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Review

Gut Feeling: How Plants and Gut Microbes Team Up

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Abstract: Plants and gut microbes work together to produce metabolites that shape immunity, metabolism, and mood. Every plant we eat brings fibres, polyphenols, and other natural compounds into the gut. Many of these arrive in large, complex forms that human enzymes cannot fully break down. Gut microbes complete the job. They convert stubborn plant molecules into smaller and more active metabolites that support the immune system, strengthen the gut barrier, regulate energy balance, and communicate with the brain. Fresh plant foods also carry their own tiny microbial communities, adding chemical variety and expanding what the gut ecosystem can do. Diets rich in whole and diverse plants encourage a more resilient microbiota and a broader pool of beneficial metabolites. Similar chemical teamwork occurs in plant roots and soils, offering a simple way to understand cooperation across ecosystems. This review introduces the core ideas behind plant-microbe collaboration and prepares the ground for the next chapter in the *Gut Feeling* series, where the journey of natural products through microbial transformation becomes the central story.

Keywords: gut microbiota; plant natural products; dietary fibre; polyphenols; microbial metabolism; microbial metabolites; gut-brain axis; precision nutrition

1. Introduction

Life on Earth has always depended on partnerships between organisms and the microbes that support survival, growth, and adaptation [1]. These long relationships shaped the evolution of plants, animals, and humans through shared biochemical abilities and co-adapted metabolic strategies [2]. Modern ecosystems still reflect these connections in plant holobionts, edible microbiomes on fruits and vegetables, and the human gut community, all functioning as integrated systems shaped by microbial activity [3,4]. Plants and humans rely on microbes for nutrient access, defence, and metabolic stability, forming a continuous link between soil, plants, food, and the gut [5,6]. This link explains how plant chemistry, microbial metabolism, and dietary patterns interact across environments to influence health [7]. It also provides the ecological and evolutionary background for understanding plant-microbe cooperation. Figure 1 maps the ecological and biochemical relationships that position plants and microbes as an interdependent team.

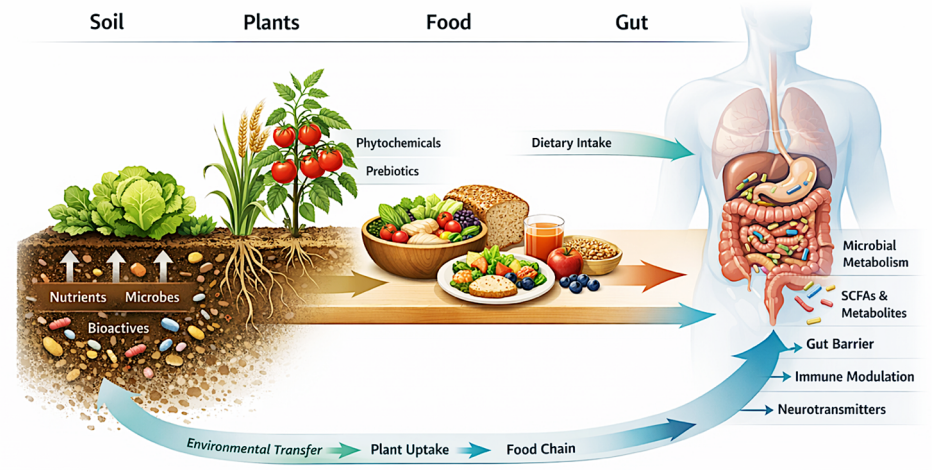

Figure 1. Plants and microbes are connected as a team.

1.1. Plants Deliver Complex Chemistry

Plants supply a wide range of chemicals that enter the gut as structured mixtures shaped by evolution and microbial signals [8,9]. Fibres, polyphenols, flavonoids, terpenoids, tannins, alkaloids, and many smaller compounds reflect defence, communication, and nutritional strategies across species [10]. Each plant food contains hundreds of molecules, and this chemical variety forms the base of dietary complexity. Plant-rich diets deliver broader chemical diversity to the gut, supporting richer microbial communities and more stable metabolic functions [11,12]. Microbes living on plants influence this output by shaping precursor availability, redox balance, and stress-linked pathways [13,14]. Plant foods act as chemical inputs rather than simple energy sources, and their composition determines how gut microbes respond and produce metabolites that influence physiology.

1.2. Many Plant Compounds Reach the Colon Intact

The digestive system absorbs simple sugars, amino acids, and fats efficiently, but most fibres, complex polyphenols, and many secondary metabolites resist breakdown in the upper gut [15,16]. These compounds keep their structure through the stomach and small intestine, and this persistence determines where microbial metabolism begins. Many dietary polyphenols reach the colon unchanged, where microbial enzymes carry out the main phase of their transformation [17,18]. The colon becomes the key site where plant chemistry meets microbial capability. The intact arrival of these compounds provides substrates for fermentation, reduction, dehydroxylation, and other microbial reactions that generate metabolites with higher bioavailability and stronger physiological effects [19,20]. Structural resilience shapes the metabolic landscape of the colon and supports the partnership between diet and the gut microbiota.

1.3. Fibres as Primary Microbial Substrates

Fibres form the largest group of plant compounds that escape digestion in the upper gut. Cellulose, hemicellulose, pectins, inulin, beta-glucans, and resistant starches pass through the stomach and small intestine intact because human enzymes cannot break their structural bonds [15]. These undigested fibres reach the colon as major substrates for microbial fermentation, driving SCFA production that supports epithelial energy needs, immune balance, and metabolic regulation [21,22]. SCFA formation lowers colonic pH and shapes ecological selection within the gut, favouring microbes adapted to complex carbohydrate breakdown [23,24]. Fibre-rich diets strengthen microbial diversity and functional stability, reflecting the central role of fibres in maintaining gut resilience [11]. Structural variety determines microbial access, fermentation capacity, and the metabolic signals that influence physiology.

1.4. Polyphenols and Other Bioactive Compounds

Polyphenols form one of the most diverse groups of plant metabolites and enter the gut in complex forms that require microbial processing before they can affect the body [10,18]. Fruits, vegetables, tea, cocoa, herbs, and spices supply large polyphenolic structures that remain poorly absorbed in the upper gut, and their biological value depends on microbial access in the colon [19]. Microbial enzymes convert these compounds into smaller and more bioavailable metabolites with stronger effects on inflammation, oxidative balance, barrier function, and metabolic pathways [25,26]. Chemical structure determines microbial accessibility, reaction sequence, and conversion efficiency [20]. Terpenoids and alkaloids follow similar principles because their activity relies on microbial modification rather than host enzymes [9,12]. These interactions explain why plant-rich diets influence gut ecology and physiology through chemical diversity and microbial transformation [27]. Table 1 outlines the major classes of plant compounds and their gut-relevant features

Table 1. Major classes of plant compounds and their gut relevant features.

Compound Class	Key Features	Microbial Transformations	Physiological Relevance	References
Fibres	Cellulose, hemicellulose, pectins, inulin, resistant starches	Fermentation to acetate, propionate, and butyrate	SCFA production, pH lowering, epithelial energy	[15,21–24]
Polyphenols	Flavonoids, phenolic acids, tannins, lignans	Deglycosylation, dehydroxylation, demethylation, ring-cleavage	Anti-inflammatory effects, redox balance	[18–20,25,26]
Terpenoids	Mono-, di-, and triterpenes	Reduction and dehydroxylation	Antioxidant and membrane effects	[9,12]
Alkaloids	Nitrogen-containing metabolites	Deamination and demethylation	Neuromodulatory and metabolic effects	[9,12]

1.5. Phytochemicals Shaping Microbial Balance

Phytochemicals act as ecological signals within the gut by supporting beneficial microbes and limiting harmful taxa. Compounds from berries, green tea, turmeric, legumes, and leafy vegetables modulate microbial composition through antioxidant activity, redox regulation, and selective effects on microbial metabolism [12,22]. Polyphenol-derived metabolites influence microbial growth by altering redox gradients and shaping competitive interactions [19]. Terpenoids and alkaloids contribute by modulating quorum sensing, membrane integrity, and metabolic flux [9,12]. These interactions stabilise the gut environment and help explain why plant-rich diets support microbial resilience [11]. Phytochemicals function as modulators of microbial ecology and metabolic output [27].

1.6. Plant-associated Microbes Entering the Gut

Fresh fruits and vegetables harbour microbial communities from the phyllosphere, endosphere, rhizosphere, and surrounding environment [3,4]. These microbes reach the gut during consumption and expand the microbial exposures that influence gut ecology. Some persist at low abundance and contribute to the metabolic potential of the gut community [5]. Plant microbiomes shape nutrient flow, redox balance, and chemical composition within plant tissues, modifying the substrates that arrive in the gut [6,28]. Although their contribution is modest compared with resident microbes, plant-associated taxa demonstrate how plants function as both chemical and microbial inputs to the gut ecosystem [27]. Figure 2 presents the soil-plant-food-gut continuum.

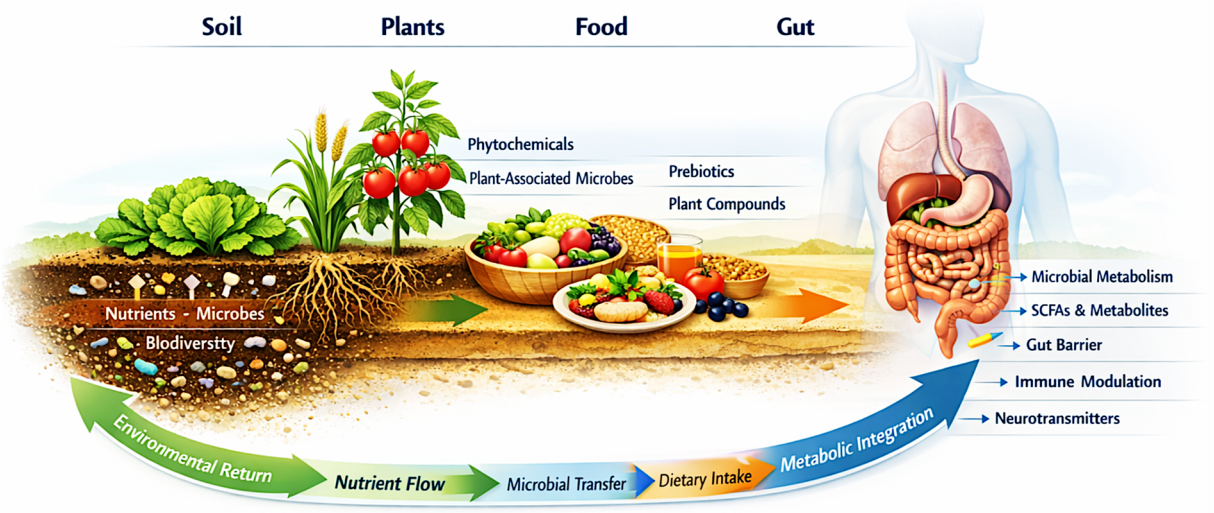

Figure 2. Soil-plant-food-gut continuum showing nutrient flow, microbial transfer, and metabolic integration.

1.7. Dietary Patterns Influence What Reaches the Gut

Dietary choices govern which plant compounds reach the colon. Whole foods and traditional plant-based diets supply higher levels of fibres, polyphenols, and other bioactive compounds, whereas processed foods limit chemical variety [11]. These patterns direct microbial metabolism by altering substrate availability, fermentation capacity, and metabolite profiles [18,25]. Plant-rich diets support microbial diversity, metabolic stability, and resilience against disturbance [29]. Daily eating habits define the chemical landscape inside the gut and steer the metabolic signals that influence physiology [27].

1.8. Aim of this Review

Plants deliver complex chemistry that enters the gut and becomes available to microbes that convert it into smaller and more active metabolites [27]. These metabolites affect immunity, metabolism, barrier integrity, and neuroimmune balance, as shown by evidence that plant-derived phytochemicals modulate microbial communities linked to metabolic, immune, and neurological functions [21,22]. Additional studies show that microbial metabolites regulate host metabolic pathways and gut-brain communication [18,30]. This review examines ecological and evolutionary links between plants, food, and the human gut microbiome [5]. It explores how plant-associated microbes add to human microbial diversity [3], how diet shapes microbial metabolism [18], and how these interactions influence health across systems [7]. The review establishes a clear foundation for understanding

the continuum that connects soil, plants, food, and the gut, preparing the ground for the next chapter in the *Gut Feeling* series.

2. Microbial Transformation of Plant Compounds

Microbes decide how much value humans gain from plant foods. They convert large phytochemicals into smaller metabolites that the body can absorb and use more effectively. This transformation depends on microbial enzymes, and these enzyme sets vary widely across species with different metabolic capacities [11,15]. Plant-associated microbes show strong biotransformation abilities in soils, roots, and other environments, offering clues about how microbial enzymes remodel plant molecules across ecosystems [31,32]. These same capacities support reactions that generate urolithins, equol, phenolic acids, indole derivatives, and SCFAs, metabolites that influence immunity, metabolism, barrier integrity, and gut-brain communication [18,19,27,33].

2.1. Deglycosylation as the Gateway to Bioactivity

Deglycosylation often forms the first step in unlocking plant compounds. This reaction removes sugar groups from glycosylated molecules and increases their ability to cross mucosal surfaces. Microbial beta-glucosidases, alpha-arabinosidases, and beta-xylosidases perform this step and convert flavonoid glycosides into aglycones that act as precursors for metabolites such as equol and urolithins [19,20]. Gut microbes possess a broad repertoire of glycoside-cleaving enzymes that grant metabolic flexibility and enable efficient processing of dietary polyphenols, a capacity mirrored in plant-associated microbial systems [13,34]. Through these shared enzymatic classes, microbial communities convert structurally complex polyphenols into smaller, bioactive intermediates that carry greater physiological relevance for the host [18,27]. Deglycosylation forms the critical entry point to this pathway, opening microbial access to otherwise inaccessible plant-derived compounds.

2.2. Demethylation and Dehydroxylation Extend Metabolic Diversity

Demethylation and dehydroxylation expand the chemical diversity of plant-derived intermediates by altering aromatic ring patterns. Microbial methylesterases, oxidoreductases, and dehydroxylases perform these reactions and generate metabolites with altered solubility, redox behaviour, and receptor affinity [19]. Stress-adapted microbial consortia, including arbuscular mycorrhizal fungi (AMF)-associated systems, show enhanced phenolic-modifying capacity during salinity and drought, reflecting coordinated metabolic responses that reshape plant chemistry [14,35]. These enzyme systems mirror gut microbial pathways that remodel lignans into enterolignans and isoflavones into equol, and they support the formation of phenylpropionic and phenylacetic acids that accumulate in the colon after flavonoid metabolism [18]. Demethylation and dehydroxylation extend metabolic diversity and generate intermediates with distinct physiological actions [27].

2.3. Ring-cleavage as a Decisive Structural Transformation

Ring-cleavage represents one of the most decisive structural transitions in plant–microbe metabolism. Gut microbial dioxygenases, hydrolases, and decarboxylases open bulky aromatic rings and convert them into smaller metabolites with distinct biological activities [19,20]. These pathways enable the breakdown of chemically stable phenolic structures in the human gut, supporting the formation of intermediates that influence inflammatory signalling, mitochondrial function, and epithelial resilience [18,27,36]. By dismantling rigid aromatic frameworks, ring-cleavage increases bioavailability and functional potency, generating physiologically active metabolites from otherwise inaccessible plant compounds. Table 2 summarises the core microbial enzymatic functions involved in transforming plant-derived substrates.

Table 2. Core microbial enzymatic functions in plant metabolism.

Enzyme Class	Reaction Type	Resulting Metabolites	Functional Significance	References
Beta-glucosidases	Deglycosylation	Aglycones	Increased absorption and bioactivity	[19,20]
Dehydroxylases	Dehydroxylation	Phenylpropionic acids	Altered redox behaviour and receptor affinity	[18,19]
Demethylases	Demethylation	Demethylated intermediates	Enhanced microbial accessibility	[18]
Dioxygenases	Ring-cleavage	Urolithins, phenolic acids	Formation of absorbable metabolites	[19,20]

2.4. Fermentation of Plant Substrates to Short-Chain Fatty Acids

Short-chain fatty acids (SCFAs) formation represents the largest quantitative output of microbial transformation of dietary plant substrates. Acetate, propionate, and butyrate arise from cooperative fermentation carried out by multi-species consortia that specialise in polysaccharide degradation within the human gut [23,24]. These metabolites support epithelial energy demands, reinforce tight-junction structure, regulate immune tone, and influence metabolic pathways through receptor-mediated and epigenetic mechanisms [21,22]. Comparative analyses of plant-associated microbial communities under nutrient-limited conditions highlight the conservation of core carbohydrate-fermenting metabolic modules across ecosystems, providing ecological context for the efficiency and resilience of analogous pathways in gut consortia [37]. Within the colon, SCFAs further shape microbial ecology by lowering luminal pH and selectively enriching taxa adapted to fibre fermentation [29]. SCFAs production connects plant substrates, microbes, and host physiology as a key metabolic pathway [27].

2.5. Conversion of Polyphenols into Bioactive Metabolites

Microbial conversion of polyphenols generates metabolites that frequently exceed their parent compounds in biological potency. Phenolic-modifying capacities observed in plant-associated microbial communities highlight the breadth of enzymatic repertoires capable of transforming complex aromatic structures, providing ecological context for analogous processes in the human gut [38,39]. Within the gastrointestinal tract, polyphenols undergo sequential deglycosylation, reduction, dehydroxylation, demethylation, and ring-cleavage, yielding phenolic acids, hydroxycinnamic derivatives, and microbially exclusive metabolites such as urolithins [18,19]. These metabolites modulate inflammatory signalling, oxidative stress, mitochondrial function, vascular tone, and metabolic resilience [25,26]. Polyphenol transformation therefore represents a central route through which plant chemistry exerts physiological influence on the host [27].

2.6. Indole and Nitrogen-Derived Metabolites

Tryptophan-modifying gut microbes generate a diverse repertoire of indole derivatives that support epithelial homeostasis, immune regulation, and neuroimmune communication. Comparative analyses of microbial communities across environments show that tryptophan-linked enzymatic pathways are widely conserved, reflecting shared biochemical strategies for nitrogen handling and secondary metabolite transformation that provide ecological context for gut microbial metabolism [40,41]. Within the gastrointestinal tract, bacteria convert tryptophan into indole-3-propionic acid, indole-3-lactic acid, tryptamine, and related intermediates that act as aryl hydrocarbon receptor ligands and regulate IL-22 production, barrier repair, and mucosal tolerance [42–44]. Additional evidence links indole metabolites to metabolic regulation, oxidative balance, and neuroprotective signalling pathways [33,45]. Indole- and nitrogen-derived metabolites therefore form a major axis through which microbial metabolism translates plant chemistry into physiological signals in the host [27].

3. Plants as Chemical Ecologies

Plants behave like living chemical ecosystems shaped by surrounding microbes [31,34,35]. Fibres, polyphenols, terpenoids, alkaloids, organic acids, and specialised metabolites accumulate under drought, nutrient stress, salinity, and pathogen pressure [31,34,35]. Microbes influence these responses by modulating nutrient flow, redox balance, phytohormone signals, and metabolic pathways that define plant tissue chemistry [13,14,46]. Plant microbiota boost chemical diversity by modifying precursors, increasing antioxidant levels, and changing phenolic and terpenoid profiles during stress [32,47]. These ecological interactions mirror human gut processes, where microbial communities remodel dietary substrates into metabolites with enhanced bioactivity [11,19,27]. Plants act as chemical ecologies whose outputs become starting materials for microbial metabolism after ingestion.

3.1. *Plants as Sources of Complex Chemical Mixtures*

Plants accumulate diverse fibres that determine microbial utilisation in soil and gut environments. Cellulose, hemicellulose, pectins, resistant starches, and arabinoxylans vary in accessibility under stress and microbial symbiosis [31,34]. Rhizosphere and endophytic communities influence fibre composition by altering growth, carbohydrate metabolism, and hormonal signals during drought and nutrient limitation [46]. Similar ecological dynamics occur in the human colon, where microbial consortia ferment non-digestible fibres into SCFAs that support epithelial integrity, immune balance, and metabolic function [21,22,27]. Fibre architecture creates selective niches that determine microbial success across the soil-plant-gut continuum [47]. Figure 3 outlines the major classes of plant compounds and their distribution across plant tissues.

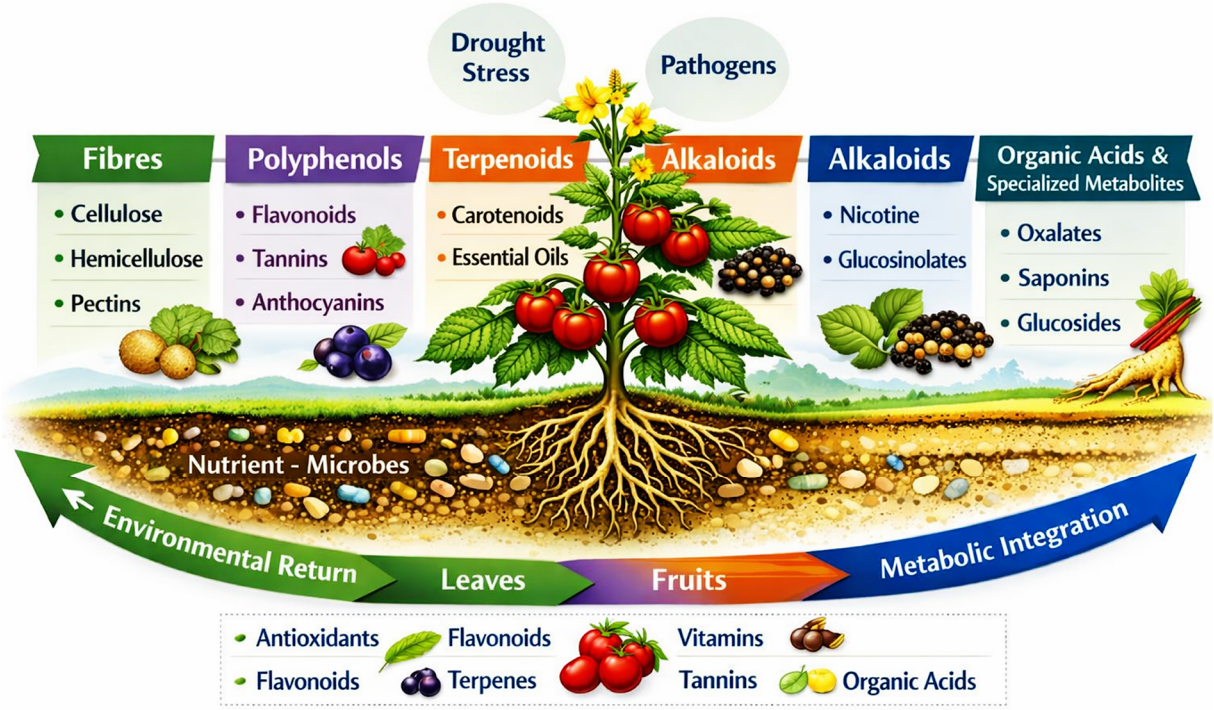

Figure 3. Major classes of plant compounds and their distribution across plant tissues.

3.2. *Structural Diversity of Plant Natural Products*

Plants generate structurally diverse natural products across multiple biosynthetic pathways shaped by ecological pressures and microbe-mediated signals at the plant-soil interface. Polyphenols, terpenoids, alkaloids, phenolic acids, and nitrogen-containing metabolites accumulate under nutrient stress, drought, salinity, and microbial association [32,46]. Microbial partners influence this diversity by modulating precursor pools, redox balance, and phytohormone regulation [13,14]. Stress-tolerant microbes further reshape metabolic profiles through enhanced antioxidant activity, polyamine regulation, and phenolic turnover under salinity and drought [34,46]. These interactions parallel the human gut, where microbial enzymes remodel plant-derived compounds into metabolites with altered solubility, stability, and bioactivity [18,19,27]. Structural diversity governs plant ecological performance and microbial accessibility during digestion.

3.3. *Dietary Fibres and Microbial Fermentation*

Dietary fibres form a central component of plant chemical ecologies because structural heterogeneity determines microbial utilisation in soil and gut environments. Plants accumulate cellulose, hemicellulose, pectins, resistant starches, and arabinoxylans whose accessibility depends on stress responses and microbial symbioses [31,34]. Rhizosphere and endophytic communities influence fibre composition by altering growth, carbohydrate metabolism, and hormonal signals during drought and nutrient limitation [38,46]. Comparable dynamics occur in the human colon, where microbial consortia ferment non-digestible fibres into SCFAs that support epithelial integrity, immune balance, and metabolic regulation [21,22,27]. Fibre architecture creates selective niches that determine microbial success across the soil-plant-gut continuum [47]. The structural complexity of plant fibres underpins plant resilience and host-microbe metabolic interactions.

3.4. *Polyphenol Subclasses and Microbial Accessibility*

Polyphenols show extensive chemical variation and remain largely unabsorbed in the upper gut, making microbial transformation essential for physiological relevance. Plants adjust polyphenol composition under salinity, nutrient limitation, and microbial colonisation, reflecting coordinated stress-response networks [13,48]. Microbes reshape polyphenolic profiles by influencing phenylpropanoid pathways and modulating antioxidant capacity during drought and metal stress [36,49]. This ecological background mirrors gut microbial activity, where polyphenols undergo sequential deglycosylation, dehydroxylation, demethylation, and ring-cleavage to form smaller metabolites with enhanced bioavailability [18,19,27]. These microbial products, including phenolic acids and urolithin precursors, influence inflammation, redox balance, vascular function, and gut-brain communication

[25,26]. Polyphenols act as ecological selectors of microbial behaviour and serve as substrates for metabolite production that extend plant chemical influence into the host.

3.5. *Terpenoid and Alkaloid Metabolism in the Gut*

Terpenoids and alkaloids form central components of plant defence chemistry and contribute to ecological communication within root-associated microbial networks. These compounds accumulate under abiotic and biotic stress, and microbial partners shape their production through redox modulation, hormone signalling, and nutrient acquisition [50,51]. Plants synthesise monoterpenes, carotenoids, triterpenoids, and diverse alkaloid subclasses, many requiring enzymatic modification before absorption. Plant-associated microbes can detoxify, degrade, or activate these compounds, suggesting parallels with gut microbial metabolism where similar transformations influence stability, toxicity, and bioactivity [39,52]. Microbial resilience under nitrogen limitation, salinity, and drought illustrates how metabolic flexibility supports plant survival and chemical turnover [40,46]. These interactions provide insight into how gut microbes modify terpenoids and alkaloids through reduction, dehydroxylation, deamination, and demethylation, yielding metabolites with altered biological properties [18,19,27].

3.6. *Plants as Ecological Inputs to the Gut Microbiome*

Plants act as ecological inputs to the gut microbiome by providing structural, nutritional, and signalling compounds that shape microbial composition and metabolic function. The chemical complexity of plant tissues reflects interactions between plants and their associated microbiota, where fibres, polyphenols, terpenoids, and nitrogen-containing metabolites arise from coordinated defence and adaptation responses [34,39,47]. Microbes influence these outputs by modulating nutrient transport, osmolyte production, and redox balance under stress [35,46]. Once ingested, these plant-derived compounds shape gut microbial behaviour by acting as substrates for fermentation, modulators of oxidative status, and drivers of quorum sensing, biofilm formation, and competitive interactions [12,19,27]. These ecological dynamics determine which microbial taxa flourish, which metabolites are produced, and how microbial biochemistry influences host physiology [11,18]. Plants therefore function not only as nutrient sources but as chemical ecosystems that regulate microbial structure and metabolic output.

4. Microbes as Translators and Amplifiers

Microbes act as biochemical translators that convert plant compounds into new metabolites with distinct functions. Human enzymes digest simple carbohydrates, proteins, and fats, but most fibres, polyphenols, and resistant starches reach the colon unchanged. Microbial enzymes continue digestion and extend chemical breakdown far beyond human capacity [15,16]. The gut microbiota carries millions of genes that support glycosidation, esterification, dehydroxylation, demethylation, and ring-cleavage reactions [18,19]. These reactions break chemical structures that mammalian enzymes cannot process. Microbial transformations produce SCFAs, phenolic acids, indole derivatives, and other intermediates that influence epithelial integrity, inflammatory balance, neuroimmune activity, and vascular function [21,27,30,33].

Plant-associated microbiomes show similar logic, where microbial activity expands chemical diversity and strengthens stress tolerance [13,46]. Microbial metabolism amplifies the biological value of plant compounds by converting complex substrates into diverse biochemical signals that support physiological resilience [27,53]. Figure 4 displays the principal microbial metabolites derived from plant compounds and their physiological actions.

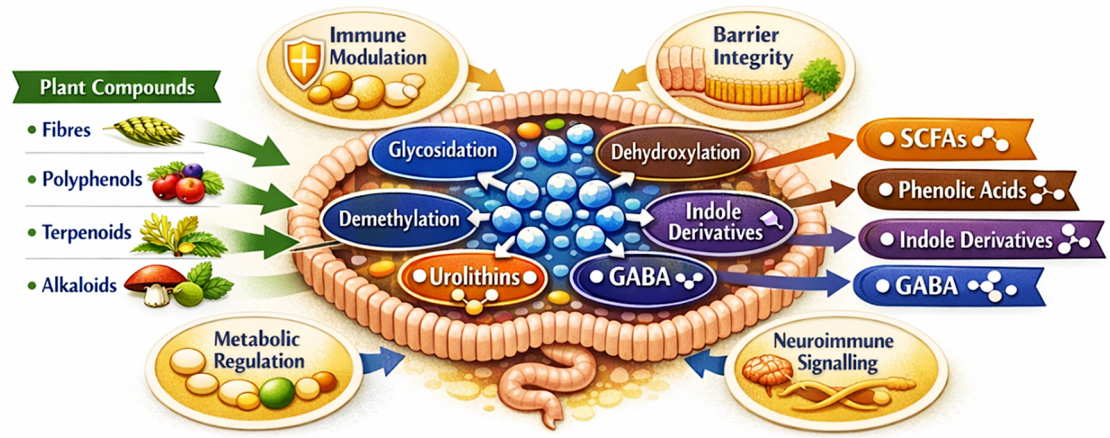

Figure 4. Major microbial metabolites derived from plant compounds and their physiological actions.

4.1. *Immune Modulation*

Immune modulation arises from the combined actions of plant compounds and microbial metabolites that influence tolerance and inflammation. SCFAs illustrate this clearly because acetate, propionate, and butyrate induce regulatory T cells through G-protein-coupled receptors and histone deacetylase inhibition [12,54]. These metabolites support epithelial homeostasis, influence dendritic-cell maturation, and promote memory T-cell formation through metabolic reprogramming that links fibre availability to immune tone [55,56]. Polyphenol-derived metabolites extend this spectrum by modulating dendritic-cell activation, limiting NF-kappa-B transcription, and reducing oxidative stress signals that drive chronic inflammation [19,26]. Nutritional ligands also engage nuclear and membrane receptors, including retinoid X receptor partners and Toll-like receptors, enabling polyphenols to exert anti-inflammatory effects through receptor-mediated pathways [54]. Indole derivatives provide a third axis of immune modulation. Microbial conversion of tryptophan produces indole-3-aldehyde, indole-3-acetic acid, tryptamine, and related intermediates that activate the aryl hydrocarbon receptor in lymphocytes and dendritic cells, supporting IL-22 production and mucosal repair [42–44]. These pathways show how plant-microbe interactions generate a metabolite landscape that shapes local and systemic immunity [27].

4.2. *Barrier Integrity*

Barrier integrity relies on continuous biochemical communication between epithelial cells, microbial metabolites, and plant-derived substrates. Butyrate supports colonocytes by providing energy, enhancing tight-junction assembly, and reinforcing cytoskeletal structure through receptor signalling and histone deacetylase inhibition [56,57]. Urolithins add complementary protection by improving mitochondrial efficiency, enhancing mitophagy, and stabilising epithelial metabolism during stress [12,18,27]. Plant fibres contribute by modulating mucin production and altering mucus properties, creating a hydrated interface that separates microbes from epithelial tissues [21,22]. This interface supports beneficial taxa that reinforce SCFA and indole production. These metabolites integrate plant chemistry with microbial activity to maintain epithelial continuity and sustain barrier function under inflammatory challenge [27].

4.3. *Metabolic Regulation*

Metabolic regulation reflects integration of dietary substrates, microbial metabolites, and host signalling pathways. SCFAs influence glucose and lipid metabolism through G-protein-coupled receptors, AMPK activation, and mitochondrial regulation [23,24]. Phenolic acids and urolithins modulate oxidative balance, endothelial function, and mitochondrial efficiency, providing benefits that arise only after microbial transformation [18,26,27]. Indole derivatives contribute by influencing insulin sensitivity, hepatic lipid handling, and enteroendocrine signalling through AHR-mediated pathways [33,42]. Microbial metabolites also shape appetite regulation, vagal signalling, and neuroendocrine communication, linking plant substrates to systemic metabolic outcomes [25,30]. These interactions show that plant-microbe metabolic cooperation forms a central axis of metabolic homeostasis [27].

4.4. *Neuroimmune Signalling*

Neuroimmune signalling arises from coordinated communication between the gut, immune system, and central nervous system, with microbial metabolites acting as primary mediators. Indole derivatives generated through tryptophan metabolism activate the aryl hydrocarbon receptor in epithelial, immune, and neural-associated cells, promoting IL-22-driven repair and neuroprotective transcriptional programmes [42–44]. Their stabilising effects on epithelial and immune networks reduce inflammatory cues that influence neural circuits.

SCFAs provide complementary regulation by shaping microglial maturation, cytokine responsiveness, and neurotransmitter processing [58]. Butyrate and propionate modulate microglial activation, regulate neuroinflammatory pathways, and support synaptic plasticity through receptor-dependent and epigenetic mechanisms [56,58]. These actions align with broader metabolic roles of SCFAs that influence energy balance and endocrine signals linked to the hypothalamic-pituitary-adrenal axis [12,15].

Gamma-aminobutyric acid producing microbes influence vagal activity and modulate anxiety-related behaviours, with vagotomy studies demonstrating neural routing rather than direct metabolite transfer [59–61]. Microbial regulation of tryptophan flux alters serotonin synthesis and reduces diversion toward the kynurenine pathway, affecting mood, neuroplasticity, and cognitive stability [44,62].

These observations show that neuroimmune signalling depends on metabolites produced through microbial processing of plant compounds. Indoles regulate transcriptional and cytokine networks [42–44], SCFAs shape microglial tone and endocrine pathways [12,15,56,58], and GABA-linked processes influence vagal activity and

emotional regulation [59–61]. This integrated system demonstrates that plant-microbe interactions extend into neural circuits and contribute to behavioural and cognitive homeostasis [27].

5. Microbial Metabolites as Systemic Signals

Microbial metabolites act as systemic messengers that carry the influence of dietary plants far beyond the gut. SCFAs, phenolic acids, urolithins, indole derivatives, and microbial neurotransmitter analogues circulate through metabolic, immune, and neuroendocrine pathways, linking plant chemistry to whole-body physiology [21,27,30,33]. These metabolites regulate mitochondrial efficiency, oxidative balance, vascular tone, immune tolerance, and neuroimmune communication, showing that microbial metabolism forms a biochemical interface between diet and host systems [18,19,27].

5.1. SCFAs as Metabolic and Immune Signals

SCFAs represent the most abundant microbial metabolites derived from dietary fibres. Acetate, propionate, and butyrate influence glucose and lipid metabolism through G-protein-coupled receptors, AMPK activation, and mitochondrial regulation [23,24]. These metabolites support regulatory T-cell differentiation, enhance epithelial barrier function, and modulate dendritic-cell maturation, demonstrating dual metabolic and immunological roles [54–56]. SCFAs influence appetite regulation, vagal signalling, and enteroendocrine activity, linking fibre fermentation to systemic metabolic outcomes [25,30]. SCFAs therefore act as central mediators that translate fibre fermentation into coordinated host responses [27]. Figure 5 highlights SCFA formation and the signalling pathways that link microbial fermentation to metabolic and immune functions.

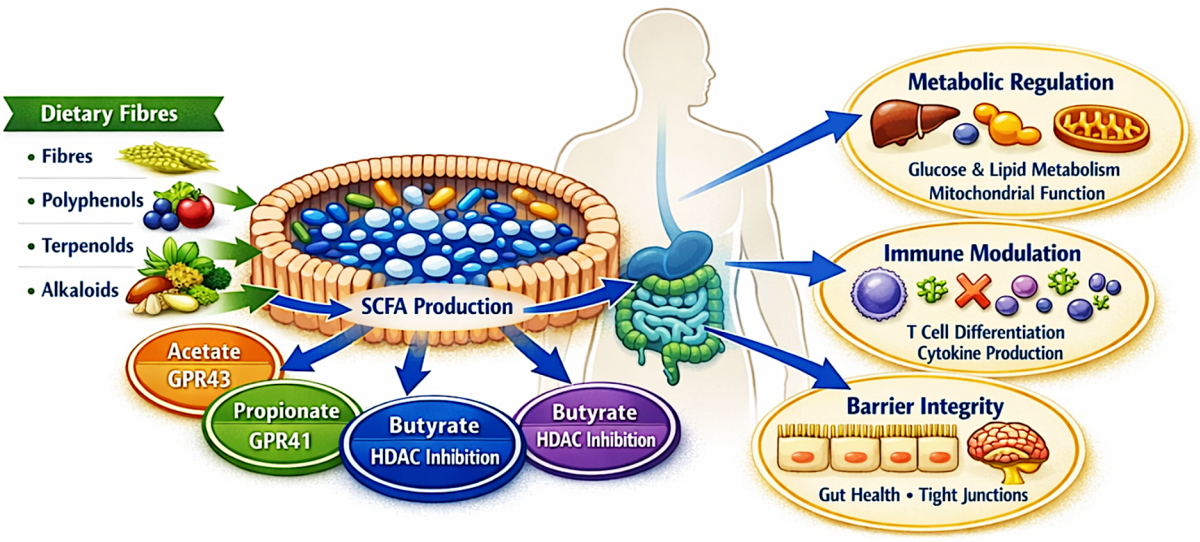

Figure 5. SCFA formation and signalling pathways linking microbial fermentation to host metabolic and immune functions.

5.2. Phenolic Metabolites and Redox-Immune Balance

Phenolic acids and urolithins arise from microbial transformation of polyphenols and often show stronger biological activity than their parent compounds. These metabolites modulate oxidative balance, endothelial function, and mitochondrial efficiency, providing metabolic and vascular benefits that depend on microbial processing [18,26,27]. Phenolic metabolites attenuate NF-κB signalling, suppress pro-inflammatory cytokine production, and stabilise redox gradients that shape immune tone [19,22]. Urolithins support mitochondrial turnover and epithelial resilience, linking polyphenol metabolism to barrier protection and systemic metabolic regulation [12,27]. These metabolites act as redox-immune modulators that extend the physiological reach of plant chemistry.

5.3. Indole Pathways and Neuroimmune Communication

Indole derivatives form a major class of microbial metabolites derived from dietary tryptophan. Indole-3-propionic acid, indole-3-lactic acid, tryptamine, and related compounds act as ligands for the aryl hydrocarbon receptor and influence IL-22 production, epithelial repair, and mucosal tolerance [42–44]. Indole metabolites regulate neuroimmune pathways by modulating vagal signalling, microglial activation, and neurotransmitter

balance, linking microbial metabolism to cognitive and emotional outcomes [33,45,60]. These metabolites also influence insulin sensitivity, hepatic lipid handling, and enteroendocrine function, demonstrating broad metabolic relevance [30,61]. Indole metabolites act as integrative signals that connect diet, microbial activity, and neuroimmune physiology [27]. Figure 6 demonstrates the microbial conversion of dietary tryptophan into indole derivatives and the downstream epithelial and neuroimmune pathways mediated through AHR activation.

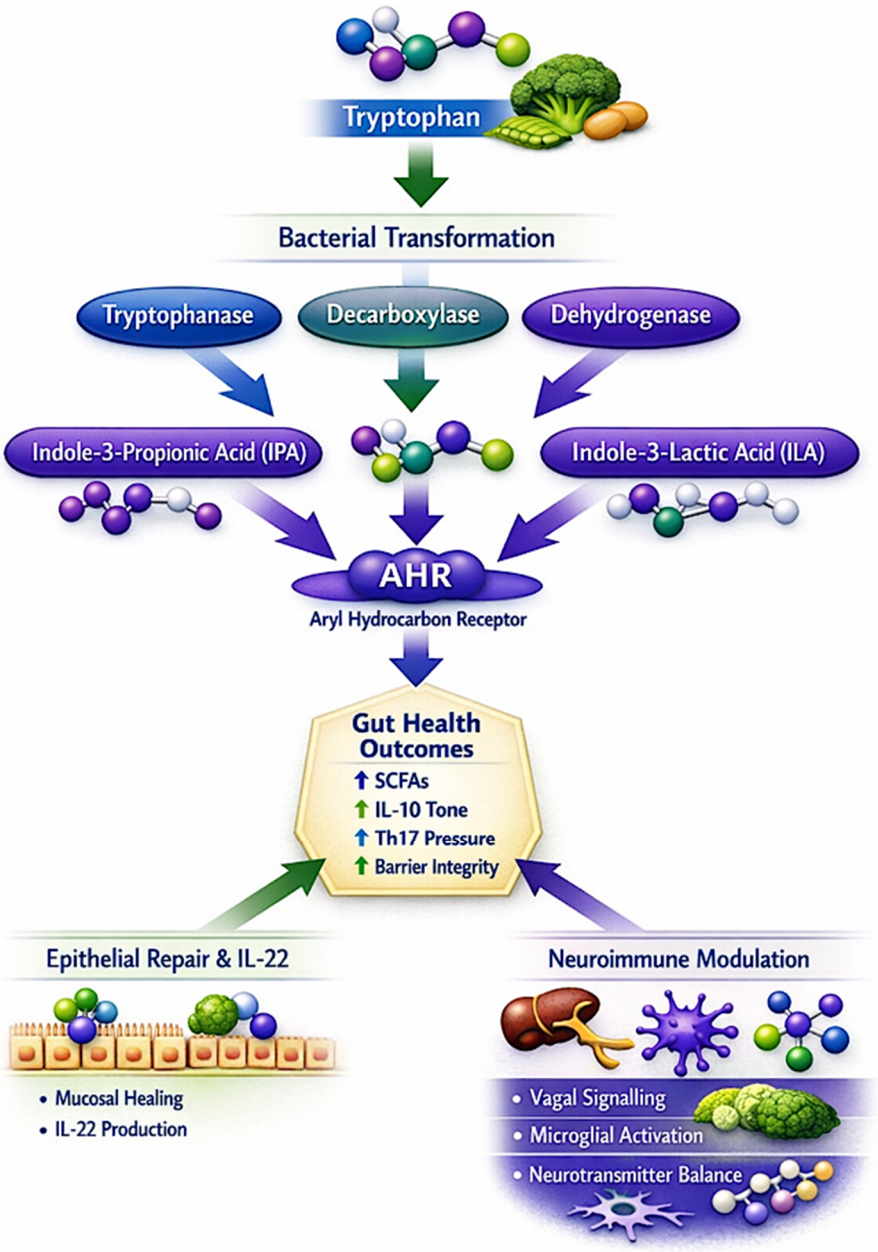

Figure 6. Tryptophan-derived indole pathways and their roles in epithelial and neuroimmune regulation.

5.4. Microbial Neuroactive Compounds

Microbial production of neurotransmitter analogues extends plant-microbe interactions into neural and behavioural domains. Gamma-aminobutyric acid, dopamine-like metabolites, serotonin-pathway intermediates, and catecholamine mimetics arise from microbial metabolism and influence gut-brain communication through receptor-mediated and vagal pathways [63–65]. These compounds act locally on epithelial and immune cells and signal centrally through vagal afferents. Microbial GABA regulates barrier integrity, microglial activation, and stress-linked endocrine responses, linking microbial metabolism to neuroendocrine control [60,61]. Additional studies show that microbial metabolites modulate hypothalamic–pituitary–adrenal axis activity, appetite circuits, and mood-associated pathways, providing mechanistic support for psychobiotic effects [66–69]. These neuroactive metabolites illustrate how plant-derived substrates, once transformed by microbes, influence neural circuits and

behavioural outcomes [27]. Their actions integrate with indole- and SCFA-mediated pathways to form a broader neuroimmune and neuroendocrine network that links diet, microbial metabolism, and brain function [27,68].

5.5. Integrated Systemic Effects

Microbial metabolites operate as integrated systemic signals that coordinate metabolic, immune, vascular, and neuroendocrine responses. SCFAs, phenolic acids, urolithins, and indole derivatives converge on shared pathways involving mitochondrial regulation, redox balance, receptor signalling, and epigenetic modification [18,27,30,33]. These metabolites influence physiology through distributed networks that link the gut to the liver, adipose tissue, immune organs, and the central nervous system [25,60]. The systemic reach of microbial metabolites shows that plant-microbe interactions extend far beyond digestion and form a biochemical framework that shapes resilience, metabolic stability, and cognitive health [27]. Table 3 highlights the major microbial metabolites derived from plant compounds and their systemic effects.

Table 3. Key microbial metabolite families and systemic effects.

Metabolite Family	Key Molecules and Origins	Main Physiological Effects	Systemic Pathways	References
SCFAs	Acetate, propionate, butyrate from fibre fermentation	Treg induction, epithelial energy, pH lowering	Metabolic and immune regulation	[21–24,55,56]
Phenolic metabolites	Phenolic acids, urolithins from polyphenols	Redox balance, anti-inflammatory effects	Vascular and mitochondrial support	[18,19,25,26]
Indole derivatives	Indole-3-propionic acid, indole-3-lactic acid from tryptophan	IL-22 induction, barrier repair	Neuroimmune communication	[42–45]
Neuroactive metabolites	GABA, dopamine analogues, serotonin intermediates	Stress modulation, mood effects	Gut-brain axis	[62–66]

6. Plants Shaping the Microbiome

Diet shapes the intestinal ecosystem through coordinated inputs that favour beneficial microbes, suppress pathobionts, and reorganise metabolic networks. Plant foods deliver three converging forces [15,57]. Fermentable fibres alter substrate flow, lower luminal pH, and enrich SCFA-producing taxa. Polyphenols act as selective modulators whose limited absorption increases colonic exposure, where microbial biotransformation yields bioactive metabolites. Plant-associated microbes and their metabolites enter the gut and participate transiently in ecological assembly. These forces interact with nutrient-sensing receptors and immune circuits that regulate Th17/Treg balance, barrier function, and colonisation resistance [15,27,57]. Dietary fibres impose ecological restructuring by favouring saccharolytic consortia over proteolytic guilds. Increased arabinoxylans, pectins, inulins, and resistant starches expand *Bifidobacterium*, *Faecalibacterium*, and *Roseburia*, increase acetate, propionate, and butyrate, and reduce luminal pH into a range that limits Enterobacteriaceae expansion. SCFAs then signal through GPR41/43 and histone deacetylase inhibition to support epithelial energy, mucin dynamics, and Treg induction, tightening permeability control and limiting pathogen overgrowth [15,27,57]. The ecological signal is competitive as well as chemical because more fibre increases cross-feeding as primary degraders release oligosaccharides that secondary fermenters convert into butyrate, locking in a stable, low-pH, pathogen-resistant state [15,54].

6.1. *Mechanistic Foundations*

Selective growth of beneficial taxa shapes microbial succession because plant fibres and polyphenols act as nutrient and signalling cues that favour saccharolytic guilds over proteolytic competitors. Fermentable substrates increase *Bifidobacterium, Faecalibacterium*, and *Roseburia*, expand SCFA production, and strengthen pH-lowering dynamics that reinforce colonisation resistance [15,27]. These effects deepen as cross-feeding establishes stable acetate-propionate-butyrate networks that support a resilient, low-inflammation state. Suppression of pathobionts follows from direct and ecological pressures. Polyphenols compromise membrane integrity, disrupt metal handling, and attenuate virulence programmes in Enterobacteriaceae, while SCFA-driven acidification constrains bloom-prone Proteobacteria [15,19]. The combined antimicrobial and ecological forces create a niche that limits opportunistic expansion without disturbing commensal stability.

Fibre-driven restructuring anchors long-term compositional shifts. Increased access to arabinoxylans, inulins, pectins, and resistant starches alters metabolic flux, enhances mucin dynamics, and delivers SCFA-mediated signals that stabilise Treg populations and strengthen epithelial energetics. Host nutrient receptors integrate these cues with microbial metabolites to maintain barrier integrity and regulate Th17/Treg balance [27,54,57]. Polyphenols function as prebiotic modulators through selective bioaccessibility and microbial biotransformation. Limited small-intestinal uptake ensures that catechins, anthocyanins, curcuminoids, flavan-3-ols, and glucosinolates reach the colon, where microbial enzymes convert them into host-active metabolites with immune-regulatory properties [19,27]. These transformations favour taxa capable of aromatic ring fission, dehydroxylation, or lactonisation, reinforcing a community enriched in SCFA producers and constrained in pathobionts.

Plant-associated microbes add a further ecological signal. Fresh produce transfers epiphytic and endophytic microbiota that persist transiently in the gut and influence assembly trajectories through metabolite pulses and microbe-associated molecular patterns. The recurring entry of plant-borne microbes acts as a soft ecological pressure that contributes to community structure [5,27,70]. Table 4 compares plant foods, their microbial transformations, and the dominant taxa they support.

Table 4. Plant foods, microbial transformations, and dominant taxa.

Plant Food	Key Transformations and Enriched Taxa	Main Metabolites	Physiological Outcomes	References
Green tea	Catechin conversion by *Bifidobacterium, Roseburia, Eubacterium*	phenyl-γ-valerolactones	Barrier support, Treg skewing	[15,19]
Berries	Anthocyanin conversion by *Akkermansia, Bifidobacterium*	Urolithins, phenolic acids	Mitochondrial and barrier support	[15,57]
Turmeric	Curcuminoid reduction by *Blautia, Lactobacillus, Bifidobacterium*	Reduced curcuminoids	NF-κB attenuation	[19]
Cocoa	Procyanidin depolymerisation by *Bifidobacterium, Lactobacillus*	phenyl-γ-valerolactones	SCFA enrichment, reduced Proteobacteria	[15,19]
Crucifers	Glucosinolate conversion by SCFA producers and *Akkermansia*	Indoles	IL-22 activation, barrier repair	[54,57]

6.2. *Phytonutrients and Gut Health*

Green tea catechins shape a selective metabolic dialogue within the gut. The unabsorbed epigallocatechin gallate reaches the colon, where Eggerthellaceae and Lachnospiraceae convert it into phenyl-γ-valerolactones that reinforce epithelial integrity and support Treg-skewing pathways. Catechins restrict Enterobacteriaceae expansion through membrane disruption and metal limitation while enriching *Bifidobacterium, Roseburia,* and *Eubacterium* [15,19]. These changes align with increased butyrate, reduced luminal redox potential, and improved colonisation resistance [27].

Berries reshape microbial networks through anthocyanin biotransformation. Poorly absorbed pigments yield urolithins and other phenolics that support mitochondrial and barrier function. The shift favours *Akkermansia* and *Bifidobacterium*, suppresses *Escherichia*/*Shigella*, and expands butyrate-producing consortia through intensified cross-feeding. The resulting SCFA and indole profiles support IL-10-rich regulatory tone and reduce Th17 pressure [15,27,57].

Turmeric influences ecological balance through curcuminoid conversion. Reductases and demethylases in Blautia, *Lactobacillus*, and *Bifidobacterium* convert curcuminoids into smaller phenolics that attenuate NF-κB activation and strengthen tight-junction stability. Selective antimicrobial pressures curb *Prevotella copri* and moderate inflammatory potential while deepening butyrate-supported epithelial resilience [19,27].

Cocoa reinforces SCFA-centred metabolism through procyanidin-fibre synergy. High-molecular-weight procyanidins and fermentable fibre enrich *Bifidobacterium* and *Lactobacillus*, increase acetate and butyrate, and suppress Proteobacteria. Microbial depolymerisation yields phenyl-γ-valerolactones that reduce inflammatory tone and strengthen colonisation resistance [15,19,27].

Cruciferous vegetables integrate glucosinolate and fibre pathways. Microbial conversion generates indoles that activate the aryl hydrocarbon receptor, strengthen IL-22-mediated repair, and support barrier integrity. The combined effects favour *Akkermansia* and SCFA producers and suppress Enterobacteriaceae through competitive

exclusion and acidification [27,54,57]. Figure 7 maps the microbial transformations and physiological effects associated with major phytonutrient groups.

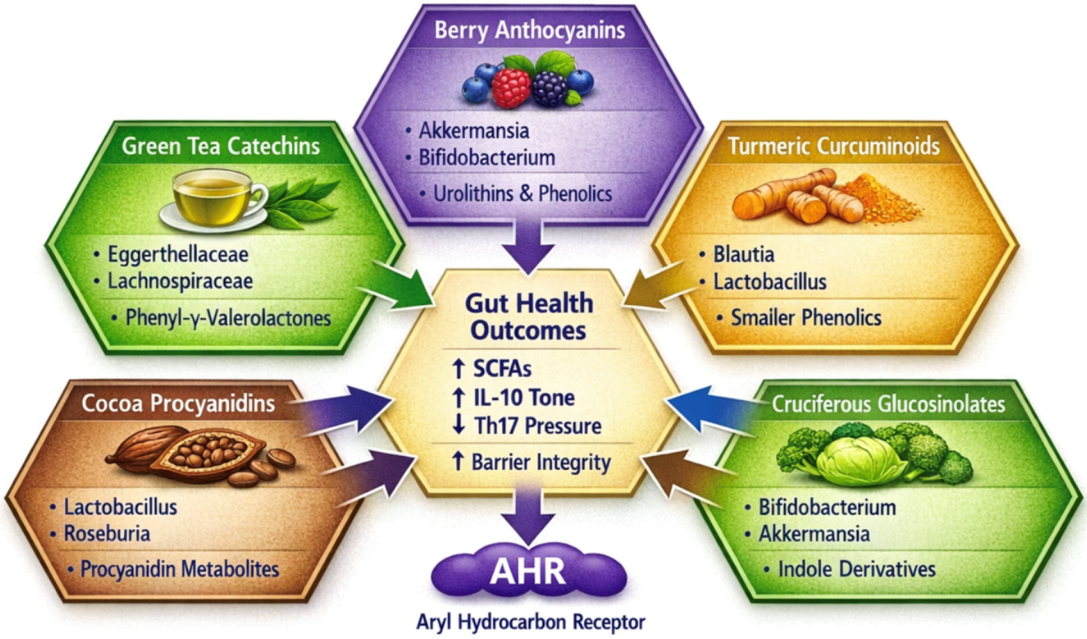

Figure 7. Comparative overview of microbial transformations and physiological effects of major phytonutrient groups.

6.3. *Integrative Interactions*

Plant-microbiome interactions converge on a shared ecological logic in which fibres, polyphenols, and plant-associated microbes reshape the gut through selective pressures that favour stability, resilience, and immune tolerance [27]. Structural carbohydrates deliver sustained metabolic flux into saccharolytic pathways, yielding SCFA profiles that anchor epithelial energetics, mucin dynamics, and Treg differentiation while lowering luminal pH to suppress opportunistic Proteobacteria [15,57]. Polyphenols add a complementary layer of selective modulation because limited bioaccessibility and extensive microbial metabolism generate phenolic and indole derivatives that engage nutrient and xenobiotic receptors to recalibrate inflammatory tone and strengthen barrier circuits [19,27,54].

Plant-borne microbial consortia reinforce these processes by entering the gut as transient ecological seeds that participate in early fermentative dynamics and contribute metabolites and microbe-associated molecular patterns that modulate mucosal vigilance [5,70]. The examples considered, green tea, berries, turmeric, cocoa, and crucifers, illustrate how diverse phytochemical architectures converge on SCFA enrichment, pathobiont suppression, and metabolite-driven immune alignment. Catechins, anthocyanins, curcuminoids, procyanidins, and glucosinolate derivatives all depend on microbial enzymes to unlock full bioactivity, situating the host response within a metabolic partnership rather than a single-compound effect [27]. These transformations increase butyrate-forming potential, promote *Akkermansia* and *Bifidobacterium*, constrain Enterobacteriaceae, and generate receptor-specific ligands that stabilise barrier integrity and support Treg-rich immune states. The ecological pathways overlap with cross-feeding networks established by fibre, ensuring that diverse plant foods produce additive and sometimes synergistic metabolic effects [27].

The broader insight aligns with principles emerging from plant-microbiome science, where ecological assembly, metabolic complementarity, and inducible defence responses underpin plant resilience and productivity [48,70]. In humans, an analogous system operates because dietary plants deliver substrates, metabolites, and microbial consortia that act through coordinated ecological shifts that strengthen colonisation resistance and modulate immune tone [15,27,57]. The integration of fibre, polyphenols, and plant-associated microbes therefore provides a coherent mechanism by which plant-rich diets stabilise gut ecology and promote a low-inflammation physiological state [5,19,27,54]. The cumulative trajectory points toward a model in which diverse plant foods, consumed consistently, create a microbiome that is more resilient to perturbation, more efficient in SCFA production, and more aligned with host immune homeostasis [15,27,57,70]. Figure 8 explores the integrative interactions between plant substrates, microbial transformations, and host responses, highlighting the ecological convergence that underpins gut stability and immune homeostasis.

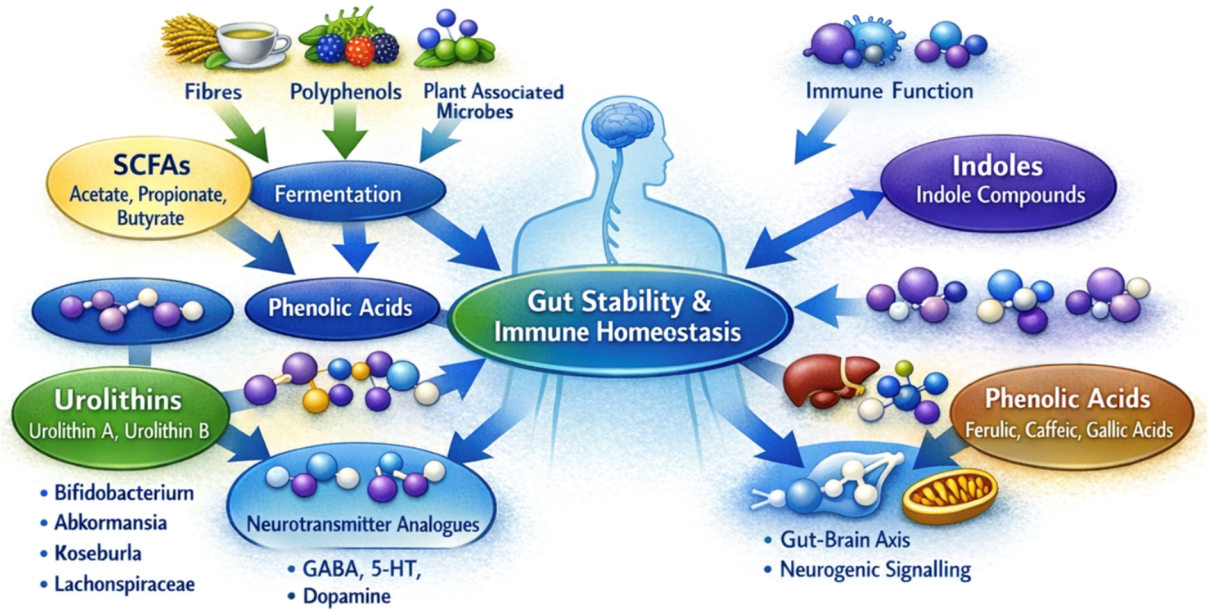

Figure 8. Integrative interactions between plant substrates, microbial transformations, and host responses.

7. Synergy between Plants and Microbes: A Great Team Player

Synergy arises when plant chemistry and microbial metabolism operate as one integrated biochemical system. Plant fibres and polyphenols enter the gut as complex substrates, but their full physiological potential appears only after microbial transformation [15,18,19,27]. Microbial enzymes perform reactions that neither plants nor humans can execute alone, including ring-cleavage, reductive tailoring, dehydroxylation, and lactonisation, generating urolithins, phenyl-γ-valerolactones, indoles, and hydrogenated metabolites with expanded bioactivity [15,19,27]. These postbiotic molecules influence barrier integrity, immune calibration, redox balance, and host energy metabolism in ways that exceed the effects of their parent compounds. Microbial metabolism acts as a biochemical amplifier that converts plant inputs into systemic signals [15,18,19,27]. Figure 9 integrates the synergistic interactions between plant chemistry, microbial metabolism, and host physiological responses.

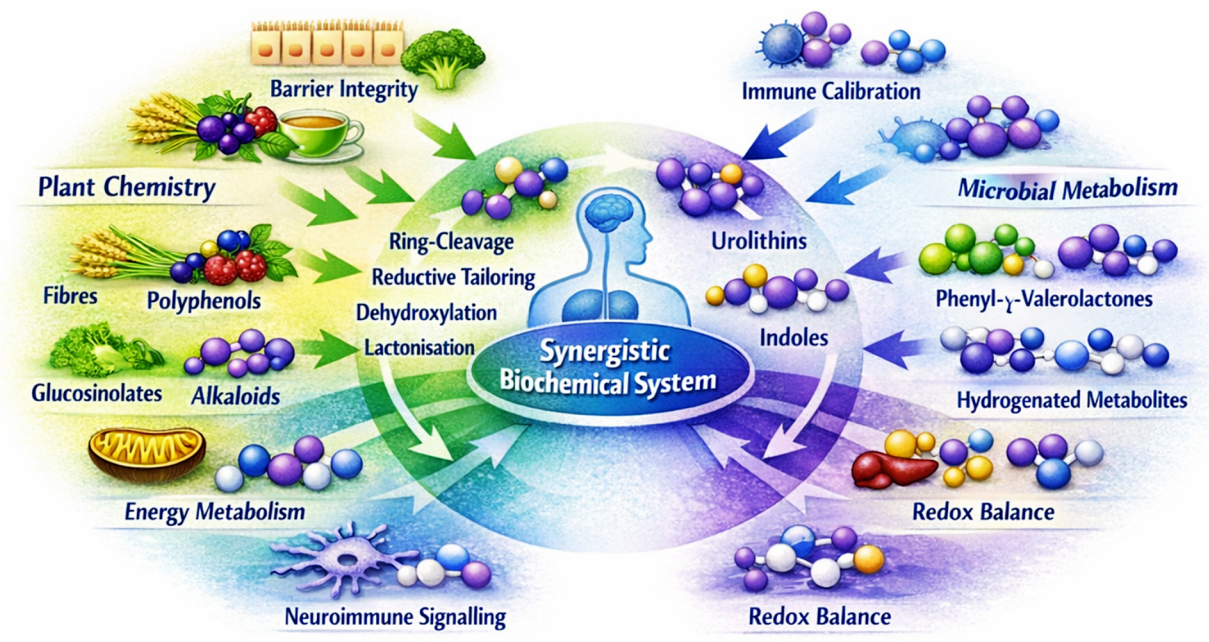

Figure 9. Synergy between plant chemistry, microbial metabolism, and host physiological responses.

7.1. *Microbial Amplification of Plant Chemistry*

Plants supply the substrates, but microbes unlock their functional value. Fermentable fibres sustain SCFA-producing consortia, while polyphenols reach the colon largely unmetabolised and undergo microbial conversion

into smaller, more potent metabolites [15,18,19]. These transformations expand chemical diversity, increase solubility and bioavailability, and generate molecules that engage host receptors involved in immune tolerance, mitochondrial regulation, and epithelial repair [15,27,57]. Microbial amplification determines the physiological reach of plant chemistry [27].

7.2. *Plants Feed Microbes That Protect the Host*

Plants feed microbes that protect the host by delivering fermentable substrates that favour saccharolytic guilds over proteolytic competitors. Increased access to arabinoxylans, pectins, inulins, and resistant starches expands *Bifidobacterium*, *Faecalibacterium*, and *Roseburia*, increases acetate, propionate, and butyrate, and lowers luminal pH into a range that suppresses Enterobacteriaceae expansion [15,57]. SCFAs then signal through GPR41/43 and histone-deacetylase inhibition to reinforce epithelial energetics, mucin dynamics, and Treg differentiation [23,24,55–57]. Fibre fermentation interlocks with polyphenol metabolism because the same saccharolytic guilds often participate in both processes, forming a metabolic network that transforms plant inputs into antimicrobial, anti-inflammatory, and mucosal-supportive outputs [15,18,19,27].

7.3. *Co-metabolism and the Creation of New Molecules*

Co-metabolism produces unique molecules that do not exist in plants or humans and that act as functional intermediates between diet, microbes, and host physiology. Urolithins, phenyl-γ-valerolactones, indole derivatives, and hydrogenated stilbenes arise only when plant substrates meet microbial enzymatic capacity [15,19,27]. Plant-associated microbes arriving with fresh produce add an ecological dimension by contributing transient metabolic pulses and microbe-associated molecular patterns that modulate mucosal vigilance and influence assembly trajectories [5,70]. Health emerges from collaborative metabolism rather than from plant or microbial activity alone [27].

7.4. *Translational Potential*

The translational potential of plant-microbe synergy lies in recognising that the health effects of plant foods depend on microbial capacity rather than intake alone. Controlled feeding trials and metabolomics studies show that fibres and polyphenols exert their strongest effects only after microbial conversion into high-value metabolites such as urolithin A, equol, phenyl-γ-valerolactones, and lunularin [15,27,71]. Inter-individual variability in these transformations underpins the concept of metabotypes, which classify individuals according to their microbial metabolic signatures [19,27,72]. These signatures influence cardiometabolic, endocrine, neurocognitive, and quality-of-life outcomes after identical polyphenol exposures. They can shift modestly with dietary interventions, indicating both biological stability and therapeutic malleability [57,72]. Translating these insights requires strategies that match plant compounds to microbial functions and use metabotypes to guide personalised nutritional interventions [27].

8. Challenges and Future Research

A major challenge lies in resolving the temporal dynamics of plant-microbe interactions because microbial metabolism, metabolite flux, and host responses fluctuate across circadian, dietary, and hormonal cycles. Capturing these oscillations will require high-resolution sampling frameworks and computational models capable of integrating time-dependent variation into predictive metabolic maps [73–75]. These rhythms shift across menopause, ageing, and immunosenescence, and this variation will guide the design of interventions that remain effective across physiological contexts [74,76]. Another priority is to disentangle host-microbe co-regulation of metabolic pathways, particularly those involving mitochondrial function, redox balance, and neuroimmune communication.

Microbial metabolites such as SCFAs, indoles, and urolithins influence mitochondrial biogenesis, neurotransmitter turnover, and inflammatory tone, yet the host factors that determine sensitivity to these signals remain poorly defined [61,63,77]. Host genetics, epigenetic states, and immune phenotypes shape responses to identical plant-derived inputs through their interaction with microbial metabolic capacity. Environmental variables also require attention. Diet diversity, antibiotic exposure, pollutants, and psychosocial stress reshape microbial metabolism and alter the production of health-relevant metabolites [78]. Longitudinal, multi-country cohorts will be essential for capturing these ecological pressures and for identifying universal versus population-specific metabolic signatures [27,79]. Such datasets will also support the development of global reference ranges for key microbial metabolites, enabling more precise clinical interpretation.

Regulatory frameworks must evolve to accommodate next-generation interventions. Engineered probiotics, targeted postbiotics, and CRISPR-edited microbial strains raise questions about safety, stability, horizontal gene transfer, and long-term ecological effects [80,81]. Safeguarding the development of next-generation microbiome technologies will depend on clear reporting frameworks, rigorous clinical validation, and internationally aligned standards that ensure methodological consistency across research settings. Maintaining fairness, reproducibility, and interpretability is equally critical for translating computational outputs into clinically meaningful insights [82–85]. Metabolomics pipelines now incorporate stronger correction strategies and cross-platform harmonisation, and these advances will support the emergence of metabolite-based diagnostics and therapeutics [29,86,87]. The expanding use of artificial intelligence in microbiome science amplifies both opportunity and responsibility because these models can accelerate biomarker discovery and personalise dietary strategies while remaining vulnerable to biases embedded within training datasets.

9. Conclusions

This review forms the second chapter in the 21-part *Gut Feeling* series, and its message remains simple. Plants and gut microbes work side by side to support human health. Plants deliver rich and complex chemistry into the gut, and microbes convert this chemistry into small, active metabolites that the body can use. These metabolites help shape immunity, metabolism, barrier strength, and the ongoing dialogue between the gut and the brain. A broader pattern also emerges. The same rules that guide microbial behaviour in the human gut also shape partnerships between plants and microbes in soils and roots. Microbes unlock plant potential in many environments, and plants provide the materials that sustain microbial communities. This shared logic helps explain why plant-rich diets offer broad and reliable benefits across populations. The next chapter will follow natural products on their journey through the gut and will map the enzymes, pathways, and metabolites that drive this partnership. These insights lay the foundation for targeted dietary strategies, microbiome-informed interventions, and natural-product-based therapeutics. As evidence grows, one message becomes clear. Plant-microbe cooperation will play a central role in the future of personalised health.

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