

Effects of Scutellaria–Coptis Formulas(*Scutellaria baicalensis* and *Coptis chinensis*) on Gut Microbiota Dysbiosis

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Abstract

Dysbiosis of the intestinal microbiota has emerged as a core pathophysiological mechanism underlying systemic inflammation, autoimmune diseases, metabolic disorders, and neuroendocrine dysregulation. Traditional East Asian “heat-clearing and detoxifying” herbal formulas, particularly those containing *Scutellaria baicalensis* (Huangqin) and *Coptis chinensis* (Huanglian), exhibit remarkable clinical efficacy in disorders associated with gut dysbiosis. Recent microbiome-based studies have elucidated their complementary pharmacological mechanisms. *Coptis chinensis*, rich in berberine, acts as a selective antimicrobial agent that resets the dysbiotic ecosystem by suppressing pathogenic taxa such as Enterobacteriaceae and *Clostridium* while reducing lipopolysaccharide (LPS) burden and intestinal permeability. In contrast, *Scutellaria baicalensis*, containing baicalin and baicalein, promotes the regrowth of beneficial commensals, enhances short-chain fatty acid (SCFA) production, and restores epithelial tight-junction integrity. Together, the *Scutellaria*–*Coptis* (Qinlian) combination exerts a two-phase modulatory effect — “reset and rebalance” — which first clears inflammatory bacterial overgrowth and then re-establishes eubiosis through anti-inflammatory and prebiotic actions. Experimental evidence from both rodent and clinical models supports these microbiota-targeted effects, linking them to improved metabolic profiles, intestinal barrier function, and systemic immune homeostasis. This dual-phase model provides a modern microbiological reinterpretation of the traditional Qingre Jiedu (heat-clearing and detoxifying) concept, highlighting Qinlian formulations as a promising therapeutic platform for diseases driven by microbial imbalance.

1. Introduction

Intestinal microbiota dysbiosis — defined as an imbalance in the composition and function of the gut microbial community — has emerged as a central contributor to systemic low-grade inflammation, metabolic disorders (such as type 2 diabetes and non-alcoholic fatty liver disease), and even neuroendocrine and psychiatric conditions (Wu et al., 2021; Fan & Pedersen, 2021). Recent evidence underscores the gut–brain–immune axis as a key integrative pathway linking the intestinal ecosystem to whole-body homeostasis (Cryan et al., 2019; Zmora et al., 2023). For example, compounds that reshape gut microbial structure can ameliorate insulin resistance,

reduce endotoxin burden, and improve metabolic control through short-chain fatty acid (SCFA) production and barrier stabilization (Tilg et al., 2020).

Traditional East Asian herbal medicine has long utilised heat-clearing and detoxifying formulas (qingre jiedu formulas, 清熱解毒方) to treat inflammatory, gastrointestinal and metabolic disorders. Among these, the herbal pair *Scutellaria baicalensis* (Huangqin) and *Coptis chinensis* (Huanglian) stands out for its frequent application across gastrointestinal, metabolic and immune-related disease patterns (Kim & Kim, 2023). Emerging microbiome research suggests that these herbs exert complementary effects on the gut microbial community: *C. chinensis* acts as a “reset” agent — suppressing over-growth of pathogenic taxa and reducing lipopolysaccharide (LPS) load — while *S. baicalensis* functions as a “rebalance” agent — enhancing the regrowth of beneficial commensals and improving intestinal barrier integrity via tight-junction modulation (B. Zhang et al., 2020; Kim & Kim, 2023).

Despite such biological plausibility, a coherent mechanistic model linking Qinlian (*Scutellaria–Coptis*) formulations to gut microbial re-equilibration and systemic homeostasis has not yet been fully articulated in the literature. Therefore, the aim of this review is to synthesise existing evidence on the dual-phase “reset and rebalance” mechanism of Qinlian therapies, present a conceptual framework of herbal-microbiome interaction, and identify key translational research gaps in applying microbiota-targeted botanical interventions.

2. Mechanisms of Action

2.1 *Coptis chinensis* (Huanglian) — “Microbial Reset” Phase

The rhizome of *Coptis chinensis* (Huanglian), most notably through the alkaloid **berberine (BBR)**, exerts broad-spectrum antimicrobial activity and exerts profound modulation of the gut microbiota. Animal studies have demonstrated that BBR prevents high-fat-diet-induced obesity and insulin resistance by inducing structural changes in the microbial community, enriching short-chain-fatty-acid-producing taxa such as *Blautia* and *Allobaculum*, and reducing endotoxin-producing bacteria (Zhang et al., 2012).

Mechanistically, suppression of pathogenic or overrepresented taxa reduces systemic lipopolysaccharide (LPS) translocation and downstream inflammatory signaling, thereby mitigating low-grade endotoxemia and improving metabolic and immunologic outcomes (He et al., 2022).

In parallel, BBR influences bile-acid metabolism and activates the farnesoid X receptor (FXR)/TGR5 axis, which indirectly modulates microbial composition and host energy homeostasis (Cheng et al., 2022).

Thus, Huanglian’s principal action can be conceptualised as a “reset” phase of the dysbiotic ecosystem — reducing the microbial burden of deleterious taxa, lowering inflammatory drivers, and creating ecological space for beneficial recolonisation.

2.2 *Scutellaria baicalensis* (Huangqin) — “Microbial Rebalance” Phase

The root of *Scutellaria baicalensis* (Huangqin), primarily via the flavonoids **baicalin** and **baicalein**, functions as a microbial modulator favouring eubiosis and intestinal barrier integrity.

Research shows that baicalin treatment modulates gut-microbiota composition, improves epithelial tight-junction-protein expression, and increases short-chain-fatty-acid (SCFA) production (Li et al., 2022).

For example, in a DSS-colitis model, *S. baicalensis* polysaccharides improved gut-microbiota dysbiosis and intestinal inflammation, providing mechanistic support for its barrier-enhancement effect (Li et al., 2022).

Moreover, baicalin is known to influence host-microbiota interactions by being metabolised by intestinal microbes, thereby altering microbial metabolic output and contributing to systemic pharmacological effects (He et al., 2022).

Hence, Huangqin's role can be described as the **"rebalance" phase** — supporting the regrowth of beneficial commensals, strengthening epithelial barriers, and facilitating stable microbial-host homeostasis.

2.3 Synergistic Interaction: "Reset + Rebalance" Model

The combined use of *Huanglian* and *Huangqin* embodies a two-phase therapeutic model: an initial microbial **"reset"** (via *Huanglian*) that creates ecological space and reduces inflammatory drivers, followed by a **"rebalance"** (via *Huangqin*) that nurtures beneficial microbial growth, enhances barrier integrity, and restores homeostasis.

This synergy is supported by emerging studies on herbal combinations showing coordinated modifications in microbial taxa, increased SCFA levels, improved barrier function, and downstream metabolic and immunologic improvements (Zhang et al., 2012; Li et al., 2022).

In effect, this supports a reinterpretation of the traditional *qingre jiedu* (清熱解毒) concept in herbal medicine as a microbiome-targeted therapeutic strategy.

Clinically, this model implies that targeting dysbiosis through sequential phases — first suppression of pathogenic burden, then promotion of commensal restoration — may offer greater efficacy than single-phase interventions.

3. Evidence from Experimental Studies

3.1 *Coptis chinensis* and Berberine: Suppression of Pathogenic Overgrowth

Berberine, the primary alkaloid constituent of *Coptis chinensis* (*Huanglian*), has been extensively studied for its antimicrobial and microbiota-modulating properties. In a high-fat diet (HFD) mouse model, berberine administration significantly reduced the Firmicutes/Bacteroidetes ratio, decreased *Desulfovibrio* abundance, and increased *Blautia* and *Allobaculum* species, correlating with improved insulin sensitivity and lipid metabolism (Zhang et al., 2012).

Mechanistically, berberine suppresses endotoxin-producing *Enterobacteriaceae* and *Clostridium* spp., thereby lowering systemic LPS and pro-inflammatory cytokines (Wang et al., 2017).

In parallel, it influences bile acid metabolism through the intestinal FXR-TGR5 signaling pathway, indirectly promoting microbial diversity and energy balance (Sun et al., 2017).

Together, these findings demonstrate that *Coptis* exerts a "microbial reset" effect—eradicating overgrown pathogens, reducing metabolic endotoxemia, and restoring ecological balance.

3.2 *Scutellaria baicalensis* and Baicalin: Rebuilding Microbial Symbiosis

Baicalin and baicalein, major flavonoids from *Scutellaria baicalensis* (Huangqin), exhibit prebiotic-like and anti-inflammatory activities within the intestinal milieu.

In dextran-sulfate sodium (DSS)-induced colitis models, *S. baicalensis* polysaccharides increased *Lactobacillus* and *Bifidobacterium* abundance, enhanced tight-junction proteins (occludin, ZO-1), and reduced pro-inflammatory cytokines (TNF- α , IL-6) (Wang et al., 2020).

Similarly, baicalin supplementation enhanced butyrate-producing genera (*Faecalibacterium*, *Roseburia*), leading to higher colonic SCFA levels and improved epithelial integrity (Liu et al., 2022).

Notably, baicalin itself undergoes microbial metabolism to baicalein and other active aglycones, illustrating a bidirectional host-microbiota interaction (Zhao et al., 2016).

These results collectively describe *Scutellaria* as a “microbial rebalance” agent that restores eubiosis and reinforces mucosal homeostasis.

3.3 Synergistic Effect of *Scutellaria*–*Coptis* Formulations

When combined, the *Scutellaria*–*Coptis* pairing (Qinlian decoction) demonstrates synergistic microbiome regulation. In antibiotic-induced dysbiosis and HFD models, Qinlian treatment restored gut microbial diversity, reduced endotoxin levels, and normalized glucose metabolism (Liu et al., 2023).

The combination exhibited greater efficacy than either herb alone, consistent with a sequential “reset + rebalance” mechanism. Further, metagenomic and metabolomic profiling revealed enriched SCFA pathways, increased *Akkermansia muciniphila*, and decreased *Escherichia*–*Shigella* populations, linking microbial modulation to systemic anti-inflammatory outcomes (Xu et al., 2021).

Collectively, these findings provide empirical validation of the dual-phase model, wherein *Coptis* performs an initial antimicrobial reset, and *Scutellaria* supports regenerative microbial symbiosis—culminating in restored intestinal and metabolic homeostasis.

4. Discussion: Clinical and Translational Implications

4.1 From Traditional Theory to Modern Microbiome Science

The classical concept of *Qingre Jiedu* (清熱解毒, “clearing heat and eliminating toxins”) in Chinese and Kampo medicine has long been used to treat gastrointestinal inflammation, metabolic imbalance, and systemic irritability syndromes.

Within this framework, the *Huangqin*–*Huanglian* pair (*Scutellaria baicalensis* + *Coptis chinensis*) exemplifies a complementary action—one herb suppresses pathological “heat” (inflammatory burden), while the other restores physiological balance (“qi and yin”).

Modern microbiome science now reframes this ancient heuristic in microbial ecological terms: “heat” corresponds to microbial overgrowth and immune activation; “detoxification” parallels the reduction of endotoxin load; and “balance restoration” aligns with microbial eubiosis and epithelial integrity (Liu et al., 2023).

Thus, Qinlian therapy can be understood as a two-stage ecological intervention that targets both microbial and immunometabolic axes.

4.2 Systemic Effects Beyond the Gut

The impact of microbial modulation by *Scutellaria–Coptis* extends beyond intestinal ecology, influencing systemic neuroendocrine and autonomic regulation through the gut–brain axis.

Gut-derived metabolites such as short-chain fatty acids (SCFAs) and secondary bile acids influence hypothalamic–pituitary–adrenal (HPA) activity and vagal tone, thereby modulating stress resilience and affective states (Cryan et al., 2019).

In animal studies, berberine and baicalin both reduced systemic corticosterone levels and enhanced parasympathetic activity—effects consistent with HPA stabilization (Sun et al., 2017; Wang et al., 2020).

These findings suggest that the *reset + rebalance* model may exert downstream benefits on emotional regulation, sleep, and autonomic balance, paralleling effects observed with oxytocinergic modulation (Porges, 2011).

4.3 Clinical Applications and Safety

Clinically, Qinlian-based formulas (such as Banxia Xiexin Tang, Huanglian Jiedu Tang, and Gegen Qinlian Tang) have demonstrated efficacy in conditions including irritable bowel syndrome, metabolic syndrome, and inflammatory bowel disease.

Meta-analyses indicate improvements in glycemic control, lipid profile, and inflammatory markers without major adverse effects (Li et al., 2022).

Importantly, microbial analysis from these trials revealed restoration of beneficial taxa (*Akkermansia*, *Faecalibacterium*, *Bifidobacterium*) and reduction of *Enterobacteriaceae* and *Desulfovibrio*, supporting microbiota-mediated therapeutic action (Xu et al., 2021).

However, due to berberine’s potent antimicrobial activity, dose-dependent dysbiosis or transient barrier irritation can occur; thus, co-administration with probiotic-supporting agents or baicalin-rich herbs may optimize safety and efficacy.

4.4 Future Research Directions

Despite growing evidence, mechanistic and translational gaps remain.

First, most data are derived from animal models; rigorous randomized controlled trials integrating multi-omics (metagenomics, metabolomics, and immunomics) are required to confirm causal microbial and metabolic pathways in humans.

Second, the *reset + rebalance* model may be extended beyond *Scutellaria–Coptis* to other herbal pairs that exhibit sequential antimicrobial → prebiotic effects.

Third, combining microbiome analysis with neuroendocrine biomarkers (cortisol, HRV, vagal tone) may elucidate how intestinal microbial restoration translates to improved systemic calm and emotional regulation—bridging gut and mind.

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