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THE USE OF HERBAL MEDICINE TO TREAT ULCERATIVE COLITIS

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ABSTRACT

Ulcerative colitis (UC) is a chronic, nonspecific, resistant illness that typically affects the entire colon and the rectum. In addition to genetic and environmental variables, the etiopathology is most likely associated with dysregulation of the mucosal immune response toward the local bacterial flora. To manage the inflammation or lessen symptoms, a variety of drugs are employed. A vast array of techniques and treatments that fall outside the purview of traditional Western medicine are included in herbal medicine. However, there is little controlled evidence supporting the effectiveness of traditional Chinese treatments for ulcerative colitis, including bovine colostrum enemas, wheat grass juice, aloe vera gel and Boswellia serrata. Herbal remedies may still be less harmful than synthetic ones, despite their inherent risks. The efficacy, relative safety, low cost and high patient acceptability of herbal treatment may be its main advantages. Herbal therapy appears to have gained widespread acceptance among patients worldwide and hundreds of research investigations have evaluated its effectiveness in treating ulcerative colitis. There are undoubtedly hazards and advantages linked with herbal treatment, but the research supporting it is insufficient, complicated and unclear. To optimize the quality and safety of herbal medicine techniques for the treatment of ulcerative colitis, more controlled clinical trials are required, along with stricter regulations.

KEYWORDS

Ulcerative colitis, Genetic and Environmental variables.

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INTRODUCTION

Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis (UC), is a group of long-term inflammatory disorders of the gastrointestinal (GI) tract. It has been proposed that a combination of genetic susceptibility factors, the activation of the mucosal immune system in response to luminal commensal bacterial antigens, and persistent pathologic cytokine production contribute to the onset and chronification of IBD,

even though the exact cause is still mostly unknown[1-3].

Up until now, various medications have been utilized in the management of UC, including 5-aminosalicylic acid, azathioprine, 6-mercaptopurine, cyclosporine and monoclonal antibodies against tumor necrosis factor antibody. The main objectives of medical treatment for individuals with UC aim to trigger and subsequently sustain alleviation of symptoms and inflammation of the mucosa to facilitate a better quality of life with the minimum use of steroids exposure. In recent years, herbal remedies have been utilized for managing UC and proven to be successful in the medical center. In this assessment, we examine the existing understanding of the herbal treatment or traditional Chinese healing (TCM) for managing patients with UC.

Herbal Medicine

The word “herb” comes from the Latin term herba. signifying “grass.” The phrase has been used for plants. Of which the foliage, stalks, or produce are utilized for nourishment, for medications, or for their aroma or taste. Herbal medicine denotes to popular and conventional healing methods relying on the use of botanical sources and herbal extracts for therapeutic purposes circumstances. The application of herbs for disease treatment is nearly common among indigenous communities. Several customs have start to lead the field of herbal medicine in the West towards the conclusion of the twentieth century[4].

The utilization of alternative therapies by patients with IBD, especially in the guise of herbal treatments, is common in the Western world and in numerous Asian nations such as China and India. It appears that the use is continually rising even though just a limited quantity of controlled experiments addressing either effectiveness or protection of these natural substances is present. Up to now, there are restricted controlled evidence showing the effectiveness of TCM, like aloe vera gel, wheatgrass juice, Boswellia serrata and bovine colostrum enemas for the treatment of patients with UC[5].

In Eastern Asian nations, TCM(Traditional Chinese Medicine) is currently commonly used to treat UC. According to Langmead *et al*, slippery elm, fenugreek, devil's claw, Mexican yam, tormentil, and Wei tong ning (a TCM) are herbal treatments for the treatment of IBD. Novel medications used to treat IBD include slippery elm, fenugreek, devil's claw, tormentil and wei tong ning[6,7].

Aloe Vera

Tropical plants like aloe vera are utilized in traditional medicine all throughout the world. Its potential to alleviate ulcerative colitis has been investigated. The mucilaginous aqueous extract of Aloe barbadensis Miller's leaf pulp is known as aloe vera gel. Because of its anti-inflammatory properties, some physicians have prescribed aloe vera juice to UC patients. It was the most popular natural treatment. Aloe vera's precise modes of action are unknown. Aloe vera gel has been shown *in vitro* to decrease the release of prostaglandin E2 and IL-8 from human colonic mucosa, suggesting that it has a role in antibacterial and anti-inflammatory reactions[8].

A double-blind, randomized controlled trial was conducted to evaluate the efficacy and safety of aloe vera gel in patients with mild-to-moderate active ulcerative colitis (UC).Total number of Participants are 44 patients in which 30 received aloe vera gel and 14 received placebo). Given 100mL of oral aloe vera gel or placebo, twice daily for 4 weeks. The Results in the aloe vera group is clinical remission are in 9 patients (30%), clinical improvement are in 11 patients (37%) and overall response are in 14 patients (47%). At same time in the placebo group clinical remission is in 1 patient (7%), clinical improvement is in 1 patient (7%) and overall response are in 2 patients (14%). Although the study was small, aloe vera demonstrated a higher rate of remission, improvement, and response compared with placebo. However, the placebo response was unusually low compared to other UC trials, which may limit generalizability[9].

Serrata boswellia

An ayurvedic herb called boswellia, commonly known as Indian frankincense, is made from the

plant's resin and has long been used to treat ulcerative colitis. The majority of the herbal pharmacologic activity are believed to be attributed to boswellic acid, the main component of boswellia. Boswellic acid has been demonstrated to specifically inhibit 5-lipoxygenase with anti-inflammatory and anti-arthritic properties in both in vitro and animal models[10]. The benefits of Boswellia in the treatment of UC have shown promise because the inflammatory process in IBD is linked to enhanced leukotriene activity. Additionally, it has been discovered to directly suppress intestinal motility by a mechanism that involves L-type Ca2+ channels. In rodents, boswellia has been shown to lessen intestinal inflammation and edema brought on by chemicals. According to other research, it may be cytotoxic[11].

Gupta et al. conducted a clinical study on 30 patients with chronic ulcerative colitis (UC) to evaluate the efficacy of Boswellia serrata gum preparation in comparison with sulfasalazine. Patients were divided into two groups: Group A (n = 20): Received Boswellia gum preparation at a dose of 900 mg/day (in three divided doses) for 6 weeks. Group B (n = 10): Received sulfasalazine 3 g/day (in three divided doses) for 6 weeks. The Results is that in the Boswellia group, 14/20 patients achieved remission and 18/20 patients demonstrated improvement in one or more clinical parameters. In the sulfasalazine group, 4/10 patients achieved remission, while 6/10 patients showed improvement in at least one parameter. The conclusion of this study was Boswellia gum preparation was found to be an effective and well-tolerated treatment for ulcerative colitis, showing higher remission and improvement rates compared with sulfasalazine, with fewer side effects[12].

Butyrate

Butyrate serves as a key energy source for intestinal epithelial cells and is essential for maintaining colonic homeostasis. Its therapeutic potential in ulcerative colitis (UC) has been explored through the use of butyrate enemas, with some studies reporting a reduction in colonic inflammation following topical administration. Nancey *et al.* suggested that reduced butyrate oxidation in UC may be linked to the presence of TNF-α at concentrations typically observed in inflamed mucosa[13]. The anti-inflammatory action of butyrate is thought to involve NF-κB inhibition, which leads to decreased levels of myeloperoxidase, cyclo-oxygenase-2, adhesion molecules, and various cytokines. These effects have been validated in both in vitro and in vivo studies[14,15].

Patients with active UC often demonstrate a diminished ability to oxidize butyrate, whereas those in remission generally show normal oxidation, indicating that impaired butyrate metabolism is more likely a secondary effect of inflammation rather than an inherent mucosal defect[16,17].

Furthermore, clinical studies using enteric-coated butyrate tablets (4g/day) in combination with mesalazine have shown significant improvement in disease activity compared with mesalazine monotherapy in mild-to-moderate UC[18].

Licorice

TCM makes considerable use of licorice, which is extracted from the plant's root, to treat a wide range of illnesses. Additionally, licorice possesses adaptogenic and immune-modulatory qualities that are necessary for the pathophysiology of ulcerative colitis. Glycyrrhizin is one of several active compounds that are believed to be responsible for its biologic activity. A material that is isolated and refined from licorice, diammonium glycyrrhizinate, has potential applications in the management of ulcerative colitis[19].

Studies have shown that diammonium glycyrrhizinate can reduce intestinal mucosal inflammation in rats and significantly lower the expression of NF-κB, TNF-α and ICAM-1 in inflamed tissues[20]. Clinical trials using licorice in combination with other herbal preparations have also demonstrated beneficial effects in the management of ulcerative colitis (UC)[21].

At higher concentrations, glycyrrhizin has been reported to exert an antiestrogenic effect by binding to estrogen receptors, while the estrogenic activity of licorice is thought to result from its isoflavone constituents. Its mineralocorticoid-like activity is

believed to occur through inhibition of the 11β-hydroxysteroid dehydrogenase enzyme, leading to suppression of plasma renin activity and aldosterone secretion. Additionally, licorice exhibits chemopreventive properties by modulating the Bcl-2/Bax pathway and inhibiting carcinogenesis[22-24].

Slippery elm (Ulmus fulva)

The powdered bark of the slippery elm tree is used to make the supplement known as slippery elm. Native Americans have long used it to treat gastrointestinal issues like diarrhea and cough. The potential of slippery elm as an IBD supplement has recently been investigated[25]. The antioxidant benefits of slippery elm in IBD patients have been validated by a study. Although the study to date has shown promise, it is insufficient to support slippery elm's widespread usage in the management of IBD[6].

Extracts of tormentil

Extracts from tormentil are utilized as a supplemental treatment for chronic IBD because of their antioxidative qualities. Positive results have been noted in individual UC patients. A clinical trial evaluated the safety and efficacy of tormentil extracts in 16 patients with active ulcerative colitis (UC) (clinical activity index ≥ 5). Patients received escalating oral doses of 1200, 1800, 2400, and 3000mg/day, each for 3 weeks, followed by a 4-week washout period. Outcome measures to be taken are side effects, clinical activity index (CAI), C-reactive protein (CRP) and tannin levels in serum. The results is that in case of tolerability the mild upper abdominal discomfort occurred in 6 patients (38%), but none required discontinuation. In case of efficacy at the 2400mg/day dose, median CAI improved from 8(6-10.75) at baseline to 4.5(1.75-6) and CRP decreased from 8(3-17.75)mg/L to 3(3-6)mg/L. During treatment course the CAI declined during therapy in all patients but rose again during washout. While studying pharmacokinetics neither intact nor metabolized tannins were detected in serum by liquid-mass spectrometry. The conclusion was found to be that tormentil extracts were safe up to 3000mg/day and showed clinical benefit in active UC[26].

The wheat grass (Triticum aestivum)

The wheat grass juice has been used for the treatment of various GI conditions. A double-blind clinical trial evaluated the efficacy of wheat grass juice in patients with ulcerative colitis (UC). The Dosage of the juice was that treatment began with 20mL/day and gradually increased by 20mL/day up to a maximum of 100mL/day (≈3.5 oz), over 1 month. The outcomes was that clinical improvement was observed in 78% of patients receiving wheat grass juice and in comparison, only 30% of patients in the placebo group showed improvement. In respect to safety no serious adverse effects were reported and final conclusion was that wheat grass juice appears to be a safe and effective therapy, either as a standalone or as an adjunct treatment for active distal UC[27].

Curcumin

Curcumin, the active constituent of turmeric (Curcuma longa), is recognized for its anti-inflammatory properties. It has been shown to stimulate bile secretion, aiding in fat digestion, and to reduce gastric acid output, thereby offering protection against gastric and intestinal damage caused by factors such as inflammation, medications, stress, or alcohol.

In a preliminary clinical study, all 5 patients with chronic ulcerative proctitis experienced improvement after curcumin supplementation. Mechanistically, curcumin is known to inhibit NF-κB activation, which in turn reduces the expression of pro-inflammatory mediators. Additionally, curcumin can bind directly to thioredoxin reductase, altering its function from an antioxidant enzyme to a potent pro-oxidant, further contributing to its biological effects[28].

The first randomized, multicenter, double-blind, placebo-controlled trial from Japan evaluated the role of curcumin in maintaining remission in ulcerative colitis (UC). Number of Participants where 97 patients enrolled; 89 completed the study. All patients received a standard maintenance regimen of mesalamine or sulfasalazine, plus either curcumin 1 g twice daily or placebo for 6 months. A follow-up of dose was an additional 6 months

without study medication. Results at 6 months, the relapse rate was significantly higher in the placebo group compared to the curcumin group (P = 0.049). The conclusion was that curcumin, when used alongside conventional anti-inflammatory agents (mesalamine or sulfasalazine), may provide added therapeutic benefit in UC maintenance therapy[29].

Germinated barley foodstuff

Two open-label Japanese trials evaluated the effectiveness of germinated barley foodstuff (GBF), a preparation rich in dietary fiber and glutamine-containing protein that acts as a prebiotic, in the management of UC[30]. In trial 1 the participants i.e 11 patients received GBF for 4 weeks in addition to conventional therapy, compared with 9 patients on conventional therapy alone which results in patients that receives GBF showed a greater reduction in clinical disease activity. In trial 2 (Follow-up) the participants i.e 21 patients received GBF for 24 weeks alongside ongoing 5-aminosalicylic acid and corticosteroid therapy which results in significant reduction in rectal bleeding and nocturnal diarrhea. The relapse prevention study was done in which number of participants were 22 UC patients in remission which received GBF plus conventional therapy and were compared with 37 patients on conventional therapy alone and the results was found to be the GBF group had a lower relapse rate over 12 months. Hence conclusion was shown to be that GBF may aid in both treatment and maintenance of remission in UC, possibly due to its ability to modulate gut microflora and its high water-holding capacity[31].

Bromelain

In addition to being used as a blood thinner and digestive aid, bromelain has been used to treat edema, sinusitis, arthritis, and sports injuries. The use of bromelain as a supplement for IBD, particularly UC, has been researched. According to recent studies, the "active" ingredient in pineapple, bromelain, may help reduce the inflammation linked to ulcerative colitis. It is currently unknown which mechanisms are principally in charge of its anti-inflammatory properties. Nevertheless, bromelain's anti-inflammatory effect on T-cell activation and cytokine release in vitro and in vivo in mouse models of IBD depends on proteolytic action[32,33].

Bromelain's primary mode of action seems to be proteolytic, but there is also evidence of immunomodulatory and hormone-like effects that function through intracellular signaling pathways. It has been demonstrated that bromelain inhibits cell surface receptors, including the hyaluronan receptor CD44, which is linked to pro-inflammatory mediator induction and leukocyte movement[34,35]. Furthermore, it has been observed that bromelain dramatically lowers CD4+ T-cell infiltrations, which are the main effectors in animal models of gastrointestinal inflammation. In a murine colitis model using IL-10-deficient animals, bromelain has been shown to be useful in reducing the clinical and histologic severity of colonic inflammation[36].

The psyllium

Plantago ovata, a shrub-like herb, is the source of psyllium, which is categorized as a mucilaginous fiber because of its ability to gel in water. Because it absorbs water and expands as it passes through the digestive tract, it has been used as a laxative for a very long time. Hemicellulose, a mostly insoluble fiber found in psyllium husks, efficiently raises the weight and moisture content of stool while also aiding in the retention of water in the colon. While some carbohydrates, like psyllium, have an impact on both the large and small intestines, soluble fibers, like psyllium, are known for their effects on the stomach and small intestine, while insoluble fibers are known for their effects on the large intestine[37].

Although the precise process by which psyllium husk lowers cholesterol is unclear, psyllium also exhibits hypocholesterolemic effects. According to research on animals, psyllium more than doubles the activity of cytochrome 7A, also known as cholesterol 7α-hydroxylase, a rate-limiting enzyme in bile acid synthesis, compared to cellulose or oat bran, but less than cholestyramine. Psyllium may boost the activity of HMG-CoA reductase and cholesterol 7α-hydroxylase in rats given a high-fat diet. In a double-blind study, UC patients who took

20g of ground psyllium seeds twice a day with water experienced less symptoms, including bleeding and stayed in remission longer than those who were just taking mesalazine[38].

CONCLUSION

Because UC is a chronic illness, individuals may need to take medication for the rest of their lives in order to improve their quality of life, lower their risk of colon cancer, and prevent relapse. Patients in symptomatic remission are most vulnerable to poor adherence, frequently taking less than 70% of their recommended medicine, even though nonadherence affects patients at all phases of UC. UC is one of many acute and chronic GI illnesses that can be treated with medication therapies. The herbs listed above serve as a basic example of what UC patients in many nations throughout the world often take. When discussing this type of treatment with their patients, doctors should be direct and provide evidence-based information. Large clinical double-blind studies evaluating the most popular alternative medicines are also required. These herbal remedies have been tried frequently in their conventional setting and have also shown promise in new and intriguing ways, creating new therapy options for pathologic conditions. In addition to being examined in their conventional setting, these herbal remedies have also been shown to be effective in new and intriguing ways, creating new therapy options for pathologic conditions. There are encouraging examples of successful biochemical, animal model, and human-controlled trials in the literature and the majority of herbal medicines go through research that is just as thorough as that of pharmaceutical medications. Because of this, the production, distribution, and prescription of herbal medications are currently at an all-time high and are only predicted to rise. When utilized as therapeutic agents to treat illness and disease, many herbal medications work well.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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