Editorial

The use of natural products in the treatment of inflammatory bowel disease

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The use of complementary medicine among patients with inflammatory bowel disease, particularly in the form of herbal therapies is widespread in the Western world as well as in many Asian countries including China and India.[1] It seems that their use is continously increasing despite the fact that only a small number of controlled trials dealing with either efficacy or safety of these natural products exist. So far, there is limited controlled evidence indicating efficacy of traditional Chinese medicines, aloe vera gel, wheat grass juice, Boswellia serrata and bovine colostrum enemas in patients with ulcerative colitis.[2] However, there is emerging evidence that many of these substances have the ability to modulate the immune system and disrupt the proinflammatory cascade through a variety of mechanisms, including antioxidant effects, alterations in cell signaling (in particular the nuclear factor kappaB pathway), cytokines, proinflammatory mediators, and disruption of bacterial flora.[3] It must be emphasized that natural therapies are not always safe as fatal hepatic and renal failure have occurred with some preparations and interactions with conventional drugs are potentially dangerous.[4]

NATURAL PRODUCTS USED IN THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

So far, several plants or their components have been used in the treatment of patients with inflammatory bowel disease with various rates of success. The available data are analysed below.

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1. Mastic gum

Mastic gum is a natural product produced by trees growing exclusively in the Greek island of Chios. Its aromatic and therapeutic characteristics are well known for centuries. It contains a large number of antioxidant substances, most of which have been recently identified. In a recent study the effectiveness of mastic administration on the clinical course and plasma inflammatory mediators of patients with active Crohn's disease was evaluated. Ten patients and 8 controls were recruited to a 4 wk treatment with mastic caps (6 caps/d, 0.37g/cap). It was found that mastic treatment significantly decreased the Crohn's disease activity index and the plasma levels of IL-6 and CRP.[5] In a subsequent study the same group of investigators evaluated the influence of mastic on some immunological parameters in patients with mildly to moderately active Crohn's disease and in healthy controls. Treating Crohn's disease patients with mastic resulted in the reduction of TNF-alpha secretion. Migration Inhibitory Factor release was also significantly increased meaning that random migration and chemotaxis of monocytes/ macrophages was inhibited. It seems that mastic acts as an immunomodulator on peripheral blood mononuclear cells, acting as a TNF-alpha inhibitor and a migration inhibitory factor stimulator.[6] Further double-blind, placebo-controlled studies are required to clarify the role of this natural product in the treatment of patients with CD.

2. Glabridin

Glabridin is a functional component of liquorice having anti-inflammatory capabilities. Oral treatment with glabridin (10 or 50 mg/kg/day for 7 days) significantly attenuated mortality, loss of body weight, shortening of the colon and severe clinical symptoms in a rat model of colitis. This was associated with significant amelioration of the disruption of the colonic architecture, reduction in colonic myeloperoxidase activity and reduction in the pro-

duction of inflammatory mediators including nitric oxide, prostaglandin E2, and proinflammatory cytokines.[7]

3. Scutellariae Radix extract

The effect of Scutellariae Radix extract on an axperimental model of colitis in rats was investigated. Treatment with this extract relieved the clinical symptoms, including reduction in body weight, and shortening and ulceration of the colon. Administration of this extract also significantly reduced the histological damage and enhanced recovery of normal colonic secretory function.[8]

4. Tormentil extracts

Tormentil extracts have antioxidative properties and are used as a complementary therapy for chronic inflammatory bowel disease. Sixteen patients with active ulcerative colitis received Tormentil extracts in escalating doses of 1200, 1800, 2400 and 3000 mg/d for 3 weeks each. Each treatment phase was followed by a 4-week washout phase. During therapy with 2400 mg Tormentil extracts per day, median clinical activity index and C-reactive protein improved from 8 (6 to 10.75) and 8 (3 to 17.75) mg/L at baseline to 4.5 (1.75 to 6) and 3 (3 to 6) mg/L, respectively. During therapy, clinical activity index decreased in all patients, whereas it increased during the washout phase. Neither undegraded nor metabolized tannins could be detected by liquid-mass spectrometry in patient sera.[9] Tormentil extracts appeared safe up to 3000 mg/d.

5. Wormwood herb

In a double-blind study, 40 patients with Crohn's disease receiving 40 mg of prednisone daily for at least 3 weeks were administered a herbal blend containing wormwood herb (3 x 500 mg/day) or placebo for 10 weeks. After 8 weeks there was almost complete clinical remission in 65% patients as compared to none in the placebo group.[10] This remission persisted till the end of the observation period. It was also noticed that wormwood had a steroid sparing effect. Wormwood also had an effect on the quality of life of Crohn's disease patients, which was not achieved by other standard medications.

6. Guggulsterone

The plant sterol guggulsterone has been shown to have anti-inflammatory properties. Administration of guggulsterone significantly reduced the severity of DSS-induced murine colitis as assessed by clinical disease activity score, colon length, and histology. Tissue upregulation of IkappaB and IKK phosphorylation induced by DSS was attenuated in guggulsterone-treated mice.[11] Guggulsterone blocks NF-kappaB signaling pathway by targeting IKK complex in IEC and attenuates DSS-induced acute murine colitis, which suggests that guggulsterone could be an attractive therapeutic option in the treatment of IBD.

7. Dietary polyphenols

Dietary polyphenols are a major source of antioxidants consumed by humans. Polyphenols possess not only antioxidant properties but also antiviral, antibacterial, anti-inflammatory and anticarcinogenic effects, as well as the ability to modulate certain signaling pathways such as nuclear factor-kappaB activation.[12]

The effects of green tea extract were tested in an experimental model of colitis in rats. Treatment with green tea extract significantly attenuated diarrhoea and loss of body weight. Moreover, a remarkable amelioration of the disruption of the colonic architecture, significant reduction of colonic myeloperoxidase and tumor necrosis factor-alpha production was noticed.[13] Green tea extract also reduced the appearance of nitrotyrosine immunoreactivity in the colon and reduced the up-regulation of ICAM-1.

The polyherbal formulation derived from an ancient authentic classical text contains four different drugs named Bilwa (Aegle marmeloes), Dhanyak (Coriandrum sativum), Musta (Cyperus rotundus) and Vala (Vetiveria zinzanioids). The influence of this polyherbal formulation was evaluated in an experimental model of colitis in rats. A significant inhibition of activity of colitis comparable with standard doses of prednisolone was found.[14]

8. Crataegifructus

The protective effect of hawthorn fruit (Crataegifructus) was examined on a murine model of colitis. Hawthorn fruit decreased signs of inflammation such as infiltration by polymorphonuclear leukocytes and multiple erosive lesions, and improved leukotriene B4 levels.[15] The results suggested that hawthorn fruit and the Kampo formula that contains this ingredient may have potential therapeutic utility in patients with inflammatory bowel disease.

9. Aloe vera

Aloe vera is an herbal preparation with significant anti-inflammatory effects. It has widely been used by patients with inflammatory bowel disease for many years. In a double-blind, randomized, placebo-controlled trial 44 hospital out-patients with mildly to moderately active ulcerative colitis were randomly given oral aloe vera gel or placebo, 100 mL twice daily for 4 weeks, in a 2 : 1 ratio. Oral aloe vera taken for 4 weeks produced a clinical response more often than placebo; it also reduced the histological disease activity and appeared to be safe.[16]

10. Triticum aestivum

The wheat grass (Triticum aestivum) juice has been used for the treatment of various gastrointestinal conditions. Patients with active distal ulcerative colitis were randomly allocated to receive either 100 cc of wheat grass juice, or placebo, daily for 1 month. Treatment was associated with significant reductions in the overall disease activity index and in the severity of rectal bleeding.[17] No serious side effects were noticed. Wheat grass juice appeared to be effective and safe as a single or adjuvant treatment of active distal ulcerative colitis.

CONCLUSION

The above mentioned results concerning the administration of extracts derived from plants and herbals represent a simple paradigm of what is in regular use by patients with inflammatory bowel disease in many countries of the world. Physicians should address their patients straightforwardly regarding this kind of treatment and offer evidence-based information about their use. At the same time, large clinical double-blind studies assessing the most commonly used alternative therapies are needed. Pharmaceutical companies should strongly support research in the field of alternative treatment even if their financial gain is be much lesser compared to other kinds of treatment including biological agents. The cost of treatment of inflammatory disease patients is rising continously and alternative medicine could represent a new effective and cheap confrontation. Meanwhile, doctors should improve their empathy and understanding about possible benefits of alternative and complementary therapies.

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