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MINIREVIEWS

Impact of curcumin on gut microbiome

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Abstract

The intricate interplay between natural compounds like curcumin and the gut microbiome has gained significant attention in recent years due to their potential therapeutic implications in various health conditions. Curcumin, a polyphenolic compound derived from turmeric, exhibits diverse pharmacological properties, including anti-inflammatory, antioxidant, and anticancer effects. Understanding how curcumin modulates gut microbiota composition and function is crucial for elucidating its therapeutic mechanisms. This review examines the current literature on the interactions between curcumin and the gut microbiome. A systematic search of relevant databases was conducted to identify studies investigating the effects of curcumin on gut microbial diversity and abundance. Key findings from studies exploring curcumin's efficacy in neurological disorders, gastrointestinal diseases, and metabolic dysfunction are synthesized and discussed. Studies have demonstrated that curcumin supplementation can

modulate gut microbiota composition and function, leading to beneficial effects on gut health and homeostasis. Mechanisms underlying curcumin's therapeutic effects include immune modulation, neuroprotection, and inflammation regulation. However, challenges such as poor bioavailability and safety concerns remain significant hurdles to overcome. The interactions between curcumin and the gut microbiome hold promise for therapeutic interventions in a diverse range of health conditions. Further research is needed to optimize curcumin formulations, improve bioavailability, and address safety concerns.

Key Words: Gut microbiome; Curcumin; Neuroprotection; Bioavailability

Core Tip: Curcumin, derived from turmeric, interacts with the gut microbiome and has a significant impact on health. Studies have revealed that curcumin modulated gut microbial composition, immune responses, and inflammation. Challenges such as bioavailability persist, but curcumin holds promise for diverse therapeutic applications.

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INTRODUCTION

Understanding the complex interactions between natural compounds and the gut microbiome has become increasingly significant in recent years as the importance of gut bacteria composition and function in maintaining human health has become apparent. The gut microbiome, comprising trillions of microorganisms, plays a crucial role in various physiological processes, including metabolism, immune function, and neurobehavioral regulation[1]. Dysbiosis, the imbalance of microbial communities within the gut, has been linked to a plethora of chronic diseases, ranging from metabolic disorders to neurodegenerative conditions[2].

Among the many natural compounds under investigation, curcumin has emerged as a promising candidate for modulating microbial composition and function within the gut. Curcumin, a polyphenolic compound derived from the rhizome of *Curcuma longa*, commonly known as turmeric, has garnered considerable attention due to its diverse pharmacological properties, including anti-inflammatory, antioxidant, and anti-carcinogenic effects[3]. Moreover, curcumin has been shown to exert significant effects on gut microbial communities, making it an intriguing subject of study in the context of microbiome modulation[4].

Investigations into the effects of curcumin on mental health have unveiled its ability to influence gut microbiota composition, thereby implicating its role in neurobehavioral regulation[5]. Several preclinical studies have demonstrated the potential of curcumin in modulating gut microbial composition to mitigate the progression of atherosclerosis, a chronic inflammatory condition characterized by the buildup of plaque within arterial walls[6]. Curcumin supplementation has been associated with reduced plaque burden and favorable alterations in gut microbiota composition, suggesting its therapeutic potential in the management of atherosclerosis[6].

Clinical studies have provided further insights into the impact of curcumin on gut microbial communities. Research investigating the effects of turmeric and curcumin on human gut microbiota composition has revealed personalized responses, with curcumin potentially driving the observed changes in microbial diversity and abundance[7]. Culinary spices like turmeric have been shown to induce beneficial alterations in gut microbial communities, promoting digestive health through increased production of short-chain fatty acids, such as butyrate[8].

Curcumin, also known as diferuloylmethane, is the primary curcuminoid found in turmeric (*Curcuma longa* L.). Its chemical designation is 1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione, and it possesses a molecular formula of $C_{11}H_{20}O_6$ with a molecular weight of 368.38 g/mol. The chemical structure of curcumin consists of two ferulic acid residues that are linked by a methylene bridge. The molecule exists in tautomeric forms, with the enol form being the dominant structure in solution. This distinctive configuration contributes to curcumin's characteristic yellow hue and its reactivity as a Michael acceptor in various chemical reactions. Within curcumin's structure, several key functional groups are present, which are fundamental to its biological activities and its interactions with a range of molecular targets. These include two aromatic rings containing ortho-methoxy phenolic groups, two α, β-unsaturated carbonyl groups, and a β-diketone moiety. Additionally, curcumin has multiple conjugated double bonds, enhancing its reactivity and interaction potential[9-12].

Despite the diverse pharmacological activities of curcumin (Table 1), its therapeutic application is significantly hindered by inherent limitations such as poor aqueous solubility, rapid metabolism, and limited systemic bioavailability. To overcome these challenges, a variety of delivery systems have been developed. These include nanoformulations, liposomal preparations, phospholipid complexes, and other novel drug delivery systems. Another important consideration in improving curcumin's bioavailability is its interaction with the gut microbiota, which plays a crucial role in its

Table 1 Pharmacological effects of curcumin

Pharmacological activity	Mechanisms/effects	Key points
Anti-inflammatory properties	Inhibition of NF-κB activation and suppression of inflammatory mediators; suppression of COX-2, LOX, and iNOS expression; modulation of pro-inflammatory cytokines (*e.g.*, TNF-α, IL-1β, IL-6); regulation of MAPK signaling pathways; inhibition of inflammatory transcription factors	Modulates gut microbiota
Antioxidant activities	Direct scavenging of free radicals; enhancement of cellular antioxidant defenses; upregulation of Nrf2 pathway; increase in antioxidant enzyme activities (SOD, CAT, GPx); metal ion chelation	Protects against oxidative stress-induced cellular damage
Anticancer properties	Cell cycle arrest and induction of apoptosis; Inhibition of cancer cell proliferation; modulation of microRNAs; suppression of angiogenesis; regulation of cancer stem cells; interference with signaling pathways (STAT3, Wnt/β-catenin, PI3K/Akt)	Gut microbiota interaction enhances effects
Immunomodulatory effects	Regulation of T cell differentiation and function; influence on B cell response; modulation of macrophage polarization; modification of dendritic cell function; alteration of natural killer cell activity	Significant impact on gut immunity
Neuroprotective activities	Protection of the blood-brain barrier; reduction of neuroinflammation; prevention of protein aggregation; enhancement of neuroplasticity; modulation of neurotransmitter systems	Gut-brain axis plays a crucial role
Cardiovascular protection	Improvement of endothelial function; reduction of atherosclerosis; modulation of lipid metabolism; prevention of cardiac hypertrophy; protection against ischemia-reperfusion injury	
Antidiabetic effects	Enhancement of insulin sensitivity; protection of β-cell function; regulation of glucose metabolism; reduction of advanced glycation end-products; amelioration of diabetic complications	Ameliorates diabetic complications
Hepatoprotective activities	Prevention of hepatic fibrosis; protection against drug-induced liver injury; reduction of hepatic steatosis; modulation of liver enzyme activities; enhancement of hepatic regeneration	
Antimicrobial properties	Broad-spectrum activity against bacterial, fungal, viral, and parasitic infections	Involves modulation of gut microbiota

TNF-α: Tumor necrosis factor-alpha; IL: Interleukin.

metabolism and overall efficacy. Recent scientific advancements have increasingly explored the relationship between curcumin and gut microbiota. Wang *et al*[13] investigated the modulatory effects of curcumin on gut microbiota as a potential therapeutic strategy[13]. Similarly, Liu *et al*[14] examined the bidirectional interaction between curcumin and gut microbiota[14], while Shen *et al*[15] emphasized the connection between curcumin, gut microbiota, and neuroprotection[15]. Further expanding on this field, Zhang *et al*[16] provided insights into how curcumin's modulation of gut microbiota may help ameliorate symptoms associated with Parkinson's disease (PD).

Despite these promising findings, there remains a need for further research to elucidate the mechanisms underlying curcumin's effects on gut microbiota and to explore its potential therapeutic applications in various disease contexts[2,3]. The personalized nature of the response to curcumin and turmeric underscores the importance of personalized medicine approaches in harnessing the therapeutic potential of natural compounds for microbiome modulation[7]. Understanding the complex interplay between curcumin and gut microbiota has substantial potential to enhance our comprehension of microbial-host interactions and facilitate the development of adjuvant therapies for an array of ailments. The aim of this study is to offer a thorough and comprehensive review of the influence exerted by curcumin on the gut microbiome, along with an exploration of its clinical applications.

CURCUMIN-AN OVERVIEW

Curcumin, a polyphenolic compound derived from the rhizome of *Curcuma longa*, commonly known as turmeric, has garnered significant attention in recent years due to its diverse pharmacological properties and potential clinical applications[17]. Curcumin is the primary bioactive constituent of turmeric and is extensively utilized in both culinary and medicinal contexts[17,18]. Despite its widespread use, curcumin exhibits poor systemic bioavailability, attributed to its low solubility and stability, which poses challenges for its therapeutic utilization[19]. Nevertheless, numerous studies have highlighted the remarkable biologic activities of curcumin, including its antioxidant, anti-inflammatory, and anticancer properties[17,20]. Additionally, curcumin has demonstrated promising effects in improving brain function, controlling obesity, and ameliorating diabetes[19].

These multifaceted pharmacological activities underscore the potential of curcumin as a therapeutic agent for various health conditions. In preclinical studies, curcumin has shown efficacy in inhibiting the proliferation of colon cancer cells and inducing apoptosis, suggesting its potential as an anticancer agent[17]. Furthermore, curcumin has been found to suppress mucosal expression of inflammatory mediators, highlighting its anti-inflammatory effects[17]. Notably, curcumin has been shown to modulate the gut microbiota, promoting the growth of beneficial bacteria such as butyrate-producing species, which may contribute to its anti-inflammatory and anticancer effects[20]. Additionally, curcumin's ability to ameliorate intestinal inflammation and modulate signaling pathways further enhances its therapeutic potential

[17].

Despite its challenges regarding bioavailability, ongoing research efforts are focused on developing novel curcumin formulations with enhanced bioavailability to maximize its therapeutic efficacy[19,20]. Moreover, studies have demonstrated the safety and tolerability of curcumin, making it an attractive candidate for clinical use[17]. Clinical trials investigating the effects of curcumin on various health outcomes, including metabolic disorders, neurodegenerative diseases, and cancer, are underway, highlighting its potential clinical applications[19].

ROLE OF GUT MICROBIOTA IN HEALTH AND DISEASE

The gut microbiome, comprising a diverse array of microorganisms, plays a crucial role in maintaining host health and homeostasis. Typically, the gut microbiome is dominated by several key phyla, including *Firmicutes, Bacteroidetes, Actinobacteria*, *Proteobacteria, Fusobacteria*, and *Verrucomicrobia*[21,22]. Among these, *Firmicutes* and *Bacteroidetes* are particularly abundant, with species such as *Lactobacillus, Bacillus*, *Clostridium, Enterococcus, Bacteroides*, and *Prevotella* commonly found[22]. Additionally, Actinobacteria, notably the Bifidobacterium genus, also contribute significantly to the gut microbiome composition. The stability of the gut microbiome is paramount, with a dynamic continuum of composition influenced by various factors such as age, diet, environment, and host genetics[21,23]. Throughout life, the gut microbiota composition undergoes changes, shaped by early microbial contact, genetic predisposition, dietary habits, and lifestyle factors[21,23].

The gut microbiome plays a critical role in numerous disease processes, impacting health outcomes through its influence on metabolism, immune responses, and physiological development. Research has identified associations between gut microbiota and a wide array of diseases, including hypercholesterolemia, respiratory allergies, anxiety, osteoarthritis, hypertension, celiac disease, inflammatory bowel disease (IBD), type 2 diabetes, hypertension, and colorectal cancer[24]. Studies have highlighted the therapeutic potential of manipulating the gut microbiota to treat diseases, with fecal microbiota transplantation emerging as a promising strategy for altering bacterial compositions and addressing conditions such as gastrointestinal disorders and metabolic diseases[25]. The gut microbiome's role in disease pathogenesis extends beyond gastrointestinal ailments, as evidenced by its involvement in allergic diseases, cancer, neurological disorders, and psychiatric illnesses[25]. Early microbial supplementation, probiotics, and specific microbial strains like *Lactobacillus johnsonii* and *Lactobacillus plantarum* may offer therapeutic benefits by promoting immune tolerance induction and restoring gut health[26]. Overall, the intricate interplay between the gut microbiome and disease processes underscores the importance of understanding and leveraging microbial contributions to develop novel approaches for disease prevention and management.

CURCUMIN AND THE GUT MICROBIOTA

Bacterial species involved: Curcumin supplementation has been associated with significant alterations in the composition and abundance of various bacterial species within the gut microbiota, with implications for health and disease. Several studies have highlighted the specific bacterial taxa affected by curcumin supplementation across different populations and health conditions[17,20,27]. Notably, *Escherichia-Shigella*, a genus encompassing pathogenic bacteria associated with gastrointestinal infections, decreased significantly following curcumin supplementation in patients with chronic kidney disease (CKD)[27]. Conversely, beneficial bacterial species such as *Lachnoclostridium* and *Lactobacillaceae spp*. showed significant increases in abundance after curcumin supplementation in CKD subjects, suggesting a potential role for curcumin in promoting gut microbial balance and diversity[27]. Moreover, curcumin intake has been shown to increase the abundance of butyrate-producing bacteria, such as *Clostridium* and *Bacteroides spp*., which are known for their anti-inflammatory and metabolic benefits[17]. A randomized controlled study found that curcumin supplementation led to changes in the abundance of *Clostridium*, *Collinsella*, and *Kluyvera*[7]. Furthermore, curcumin has been shown to reduce the relative abundance of potentially pathogenic bacteria such as *Blautia spp.* and *Ruminococcus spp*., which are associated with gut dysbiosis and inflammation[7]. In addition to promoting the growth of beneficial bacterial species, curcumin supplementation has been found to modulate the relative abundance of specific bacterial taxa associated with disease pathogenesis[28]. Curcumin has been found to increase butyrate production in the gut, which has important implications for gut health and immune function. Butyrate, a short-chain fatty acid produced by certain gut bacteria, serves as a crucial energy source for colonocytes and exhibits anti-inflammatory properties[8,17]. Table 2 shows the altered bacterial species in the gut due to curcumin.

MECHANISM OF ACTION OF CURCUMIN ON THE GUT MICROBIOME

Several studies elucidate the intricate interplay between curcumin and gut microbial composition, shedding light on its therapeutic potential in various health conditions[29,30]. One key mechanism by which curcumin influences the gut microbiome is through its ability to regulate microbial diversity and abundance. Xiao *et al*[30] revealed that curcumin supplementation can restore homeostasis in Th17/Treg responses within the gut, thereby modulating the composition of gut microbiota in mice with diabetic complications[30]. Additionally, curcumin has been shown to regulate the diversity and abundance of intestinal microbiota at various taxonomic levels, suggesting a broad-spectrum impact on microbial

Table 2 Altered bacterial species in the gut due to curcumin

Bacterial species altered	Ref.
Escherichia-Shigella, Lachnoclostridium, Lactobacillaceae spp.	[27]
Clostridium, Bacteroides, Parabacteroides, Collinsella, Kluyvera, Enterococcus spp., Blautia spp., Ruminococcus spp.	[7]
Butyrate-producing bacteria, Clostridium, Bacteroides spp., Beneficial gut microbiota	[17]
Blautia spp. MRG-PMF1	[20]
Lactobacilli, Clostridium perfringens, Anaerobic bacteria producing butyric acid	[18]
Akkermansia, Firmicutes/Bacteroidetes ratio	[6]

communities within the gut[30].

Findings from Burge *et al*[29] and Di Meo *et al*[28] highlight curcumin's ability to favor the growth of beneficial bacteria while reducing the abundance of pathogenic strains in the gut microbiome[29]. This modulation of microbial balance by curcumin is accompanied by a decrease in microbial richness and diversity, as well as the modulation of molecular pathways involved in intestinal inflammation[28]. For example, curcumin influences the intestinal barrier function by modulating tight junction proteins, thus protecting against inflammation-induced disruption of gut integrity. Mechanistically, curcumin attenuates lipopolysaccharide-induced inflammation by reducing the activation of p38 MAPK and myosin light chain kinase, as well as preventing the disruption of tight junction proteins[31]. Moreover, curcumin's interaction with gut microbiota indirectly influences neuroprotection through modulation of signaling pathways such as NF-kB and AP-1, which are involved in inflammatory responses within the gut[28]. The summarized mechanisms of action are presented in Table 3 and Figure 1.

EFFECT OF GUT MICROBIOME ON CURCUMIN

Conversely, emerging evidence suggests that the gut microbiome plays a crucial role in mediating the bioavailability, metabolism, and therapeutic effects of curcumin within the body. Pluta *et al*[32] and Augusti *et al*[33] underscore the impact of gut microbial composition on curcumin's pharmacokinetics and pharmacodynamics[32,33]. Gut microbiota influences curcumin bioavailability and transformation during digestion, with unique human phenolic metabotypes yielding different responses to curcumin[33]. Moreover, the metabolization of curcuminoids by human gut microbiota generates new colonic metabolites with potent pharmacological activities, suggesting a symbiotic relationship between curcumin and gut microbial communities[32].

The gut microbiome acts as a crucial determinant of curcumin's efficacy in various disease states. Zhang *et al*[34] elucidated how curcumin protects against cadmium-induced atherosclerosis by remodeling gut microbiota, restoring bacterial diversity, and reducing pathogenic loads[34]. The modulation of gut microbiota by curcumin contributes to its cardioprotective effects by reducing cadmium absorption and restoring microbial balance[34]. Additionally, the gut microbiota regulates curcumin's effects on microbial richness, diversity, and composition, further underscoring the bidirectional relationship between curcumin and gut microbial communities[35]. Moreover, curcumin enhances response to cytarabine therapy in acute myeloid leukemia by regulating gut microbiome composition, highlighting the therapeutic potential of targeting gut microbiota in conjunction with curcumin-based interventions[36]. Overall, the gut microbiome exerts a profound influence on curcumin's pharmacokinetics, pharmacodynamics, and therapeutic efficacy, highlighting the importance of considering microbial factors in optimizing curcumin-based interventions for various health conditions.

HEALTH IMPLICATIONS

Neurologic diseases: Curcumin exhibits promising therapeutic potential in various neurologic disorders, including Alzheimer's disease (AD), PD, multiple sclerosis (MS), ischemic brain injury, and anxiety (Figure 2). In AD models, curcumin demonstrates neuroprotective effects by mitigating memory impairment and metabolic dysfunction. Moreover, it modulates synaptic plasticity and metabolic pathways, potentially ameliorating AD-related symptoms. Additionally, curcumin enriches beneficial gut microbiota, thereby influencing cognitive functions indirectly[32,37]. In PD, curcumin improves motor deficits and neuroinflammation through modulation of the gut microbiota-metabolite axis. Furthermore, it provides neuroprotective effects and ameliorates motor deficits in PD models[38]. In MS, the curcumin derivative CMG alters gut microbiota composition, suppressing experimental autoimmune encephalomyelitis severity. This suppression correlates with changes in specific bacterial species abundance in feces and ileal contents[39]. In ischemic brain injury, curcumin reduces infarct volume, brain edema, and blood-brain barrier permeability while inhibiting tau protein hyperphosphorylation and disintegrating its fibers. Moreover, it improves cognitive deficits and neurological outcomes post-ischemia[32]. Curcumin treatment demonstrated significant improvements in brain connectivity and social behavior in mice, alongside alterations in gut microbiota composition[40]. In anxiety disorders, curcumin alleviates anxiety-like

Table 3 Mechanisms of action of curcumin

Mechanism of action	Ref.
Regulation of Th17/Treg balance	[30]
Modulation of microbial diversity and abundance	[30]
Improvement of gut microbiota composition	[30]
Influence on immune modulation	[29,50]
Restoration of gut flora balance	[17,29,34,35,50]
Enhancement of cytarabine response in acute myeloid leukemia	[36]
Indirect influence on neuroprotection through modulation of signaling pathways	[28,32]
Modulation of intestinal barrier function	[31]
Biotransformation by gut microbiota	[20,33,35]

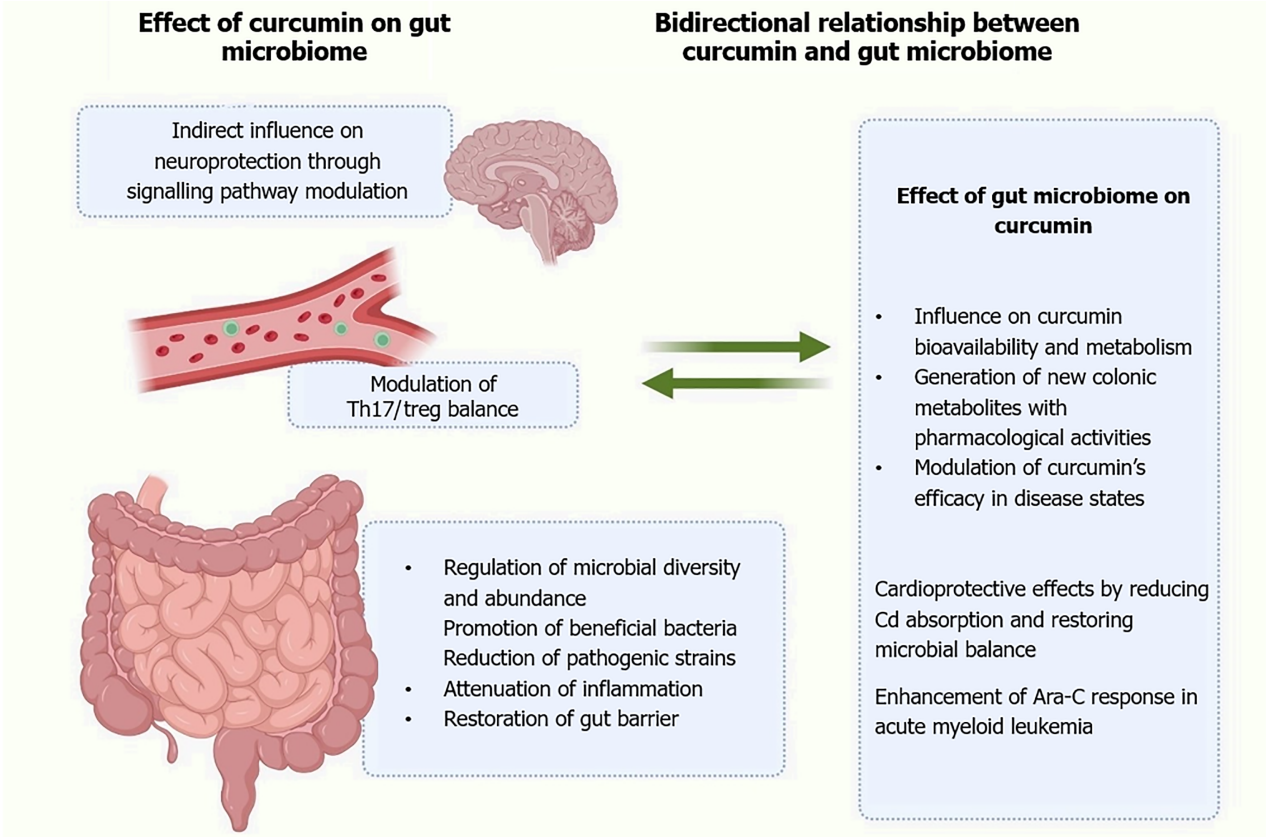

Figure 1 Effect of curcumin on the gut microbiome.

behaviors by modulating the microbiota-gut-brain axis and increasing phosphatidylcholine levels in the prefrontal cortex. Additionally, it influences lipid metabolism and gut microbiota composition to relieve anxiety symptoms[41]. Notably, curcumin's effects on working memory are independent of insulin and linked to body fatness in pre-diabetic individuals, suggesting its potential in cognitive enhancement[42]. Collectively, curcumin exerts its neuroprotective effects through various mechanisms, including scavenging free radicals, modulating synaptic plasticity, regulating neuroinflammation, and altering gut microbiota composition[28]. These multifaceted actions make curcumin a promising candidate for therapeutic intervention in neurologic diseases. Further research exploring curcumin's mechanisms of action and clinical efficacy is warranted to fully harness its therapeutic benefits in neurologic diseases.

GASTROINTESTINAL DISEASES

Numerous studies have demonstrated that curcumin supplementation can exert beneficial effects on gastrointestinal system health by modulating the composition and diversity of the gut microbiota. For instance, Xiao *et al*[30] found that

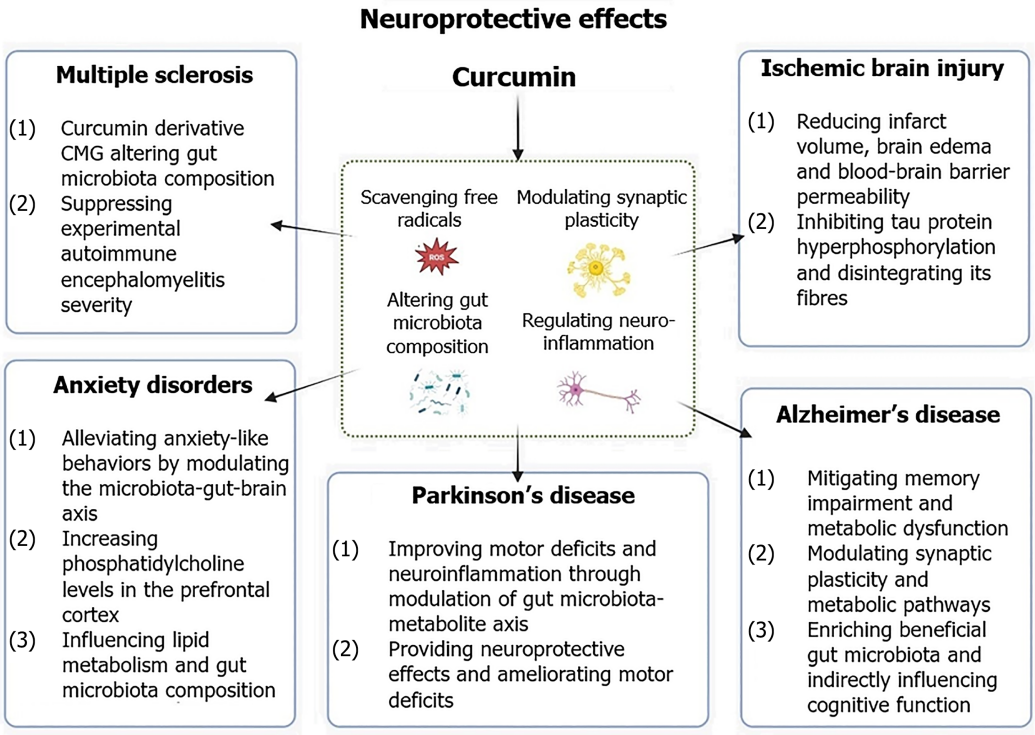

Figure 2 Neuroprotective effects of curcumin.

curcumin improved colitis in diabetic mice by regulating the balance of Th17/Treg cells and restoring intestinal microbiota composition[30]. Similarly, Burge *et al*[29] noted that curcumin supplementation can shift gut microbiota composition towards a profile enriched in short-chain fatty acid-producing bacteria, thereby promoting intestinal mucosal protection and mitigating inflammation associated with intestinal diseases[29]. Lopresti *et al*[43] found that curcumin extract was found to reduce gastrointestinal symptoms in adults. Despite not showing significant effects on the intestinal microbiota, the study observed a reduction in gastrointestinal symptoms following curcumin supplementation [43]. Curcumin's influence on the gut microbiome extends to diseases such as colorectal cancer. Farhana *et al*[44] demonstrated that a combination of curcumin and tocotrienol-rich fraction altered microbial diversity in colorectal cancer cells, suggesting a potential therapeutic synergy in inhibiting colon cancer cell growth[44]. Gan *et al*[45] reported that curcumin and resveratrol, when supplemented in the diet, alleviated intestinal inflammation and regulated gut microbiota composition in piglets, highlighting their potential as dietary interventions for improving gastrointestinal health[45]. In addition to its direct effects on gut microbiota, curcumin also exerts beneficial effects on the gastrointestinal system by enhancing intestinal barrier function. It does so by modulating tight junction proteins, which play a crucial role in maintaining the integrity of the intestinal barrier. By attenuating inflammation and enhancing barrier integrity, curcumin may help protect against gastrointestinal diseases characterized by intestinal barrier dysfunction, such as IBD and leaky gut syndrome[31]. Through its ability to modulate gut microbial composition, attenuate inflammation, and enhance intestinal barrier function, curcumin holds promise as a natural therapeutic agent for promoting gastrointestinal system health and potentially ameliorating a range of gastrointestinal disorders (Table 4). The mechanisms of action of the gut microbiome in gastrointestinal disorders are shown in Table 5.

METABOLIC DYSFUNCTION

Curcumin has garnered significant attention due to its potential therapeutic effects on metabolic dysfunction, particularly in relation to glucose regulation, insulin sensitivity, and diabetes management. Several studies have demonstrated that curcumin supplementation can lead to favorable alterations in gut microbiota composition. For instance, in a study by Hong *et al*[46], curcumin was found to increase the abundance of beneficial bacterial taxa such as *Lachnoclostridium* and *Lactobacillaceae*, while decreasing the levels of potentially harmful bacteria like *Escherichia-Shigella* in CKD patients[46]. Similarly, Zhang *et al*[34] observed that curcumin restored gut microbiota diversity and decreased the abundance of *Lactobacillus*, while increasing levels of *Akkermansia*, thereby mitigating cadmium-induced atherosclerosis[34].

These changes in gut microbial composition induced by curcumin supplementation have been linked to improvements in metabolic parameters. Huang *et al*[47] found that curcumin supplementation improved gut microbiota dysbiosis in diabetic rats, leading to enhanced intestinal barrier function and reduced blood glucose levels[47]. Xiao *et al*[30] reported that curcumin improved diabetes complications by modulating the balance between Th17 and Treg cells in conjunction with regulating gut microbiota composition, underscoring the interplay between immune regulation, gut microbiota, and

Table 4 Implications of gut microbiome in gastrointestinal disorders

Gastrointestinal disorder	Curcumin's effects	Mechanisms of action	Clinical implications
Inflammatory bowel disease	Ulcerative colitis. Reduces disease activity index and endoscopic scores. Increases beneficial bacteria (*Lactobacillus, Bifidobacterium*). Decreases pro-inflammatory bacterial species	NF-κB pathway inhibition; Modulates Th17/Treg balance through microbiota alterations; Improves barrier function	Efficacious as adjunct therapy with mesalamine
	Crohn's disease. Reduces inflammatory markers (TNF-α, IL-1β, IL-6). Strengthens epithelial barrier integrity	Modifies intestinal microbiota composition. Influences bacterial metabolite production	Shows promise in maintaining remission
Colorectal cancer	Suppresses growth of pro-carcinogenic bacteria. Enhances production of beneficial metabolites	Alters microbial diversity in colorectal cancer microenvironment; modulates bacterial enzyme activities related to carcinogenesis	Synergistic effects with conventional chemotherapy
IBS	Reduces abdominal pain and bloating. Normalizes bowel habits	Modifies gut microbiota composition. Improves gut-brain axis signaling	Effects vary across IBS subtypes (IBS-D *vs* IBS-C)
Celiac disease	Reduces intestinal inflammation	Modifies intestinal permeability. Influences microbiota adaptation to gluten-free diet	Potential role in managing non-responsive celiac disease
Gastric Disorders	*Helicobacter pylori* infection. Modification of gastric microbiota	Direct antimicrobial effects. Enhancement of mucosal defense	Synergistic effects with standard triple therapy
	Gastric cancer. Influences *Helicobacter pylori*-associated dysbiosis. Affects cancer stem cell populations	Modulates inflammatory responses	Potential role in prevention and therapy
Small intestinal bacterial overgrowth	Reduces bacterial overgrowth	Modifies small intestinal microbiota composition. Improves intestinal motility	Alleviates small intestinal bacterial overgrowth-associated symptoms
Radiation-induced enteritis	Reduces oxidative stress	Preserves beneficial microbiota. Modulates inflammatory response	Maintains intestinal barrier function
Drug-induced gastrointestinal injury	Non-steroidal anti-inflammatory drugs-induced damage. Maintains microbial homeostasis	Protects against mucosal injury; Reduces oxidative stress	Enhances mucosal recovery
	Chemotherapy-induced mucositis. Preserves microbiota diversity. Reduces inflammatory damage	Supports mucosal healing	Improves treatment tolerance

IBS: Irritable bowel syndrome; TNF-α: Tumor necrosis factor-alpha; IL: Interleukin.

metabolic health[30]. The influence of curcumin on gut microbiota appears to extend beyond direct modulation of microbial populations to impact metabolic pathways. As highlighted by Shen and Ji, polyphenols like curcumin may exert therapeutic effects on metabolic diseases by regulating the gut microbiota[48]. By promoting a microbial profile associated with improved metabolic outcomes, curcumin holds promise as a potential therapeutic agent for addressing metabolic disorders through microbiota-targeted interventions.

MISCELLANEOUS

Cai *et al*[49] investigated curcumin's role in alleviating psoriasis-like inflammation by modulating gut microbiota composition, revealing a correlation between curcumin-induced gut microbiota changes and reductions in psoriasis-related inflammatory factors[49]. Augusti *et al*[33] explored the immunomodulatory properties of curcumin, highlighting its ability to combat inflammatory storms, such as those observed in coronavirus disease 2019. Importantly, curcumin's modulation of the gut microbiota was implicated in influencing disease outcomes, suggesting a potential mechanism by which curcumin exerts its immunomodulatory effects[33]. Liu *et al*[36] investigated curcumin's role in enhancing the response to cytarabine chemotherapy in AML, revealing that curcumin-mediated alterations in the gut microbiota sensitized the response to cytarabine treatment[36].

Collectively, these studies underscore the intricate relationship between curcumin, the gut microbiome, and disease modulation. By influencing gut microbiota composition and function, curcumin holds promise as a therapeutic agent for a wide range of diseases, including neurological disorders, inflammatory conditions, infectious diseases, and cancer. Further research elucidating the mechanisms underlying curcumin-gut microbiome interactions will be crucial for harnessing the full therapeutic potential of this natural compound in disease management and prevention.

Table 5 Mechanism of action of gut microbiome in gastrointestinal disorders

Mechanisms of action	Description	Implications
Direct effects on gut microbiota	Selective pressure on bacterial populations: Curcumin selectively inhibits harmful bacteria while promoting the growth of beneficial microbes	Helps restore a balanced gut microbiome
	Modification of Bacterial Metabolism: Alters metabolic pathways of gut bacteria, affecting their growth and activity	May reduce production of harmful bacterial metabolites
	Influence on bacterial adhesion and biofilm formation: Disrupts bacterial adhesion to gut mucosa and inhibits biofilm formation	Reduces infection risk and persistence of pathogens
	Effects on bacterial virulence factors: Curcumin can suppress the expression of bacterial virulence factors	Lowers pathogenicity of harmful bacterial strains
Host-microbiota interactions	Modulation of immune responses: Modulates gut-associated immune cells, reducing excessive inflammatory responses	Helps in managing inflammatory bowel conditions
	Enhancement of barrier function: Strengthens the intestinal epithelial barrier, preventing translocation of pathogens	Prevents gut permeability ("leaky gut")
	Regulation of mucus production: Promotes mucus secretion in the gut, aiding in the protection of the mucosal lining	Provides an additional layer of defense against pathogens
	Influence on enterocyte function: Enhances the function of enterocytes, the absorptive cells of the intestinal lining	Improves nutrient absorption and gut health
Metabolic effects	Alteration of short-chain fatty acid production: Modulates the production of short-chain fatty acids like butyrate.	Supports gut barrier integrity and reduces inflammation
	Modification of bile acid metabolism: affects the synthesis and transformation of bile acids, impacting digestion and gut health	May alter gut microbial composition and metabolism
	Influence on tryptophan metabolism: Modifies tryptophan metabolism, affecting serotonin production and gut-brain axis signaling	Potentially improves gut-brain communication and mood
	Effects on bacterial enzyme activities: Alters the activities of bacterial enzymes involved in various metabolic processes	Influences gut homeostasis and metabolic health

CHALLENGES AND FUTURE DIRECTIONS

Curcumin, despite its potential therapeutic benefits, faces numerous limitations and challenges that hinder its effectiveness in various disease contexts. One of the primary obstacles is its poor bioavailability, characterized by inadequate absorption and rapid metabolism[32,33,40]. This limitation impedes the attainment and maintenance of therapeutic concentrations of curcumin in the body, thereby limiting its clinical efficacy. Moreover, the bioavailability issues are compounded by challenges in achieving stable concentrations in target tissues[29,40]. These factors pose significant hurdles in realizing its therapeutic potential[28,39,41]. Furthermore, the lack of standardized formulations and inconsistent results from clinical trials contribute to the uncertainty surrounding curcumin's efficacy and safety[19,50]. Curcumin's safety profile is a concern, as evidenced by its cytotoxicity and potential DNA damage, particularly at high doses[42]. These limitations underscore the need for further research to overcome the challenges associated with curcumin's bioavailability, efficacy, and safety to fully harness its therapeutic potential.

Recent advances in understanding curcumin-gut microbiota interactions have opened new avenues for therapeutic applications while raising important questions for future research. Unlike previous reviews that focused on specific aspects of this relationship, our analysis reveals several critical areas requiring further investigation: (1) Temporal dynamics of microbiota changes; (2) Need for longitudinal studies examining the sustainability of curcumin-induced microbiota changes; (3) Investigation of optimal dosing schedules for maintaining beneficial microbiota alterations; (4) Population-specific responses; (5) Examination of genetic and environmental factors influencing individual responses to curcumin; (6) Development of predictive models for personalized curcumin interventions; (7) Novel delivery systems; (8) Investigation of microbiota-targeted delivery systems for enhanced curcumin efficacy; (9) Development of synbiotic formulations combining curcumin with specific probiotic strains; (10) Mechanistic studies; (11) Elucidation of direct *vs* indirect effects of curcumin on specific bacterial populations; (12) Investigation of bacterial metabolites mediating curcumin's therapeutic effects; (13) Clinical applications; (14) Design of microbiota-focused clinical trials for specific disease conditions; and (15) Development of biomarkers for monitoring curcumin-induced microbiota changes. These research directions represent important opportunities for advancing our understanding of curcumin-microbiota interactions and their therapeutic applications.

CONCLUSION

Curcumin, a polyphenolic compound derived from turmeric, exhibits multifaceted pharmacological properties, including

anti-inflammatory, antioxidant, and anticancer effects. Its ability to modulate gut microbiota composition and function further enhances its therapeutic potential. Through the regulation of microbial diversity and abundance, curcumin contributes to the maintenance of gut health and homeostasis, thereby exerting beneficial effects on various disease processes. Studies have demonstrated curcumin's efficacy in neurological disorders, gastrointestinal diseases, metabolic dysfunction, and beyond, with mechanisms involving immune modulation, neuroprotection, and inflammation regulation. However, challenges such as poor bioavailability, inconsistent formulations, and safety concerns warrant further investigation to optimize curcumin's therapeutic utility.

FOOTNOTES

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