism modulation. Industrial Crops & Products, 226, 122574. https://doi.org/10.1016/j.indcrop.2025.122574 .

137. Zhu, J., Tao, K., Prakash, S., Zhang, C., Gilbert, R. G., & Liu, Q. (2023). Using starch structure to choose rices with an optimal combination of palatability and digestibility. Food Hydrocolloids, 141, 108763. https://doi.org/10.1016/j.foodhyd.2023.108763 .