



Exploring Immunological Strategies of Traditional Chinese Medicine in the Treatment of Ulcerative Colitis Based on the Theory of "The Spleen as the Defender"

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Abstract: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by immune dysregulation, mucosal barrier damage, and gut microbiota imbalance. Despite advances with biologics and immunosuppressants, long-term efficacy remains limited. In traditional Chinese medicine (TCM), UC is classified under "dysentery" or "diarrhea," with spleen deficiency and damp-heat excess as key mechanisms, reflecting the theory of "the spleen as the defender." This paper integrates this theory with modern immunology to explore how TCM interventions — such as strengthening the spleen and qi, clearing heat and dampness, and protecting intestinal collaterals — regulate immune responses. Clinical and experimental evidence indicates that TCM can modulate cytokine networks, restore mucosal barrier integrity, and reshape gut microbiota. These findings highlight the unique value of TCM in UC treatment and suggest new directions for integrative approaches to immune-related diseases.

Keywords: spleen as the defender; ulcerative colitis; immunology; traditional Chinese medicine; gut microbiota

1. Introduction

Ulcerative colitis (UC) is a chronic and relapsing inflammatory bowel disease characterized by immune dysregulation, mucosal barrier disruption, and gut microbiota imbalance. Although corticosteroids, immunosuppressants, and biologics have improved disease management, long-term efficacy remains limited and relapse rates are high. In traditional Chinese medicine (TCM), UC is classified under "dysentery" or "diarrhea," with a core pathogenesis of spleen deficiency and damp-heat accumulation. The classical concept of "the spleen as the defender" highlights the spleen's role in maintaining defense and immune balance. Recent studies suggest that TCM therapies, such as invigorating the spleen and qi, clearing heat and dampness, and protecting intestinal collaterals, can regulate immune cells, suppress inflammatory cytokines, repair mucosal barriers, and modulate gut microbiota. Integrating this theoretical framework with modern immunology provides a promising direction for developing novel strategies in UC treatment.

2. Immunological Research on TCM Treatment of Ulcerative Colitis

In traditional Chinese medicine (TCM), ulcerative colitis (UC) is categorized as "dysentery" or "chronic diarrhea," with a pathogenesis of "deficiency in origin and excess in superficial manifestation." Spleen deficiency impairs transformation and transportation, weakens defense, and leads to qi and blood insufficiency, while damp-heat and toxins damage intestinal collaterals and cause relapse. The *Suwen* describes the spleen as "the foundation of acquired constitution" and "the defender," underscoring its role in immunity[1]. Based on this theory, TCM treatment emphasizes strengthening the spleen and qi, clearing heat and dampness, and consolidating the intestines. This aligns with modern immunology, where spleen deficiency parallels impaired gut immunity and damp-heat resembles inflammation. Studies show TCM interventions exert broad immunomodulatory effects. Formulas such as Buzhong Yiqi Tang and Huangqi Jianzhong Tang enhance immune tolerance by increasing Treg cells and reducing Th17 activity[2]. Heat-clearing prescriptions like Baitouweng Tang and Huanglian Jiedu Tang suppress pro-inflammatory cytokines (TNF- α , IL-6, IL-17) while upregulating IL-10. Spleen-strengthening herbs promote mucosal barrier integrity by enhancing mucin and tight junction proteins, and compound prescriptions reshape gut microbiota by enriching beneficial species. Together, these multi-target effects—immune regulation, cytokine balance, barrier repair, and microbiota modulation—highlight the therapeutic value of TCM in UC and its consistency with modern immunological insights[3].

3. Modern Interpretation of "The Spleen as the Defender" and Immune Defense

In traditional Chinese medicine (TCM), the spleen is described as "the foundation of acquired constitution and the source of qi and blood," responsible for nutrient transformation, body nourishment, and generation of defensive qi. The theory of

"the spleen as the defender" emphasizes its role in resistance and disease prevention. Impaired spleen function weakens defense, leaving the body vulnerable to dampness, heat, and recurrent diarrhea or dysentery. Modern immunology provides a parallel perspective, recognizing the spleen as both a hematopoietic and immunoregulatory organ rich in macrophages, dendritic cells, T cells, and B cells. It serves as a hub for antigen presentation, immune activation, and pathogen clearance[4]. This aligns with the TCM view of the spleen as central to defense and homeostasis. At the cellular level, the spleen regulates Treg/Th17 and Th1/Th2 balance, determining immune tolerance versus inflammation. "Spleen deficiency" thus parallels immune suppression or dysregulation, often with reduced IL-10 and elevated TNF- α and IL-6. The spleen also interacts with gut-associated lymphoid tissue (GALT), influencing barrier integrity and microbial balance. TCM's view that spleen deficiency produces internal dampness and damages intestinal collaterals corresponds with findings that impaired splenic function leads to barrier dysfunction, dysbiosis, and ulcerative colitis. Overall, the theory can be scientifically interpreted within immunology, providing a foundation for TCM interventions in UC[5].

4. Immunological Mechanisms of TCM in the Treatment of Ulcerative Colitis

Traditional Chinese medicine (TCM) treatment of ulcerative colitis (UC) follows the classical principles of "strengthening the spleen and qi, clearing heat and dampness, and consolidating the intestines," while modern immunology provides mechanistic insight. Increasing evidence shows that TCM formulas and single herbs modulate immune responses through multiple pathways, improving mucosal inflammation and restoring intestinal homeostasis. As illustrated in Figure 1, TCM exerts broad effects on immune-related cellular and molecular mechanisms.

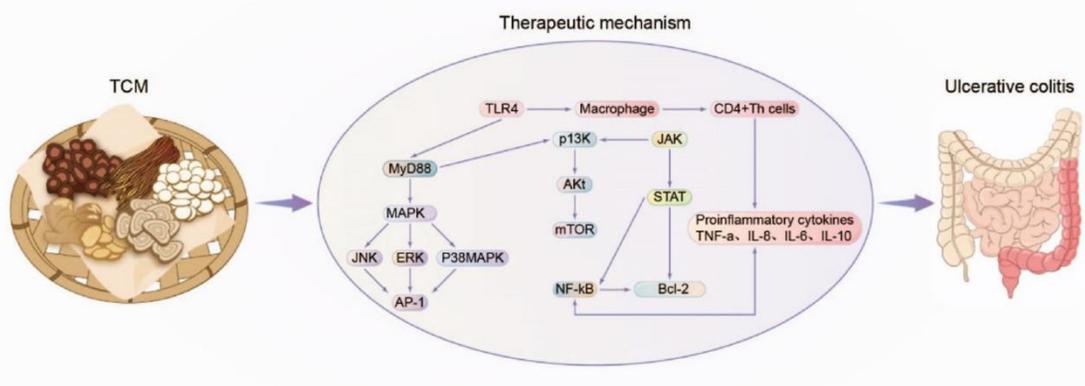


Figure 1. Schematic diagram of the immunological mechanisms of TCM interventions in ulcerative colitis

At the level of innate immunity, TCM regulates the TLR4/MyD88-MAPK pathway, reducing overactivation of JNK, ERK, and p38 MAPK, and inhibiting AP-1 transcription, thereby preventing amplification of inflammation. It also modulates macrophage activity, suppressing abnormal activation and limiting pro-inflammatory mediator release. For adaptive immunity, TCM influences the JAK/STAT pathway, adjusting CD4+ T cell differentiation. By suppressing Th17 overactivation and enhancing Treg restoration, it reestablishes immune balance. Spleen-strengthening and qi-replenishing formulas often act through this mechanism, supporting the principle of "restoring the foundation." Moreover, TCM regulates the PI3K/Akt/mTOR pathway, central to apoptosis, inflammation, and metabolism. By downregulating mTOR and NF- κ B activity, TCM decreases pro-inflammatory cytokines, increases Bcl-2 expression, and promotes mucosal repair and barrier integrity. Finally, TCM rebalances the cytokine network by downregulating TNF- α , IL-6, and IL-8 while enhancing IL-10, breaking the cycle of persistent inflammation. These immunological actions align with the TCM concept of "the spleen as the defender," emphasizing defense enhancement and stability. In summary, TCM's mechanisms extend beyond single targets to comprehensive regulation of innate and adaptive immunity, signaling pathways, and cytokine networks. These multifaceted effects, illustrated in Figure 1, highlight TCM's advantages in UC management and provide a strong foundation for integration with modern medicine.

5. Conclusion

The development of ulcerative colitis is closely associated with immune dysregulation, mucosal barrier impairment, and gut microbiota imbalance. The TCM theory of "the spleen as the defender" offers a unique perspective for understanding its pathogenesis and treatment. By strengthening the spleen and replenishing qi, clearing heat and dampness, and consolidating the intestines, TCM can regulate immune cell function, suppress inflammatory mediators, restore mucosal barrier integrity,

and optimize gut microbiota, thereby achieving holistic immune modulation. Clinical and experimental studies have demonstrated that TCM has significant advantages in symptom relief, recurrence reduction, and improvement of the inflammatory environment.

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