

MODULATORY EFFECTS OF BERBERIS SPECIES ON GUT MICROBIOTA AND THEIR SYNERGISTIC INTERACTION WITH PROBIOTIC STRAINS

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Annotation: This article provides a comprehensive literature-based analysis of the modulatory effects of Berberis species, particularly *Berberis vulgaris* L., on gut microbiota and their synergistic interactions with probiotic strains. The findings demonstrate that the bioactive compounds of Berberis, including isoquinoline alkaloids (berberine, palmatine, jatrorrhizine, berbamine) and phenolic constituents, selectively modulate the gut microbial composition by enhancing beneficial taxa such as *Bifidobacterium*, *Lactobacillus*, and *Akkermansia muciniphila*, while suppressing pathogenic bacteria. Additionally, Berberis extracts strengthen intestinal barrier integrity through the upregulation of tight junction proteins and contribute to metabolic stabilization via the microbiota-gut-liver axis, including AMPK pathway activation, improved glucose utilization, and lipid metabolism regulation. Recent evidence further supports the synergistic effects between Berberis extracts and probiotics, which enhance microbial resilience, increase SCFA production, and accelerate the reduction of inflammatory markers. Collectively, these findings position Berberis as a highly promising phytobiotic and a foundational component in developing next-generation symbiotic nutraceutical formulations.

Keywords: *Berberis vulgaris*; berberine; gut microbiota; probiotics; symbiotic interaction; intestinal barrier; tight junction proteins; SCFA; AMPK signaling; dysbiosis; metabolic syndrome; phytobiotics; nutraceuticals.

INTRODUCTION

In recent years, scientific perspectives on the role of the gut microbiota in human health have expanded dramatically. A growing body of evidence indicates that the intestinal microbial community exerts direct influence on immune regulation, metabolic processes, central nervous system function, endocrine balance, and even psycho-emotional well-being. Consequently, disruptions in microbial homeostasis are now regarded as major pathogenic factors contributing to metabolic syndrome, obesity, insulin resistance, inflammatory bowel diseases, dysbiosis, autoimmune disorders, and various neurological conditions.

Within this context, the role of natural bioactive substances in modulating the gut microbiota has become a central topic in contemporary phytobiotics and nutraceutical science. Among medicinal plants, species belonging to the *Berberis* genus, particularly *Berberis vulgaris* L., are emerging as some of the most promising candidates for microbiota-targeted interventions. The plant's principal isoquinoline alkaloid, berberine, along with palmatine, berbamine, jatrorrhizine, and other phenolic compounds, has been shown to selectively modify microbial composition, suppress pathogenic organisms, and promote the growth of beneficial bacteria.

Scientific literature highlights several multidirectional mechanisms through which berberine modulates gut microbiota, including: normalization of the Firmicutes/Bacteroidetes ratio; stimulation of *Lactobacillus* and *Bifidobacterium* populations; reduction of lipopolysaccharide

(LPS) production in Gram-negative bacteria; suppression of pro-inflammatory cytokines such as TNF- α and IL-6; strengthening of intestinal barrier integrity via upregulation of tight junction proteins; enhancement of the biosynthesis of short-chain fatty acids (SCFAs).

Notably, recent research demonstrates that Berberis extracts exhibit synergistic interactions with probiotic strains. Low concentrations of berberine have been shown to enhance probiotic viability, promote bacterial fermentation, and reduce inflammatory mediators. As a result, combinations of plant-derived phytobiotics and probiotics are now being proposed as next-generation therapeutic strategies for intestinal health.

Furthermore, many of berberine's metabolic benefits-such as activation of AMPK signaling, improved glucose utilization, stabilization of lipid metabolism, and increased insulin sensitivity-are now understood to be partially mediated through microbiota-dependent mechanisms. The synergistic interaction between Berberis extracts and probiotics not only restores gut microbial balance but also enhances therapeutic outcomes in metabolic syndrome, type 2 diabetes, hepatic steatosis, irritable bowel syndrome (IBS), and inflammatory bowel diseases such as Crohn's disease and ulcerative colitis.

Therefore, Berberis represents a highly promising phytobiotic candidate, and its combination with probiotics provides the scientific foundation for developing a new generation of "symbiotic phytocomplexes" designed to optimize gut and metabolic health.

LITERATURE REVIEW

Over the past 10–15 years, research on the gut microbiota has become one of the fastest-growing fields in biomedical science. The microbiota is now regarded not only as a digestive component but as a "meta-organ" involved in immune regulation, endocrine signaling, inflammatory pathways, neuroprotection, metabolic homeostasis, and psycho-emotional regulation. Studies show that microbial imbalance (dysbiosis) plays a central role in the pathogenesis of metabolic syndrome, type 2 diabetes, hepatic steatosis, irritable bowel syndrome (IBS), Crohn's disease, autoimmune disorders, heightened sensitivity to environmental toxins, and chronic systemic inflammation.

Within the scientific research focused on herbal modulation of the microbiota, the Berberis genus stands out as one of the most thoroughly examined. Its primary alkaloid, berberine, is widely recognized as a potent phytobiotic capable of modulating disrupted microbial composition, restoring the Firmicutes/Bacteroidetes ratio, reducing inflammation-associated lipopolysaccharide (LPS) production, and promoting probiotic bacterial growth. **Effects on microbial composition.** Scientific sources confirm that berberine: stimulates beneficial genera such as Lactobacillus, Bifidobacterium, and Akkermansia; suppresses pathogenic bacteria, including E. coli, Salmonella, and Clostridium spp, and reduces local inflammatory mediators within the gut. **Restoration of intestinal barrier integrity-** Research indicates that berberine: upregulates tight junction proteins such as ZO-1 and occludin; decreases intestinal permeability ("leaky gut"); enhances mucosal barrier function in inflammatory conditions.

Modulation of metabolic pathways via the microbiota, through the gut-liver-metabolic axis, berberine: increases the production of SCFAs (butyrate, propionate); stabilizes glucose and lipid

metabolism; activates the AMPK signaling pathway, one of the most crucial pathways in metabolic disease modulation.

Synergistic interactions with probiotics-Recent evidence demonstrates strong synergy between Berberis extracts and probiotic strains: Berberine enhances probiotic viability and growth; probiotics improve the intestinal bioavailability of berberine; the combination reduces inflammatory markers 2-3 times faster than either agent alone; synergistic activity produces a clear "symbiotic effect" in dysbiosis correction. Overall, the literature strongly supports the conceptualization of Berberis as a microbiota-modulating phytobiotic and as a scientifically grounded component in the development of symbiotic formulations when combined with probiotics.

RESULTS AND DISCUSSION

Based on the literature, the modulatory influence of Berberis extracts on gut microbiota manifests through several key biological pathways. Normalization of Gut Microbial Composition- Research findings indicate that berberine, the primary alkaloid of Berberis, has the capacity to selectively reshape gut microbial communities. Multiple studies confirm that berberine increases the abundance of beneficial bacterial taxa, including: Bifidobacterium- an essential immunostimulatory probiotic genus, Lactobacillus- a key contributor to intestinal barrier reinforcement, and Akkermansia muciniphila - a species linked to protection against metabolic syndrome and obesity

Simultaneously, berberine markedly suppresses the growth of pathogenic bacteria such as Escherichia coli, Clostridium perfringens, Salmonella, and Klebsiella. These microbiota-restoring effects are strongly associated with improvements in metabolic homeostasis. Restoration of Intestinal Barrier Integrity- According to literature reports, Berberis extracts enhance the expression of tight junction proteins, thereby restoring the physiological integrity of the intestinal epithelium. This mechanism contributes to the reduction of intestinal inflammation, prevention of systemic endotoxin translocation, and attenuation of excessive immune activation. Such protective effects are especially relevant in autoimmune disorders and irritable bowel syndrome (IBS).

Metabolic Stabilization via Microbiota-Dependent Mechanisms- Studies consistently show that berberine exerts metabolic improvements through interconnected pathways, including activation of the AMPK signaling pathway, increased glucose uptake, reduced insulin resistance, attenuation of hepatic steatosis (NAFLD), and enhancement of short-chain fatty acid (SCFA) production. Collectively, these outcomes support the therapeutic potential of Berberis-probiotic combinations in metabolic syndrome, type 2 diabetes, and dyslipidemia.

Synergistic Interactions with Probiotics-Scientific publications highlight several mechanisms underlying the synergy between Berberis extracts and probiotic strains: probiotics significantly increase the intestinal bioavailability and metabolic activation of berberine; berberine enhances probiotic viability and fermentation efficiency; combined administration boosts SCFA production by 1.5-2 fold; inflammatory markers such as IL-6 and TNF- α decline more rapidly. These findings provide strong theoretical foundations for designing next-generation symbiotic phytocomplexes.

CONCLUSION

The literature-based analysis allows the following scientific conclusions: Modulation of Microbiota: Berberis extracts significantly modify the composition and functional activity of gut microbiota, promoting beneficial species while inhibiting pathogenic strains. Enhancement of Intestinal Barrier Integrity: The restoration of tight junction protein expression strengthens epithelial integrity and reduces inflammatory responses. Metabolic Stabilization: Through the gut–intestinal–hepatic axis, Berberis activates AMPK signaling, enhances glucose utilization, and regulates lipid metabolism. Synergy with Probiotics: Combined use of Berberis extracts and probiotics accelerates microbiota recovery, enhances antioxidant defense, and markedly reduces inflammatory biomarkers. Therapeutic Potential: These outcomes provide a robust scientific foundation for incorporating Berberis extracts into modern phytotherapy, nutraceuticals, and symbiotic formulations aimed at improving gut and metabolic health.

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