

# HERBAL THERAPIES IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASES: A HISTORICAL AND CONTEMPORARY REVIEW

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## SUMMARY

*Inflammatory bowel diseases (ulcerative colitis and Crohn's disease) are chronic, relapsing disorders of the digestive tract, the etiology of which is complex and includes genetic, immunological, microbiological and environmental factors. Standard therapeutic options often have limited efficacy and significant side effects, which is why interest in complementary and alternative approaches, especially phytotherapy, is growing. Historically, medicinal plants have played a key role in the medical traditions of many civilizations, and modern research confirms the effectiveness of some herbal preparations in modulating the immune response, anti-inflammatory effects and maintaining intestinal homeostasis. This paper presents a historical overview of the use of plants in traditional medicine and modern knowledge about their role in the treatment of inflammatory bowel diseases. Special emphasis is placed on plants such as marshmallow, plantain, flax, licorice, sage, mint, cannabis and turmeric. Although the results of numerous studies confirm their potential in symptomatic relief and reducing inflammatory markers, additional randomized clinical trials are needed to confirm their safety and efficacy. The integration of phytotherapy into standard therapeutic protocols could represent a significant step forward in the holistic approach to patients with IBD.*

**Key words:** inflammatory bowel disease, ulcerative colitis, Crohn's disease, phytotherapy, herbal preparations.

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## INTRODUCTION

The connection between humans and plants dates back to the earliest history – from nutrition, through healing, to ritual and cultural use. The oldest civilizations, such as the Chinese, Egyptians, Indians, Greeks and Romans, knew a large number of medicinal plants whose use has shaped the foundations of medicine for centuries (1–4). Today, in the era of modern medicine, more and more research is focused on the potential of plants in the treatment of chronic diseases, including inflammatory bowel disease (IBD). IBD includes Crohn's disease and ulcerative colitis – chronic inflammatory diseases that significantly impair the quality of life of sufferers. Conventional therapies, although effective in many cases, often fail to lead to permanent remission or cause serious side effects. Therefore, interest in complementary and alternative medicine (CAM), especially phytotherapy, is growing (12–14).

The aim of this review is to unify historical and contemporary knowledge about the use of medicinal plants in the treatment of inflammatory bowel disease and to demonstrate their potential in modern medicine.

## HISTORICAL OVERVIEW OF MEDICINAL PLANT USE

From the Sumerians and Egyptians to ancient Greece and Rome, herbal remedies have been used to treat digestive and inflammatory conditions. Hippocrates described more than 300 plants for therapeutic purposes, while Dioscorides and Galen laid the foundations of European herbal medicine (1,4,6). Monastic medicine played a significant role in the Middle Ages, and the Franciscans in Dubrovnik opened the first pharmacy in 1271, which operated continuously for centuries (10,11). Plants such as flax, licorice, mint, and sage have been used for centuries to treat digestive disorders, while turmeric and cannabis are part of the Eastern medical tradition (5,8,9). Interestingly, much of the traditional knowledge has been confirmed by modern scientific research, highlighting the continuity of the use of plants in medicine (7,22).

## PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE

IBD is a multifactorial disease. Genetic predisposition, immune dysregulation, changes in the gut microbiota, and environmental factors are involved in its pathogenesis (15–19). In patients with IBD, the intestinal barrier is disrupted, leading to increased permeability, abnormal cytokine secretion, and inflammatory response (18). Standard therapy includes corticosteroids,

immunomodulators, and biologics, but side effects and resistance to therapy prompt the need for new therapeutic options (19,20). Toxicity often occurs in patients treated with biologic therapy (62). A significant number of patients with inflammatory bowel disease do not respond to anti-TNF therapy and require more effective treatment (63). Also, due to the lack of primary or secondary response to anti-TNF therapy in a certain number of patients, corticosteroid therapy must be included more often, which opens the possibility of steroid dependence.

## **HERBAL REMEDIES FOR INFLAMMATORY BOWEL DISEASE**

### **Mallow root (*Althaeae radix*)**

It contains high amounts of mucilage, which coats and soothes the lining of the digestive tract. It has been traditionally used for gastritis, enteritis, and irritable bowel syndrome, and clinical experience has shown its effectiveness in alleviating symptoms of IBD (38). Several studies have shown that mallow extract contains a variety of compounds, including phenolic derivatives, flavonoids, terpenoids, catalase enzymes, sulfite oxidase, fatty acids and certain sterols (especially essential fatty acids such as omega-3 and omega-6), beta-carotene, and vitamins C and E, which have anti-inflammatory and antioxidant properties (57, 58).

### **Psyllium seeds (*Psyllium*)**

Acts as a mechanical laxative, improves stool regulation and reduces CRP levels in patients with irritable bowel syndrome. In IBD, it helps with constipation and diarrhea, contributes to the regulation of intestinal microbiota and reduces symptoms (39,40). The seeds contain the monosaccharides glucose, fructose, xylose and rhamnose, as well as the disaccharide sucrose and the trisaccharide planteose (59). Planteose acts as a reserve carbohydrate in the seeds (60). Research has identified biologically active substances such as polysaccharides, lipids, flavonoids, terpenes. Also, analyses have identified certain organic acids and alkaloids. The positive health effect is attributed to these biologically active substances, which were discovered in plantain extracts based on appropriate analyses. The outer shell of the seeds contains polysaccharides that swell in contact with water and form a highly viscous mucus.

### **Flaxseed (*Linum usitatissimum*)**

Flaxseed is rich in fiber and omega-3 fatty acids, and has anti-inflammatory and laxative properties. Active ingredients in flaxseed also include lignin and protein, as well as a number of vitamins and minerals, such as vitamin B1 (thiamine), magnesium, copper, and manganese. Studies have shown a reduction in inflammatory markers and improvement in symptoms in patients with ulcerative colitis (41).

### **Licorice root (*Glycyrrhiza glabra*)**

Active substances in licorice root include triterpenoids and phenols, the most important of which is glycyrrhizin. It is fifty times sweeter than sugar and has potent anti-inflammatory, antioxidant, and immunomodulatory properties. Experimental models have shown suppression of NF- $\kappa$ B and TNF- $\alpha$  and protection of the colonic mucosa (42–45).

### **Sage (*Salvia officinalis*)**

Its antiseptic and anti-inflammatory effects may alleviate symptoms of colitis. Active substances in sage include essential oils (composed of thujone and other compounds), phenolic acids (such as caffeic and ursolic acids), tannins, flavonoids, triterpenes, steroid compounds, and minerals (calcium, magnesium, iron, copper, zinc) and vitamins (B-groups, C, A). Its antiseptic and anti-inflammatory effects may alleviate symptoms of colitis. Preclinical studies suggest the possibility of preventing colon cancer (46,47).

### **Peppermint (*Mentha piperita*)**

The main active ingredients of peppermint are compounds within its volatile essential oil, primarily menthol, which provides a cooling sensation and has therapeutic properties, and menthone, which contributes to the taste and aroma of mint. Other significant constituents include menthyl acetate, the compound responsible for the smell and taste of mint, and other terpenes such as limonene and 1,8-cineole. Peppermint essential oil has been shown to have antispasmodic and analgesic effects. Clinical trials have shown a reduction in abdominal pain and an improvement in quality of life in patients with irritable bowel syndrome and IBD (48–50).

### **Cannabis (*Cannabis sativa*)**

Cannabinoids, primarily CBD and THC, but also lesser-known compounds such as CBG and terpenes that have synergistic effects, are attracting particular attention in the treatment of IBD. CBD is noted for its potent anti-inflammatory and immunomodulatory properties without psychoactive effects. Studies show that CBD reduces intestinal hyperpermeability and regulates T-lymphocyte activity, while THC acts primarily to reduce pain and improve appetite. Although small clinical trials have shown significant symptom relief in patients with Crohn's disease, the results for maintaining remission are not clear. The active ingredients (THC, CBD) act through the endocannabinoid system, modulating intestinal motility and inflammatory processes. Clinical studies have shown improvement in symptoms and a decrease in the need for corticosteroids in patients with Crohn's disease (51–54). There are more than 400 different structurally recognizable compounds in the biological structure of hemp. Among the ingredients are a large number of cannabinoids (depending on the cultivation and type of hemp, the number varies from 60 to 110), nitrosamines,

polycyclic aromatic hydrocarbons, aromatic amines, proteins, glycoproteins, enzymes, sugars, hydrocarbon compounds, alcohols, aldehydes, fatty acids, esters, steroids, terpenes, phenols, flavonoids, etc. Cannabinoids are not evenly distributed in the plant. The dried leaves of the female plant contain the highest amount of THC 2-3%, followed by the lower leaves where the content is less than 1% and the stem with a content  $\leq 0.3\%$ , while cannabinoids are not present in the seeds and roots. Differences in concentrations are due to the presence of glandular hairs.

### **Turmeric (*Curcuma longa*)**

Recent research shows that curcumin also affects the expression of genes involved in the regulation of the immune response, in particular by modulating the balance between anti-inflammatory and pro-inflammatory cytokines. In addition to the NF- $\kappa$ B pathway, curcumin also inhibits the JAK/STAT signaling pathways, thereby reducing the expression of inflammatory mediators. Clinical meta-analyses highlight its potential in maintaining remission in ulcerative colitis, and the safety profile is considered favorable even with long-term use. However, the problem of low bioavailability is being addressed by new pharmaceutical forms such as nanoparticles and liposomes. Turmeric is also being investigated in the context of protecting the intestinal barrier, as it promotes the renewal of epithelial cells and reduces oxidative stress.

The main active ingredient of turmeric is curcumin, a polyphenol that gives turmeric its characteristic yellow color and strong antioxidant and anti-inflammatory properties. In addition to curcumin, turmeric also contains other active ingredients such as polyphenols, diterpenes, sesquiterpenes, sterols, triterpenoids and alkaloids. The active substance curcumin strongly inhibits inflammatory pathways (NF- $\kappa$ B, TNF- $\alpha$ , IL-6). Randomized studies have demonstrated induction of remission and reduction of endoscopic activity of ulcerative colitis (55).

## **DISCUSSION**

It is important to emphasize that despite a large number of studies, the exact causes of IBD remain unknown. Although genetic predisposition, changes in the microbiota and dysregulation of the immune system are recognized in the pathogenesis, none of these factors can be considered the exclusive cause of the disease. It is precisely this unknown that opens up the possibility of using herbal preparations as supportive therapies, since they act in multiple ways and can contribute to reducing symptoms and improving quality of life. The emergence of IBD in newly industrialized regions coincides with the westernization of dietary habits, which potentially changes the gastrointestinal microbiota, which can impair the immune system leading to the occurrence of IBD. The Western diet consists of processed foods high in saturated fats, animal proteins, refined sugars, food additives

combined with low intake of fruits and vegetables, fiber and raw foods (61). Inflammatory bowel disease (IBD) mainly includes ulcerative colitis (UC) and Crohn's disease (CD), with symptoms such as abdominal pain, diarrhea, and weight loss. Barnell et al. (64) reported that more than 50% of patients with Crohn's disease require resection at some point, and Regueiro et al. (65) reported that more than 30% of patients with Crohn's disease (CD) develop perianal fistulas. Due to the long duration of the disease and frequent relapses, IBD represents a major economic burden and psychological stress for the patient, and therefore the quality of life can be extremely impaired (66). In ulcerative colitis, more than 20% of patients progress to colectomy (67). Recent research suggests that herbal preparations, especially turmeric and hemp, can modulate key signaling pathways involved in chronic inflammation. However, well-designed, multicenter, larger-scale studies are needed to confirm their efficacy and safety. Herbal preparations in the treatment of inflammatory bowel diseases offer significant potential, but also challenges. Their value stems from their multicomponent composition that enables the synergistic action of various phytochemicals – flavonoids, phenolic acids, saponins, terpenes and essential oils (22,42). These compounds simultaneously act on various molecular pathways involved in the pathogenesis of IBD, including inhibition of NF- $\kappa$ B, reduction of pro-inflammatory cytokine expression (TNF- $\alpha$ , IL-1 $\beta$ , IL-6), modulation of oxidative stress and regulation of the intestinal microbiota (28–30,43). Clinical studies have particularly highlighted the effectiveness of curcumin, cannabis and probiotics in maintaining remission and improving the quality of life of patients (31,32,53,55). For example, randomized trials with curcumin showed significantly higher remission rates compared to placebo, while cannabis in studies of patients with Crohn's disease reduced the need for corticosteroids (53). Studies in cell cultures, animal models, and clinical trials have suggested that curcumin is a potential agent for the treatment of not only IBD, but also pancreatitis, arthritis, chronic anterior uveitis, and certain types of cancer. Curcumin has a significant effect on the repair of the intestinal mucosa and the maintenance of its morphology (68). Licorice and sage show promising results in experimental models of colitis, while plantain and flaxseed are useful in regulating stool and reducing CRP (39,41,42,46). Supplementation with peppermint oil, in addition to pharmacological standard treatments, is beneficial in patients with constipation-predominant IBD and in patients with bowel-emptying IBD (40). However, limitations are recognizable and obvious. Most studies are based on small samples, short duration, and large variations in dosage and formulation. Standardization of formulations and clear definition of active ingredients remain key research challenges (20,33,34). Also, the interactions of herbal preparations with conventional drugs have not been sufficiently investigated (42,51). Despite these limitations, the

potential of herbal therapies in IBD is undeniable. The use of complementary medicine among patients with IBD, especially in the form of herbal therapies, is widespread in the Western world, as well as in many Asian countries (69). Also, the most commonly used forms of treatment for children with IBD are medicinal plants (turmeric, cannabis), probiotics, fish oils, acupuncture, dietary nutrition and multivitamin therapy (70). Considering that when treating Crohn's disease (CD) with biological therapy, more than 50% of patients do not respond to therapy with deep remission, we are forced to look for other treatment modalities, even dual biological therapy (71,72). The greatest obstacle to optimal combination treatment remains toxicity (62). Herbal preparations should not replace conventional therapy, but complement it, especially in patients with milder forms of the disease or those who want a holistic approach to treatment (12,21,22). The integration of phytotherapy into standard therapeutic protocols could contribute to a more individualized and humane medicine (23,55,56).

## CONCLUSION

Inflammatory bowel disease (IBD) remains a therapeutic challenge despite significant advances in pharmacotherapy. Medicinal plants, used for thousands of years in traditional medicine, are regaining importance thanks to modern scientific evidence. Herbal preparations such as mallow, plantain, flax, licorice, sage, mint, cannabis and turmeric have shown promising results in reducing symptoms and inflammatory markers in patients with IBD. Although herbal therapy cannot yet be considered a substitute for conventional drugs, it can represent a valuable complementary approach. Further research is needed to ensure the standardization, safety and efficacy of these preparations and their integration into official IBD treatment guidelines.

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