

# Complementary and alternative medicine for gastrointestinal disorders

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*Clin Med*  
2007;7:224-7

**ABSTRACT – Complementary and alternative medicine (CAM) is a growing area of public interest. With increasing numbers of patients using these modalities, it is essential that Western medical practitioners become familiar with the available CAM literature to facilitate better patient care. While the volume of CAM research in gastrointestinal disorders has increased, there are still few modalities for which definitive conclusions can be made. This review will provide an overview of current knowledge of CAM therapies for functional gastrointestinal disorders, inflammatory bowel disease and liver disease. An understanding of this evolving literature is useful in discussing these therapies with patients who use, or are considering using, them. As we learn more about these CAM modalities, integration of those shown to be effective into our conventional practice and avoidance of those shown to be risky or of little use will be of benefit both to patients and practitioners.**

**KEY WORDS:** acupuncture, alternative medicine, complementary medicine, functional dyspepsia, functional gastrointestinal disorder, herbal medicine, irritable bowel

## Introduction

The use of complementary and alternative medicine (CAM) in the West has been on the rise in the past few decades, fuelled by popular media, widespread marketing of commercial products, and possibly an increasing disenchantment with the contemporary practice of Western medicine. In the area of gastrointestinal (GI) illness, CAM use appears to be most prominent in the functional gastrointestinal disorders (FGIDs). For example, in a UK sample, 26% of patients with GI symptoms and 48% of those with irritable bowel syndrome (IBS) used CAM.<sup>1</sup> The costs of CAM therapies is great, as much as \$34 billion in out-of-pocket expenses per year in the United States, and the value of the treatments remains poorly examined.<sup>2</sup> To adequately advise patients in the use, or avoidance, of CAM treatments it is essential that primary care physicians and specialists are aware of the types of modalities available and the efficacy data or lack thereof.

CAM modalities can be categorised into several main classes including herbal/nutritional, mind-body, body-based, and energetic. Some CAM treatments, such as traditional Chinese medicine (TCM), homeopathy, and Ayurvedic medicine, exist within an entire framework of medical and, in some cases, spiritual philosophy. The use of specific CAM modalities varies by nationality and by the specific illness.<sup>3,4,5,6</sup> Homeopathy, for example, is quite common in France, whereas herbal treatment is more common in the US. Several studies have shown that female gender is most predictive of CAM use.<sup>4,5,6</sup> Dissatisfaction with the patient's Western medical practitioner appears to also play a role.<sup>4</sup> Herbal treatment (including single herbs and combination therapy), acupuncture, and hypnotherapy are among the most extensively studied CAM treatments for GI illness in Western literature and will be the focus of this review.

## CAM for functional gastrointestinal disorders

### *Traditional Chinese medicine-based herbal therapy*

Two double blind, randomised controlled trials have been published on the use of TCM for IBS. The most recent studied diarrhoea in patients with a specific TCM diagnosis of 'stagnation of liver energy and asthenia of spleen'.<sup>7</sup> This is a pattern based on symptoms and physical examination but not related to the anatomic liver and spleen. Subjects were treated for eight weeks with extracts from 11 herbs commonly used for this TCM pattern and were then studied for another eight weeks post treatment. No improvement over placebo was seen in the primary outcome measure of global symptom improvement (35% and 44% had improvement in the treatment and placebo groups respectively). The treatment group actually had a worsening of diarrhoea. The earlier study had three treatment arms: a standardised herbal combination, a placebo and a herbal combination individualised to patients' global symptom pattern under the TCM paradigm, adjusting this formula at each visit as symptoms changed.<sup>8</sup> All TCM diagnostic patterns were included. Both standardised and individualised treatment groups showed a substantial

benefit over placebo after 16 weeks of therapy and the individualised treatment showed continued benefit 14 weeks after treatment ended. The vast difference in results between these two trials may be due to a number of factors including duration of treatment, type of herb preparation (raw herbs *v* extracts), variety of herbs used, and choice of primary outcome measures.

### Combination herbal therapy

A commercial compound of nine herbs, STW 5, has been studied in animal models and humans for its effects on gastrointestinal function. Rodent models show that STW 5 alters small intestinal smooth muscle function,<sup>9</sup> decreases small intestinal afferent nerve discharge in response to distension (a model of visceral hypersensitivity),<sup>10</sup> and leads to fundic muscle relaxation with increased antral contractility on *in vitro* gastric muscle strips.<sup>11</sup> STW 5 appears to act as an anti-spasmodic via calcium channel blockade.<sup>9</sup> Several clinical trials for functional dyspepsia (FD) and one for IBS have supported a possible role for STW 5 in FGIDs.<sup>12–15</sup> Melzer *et al* performed a meta-analysis of the randomised placebo controlled STW 5 trials for FD.<sup>16</sup> In a pooled analysis of data from three of the trials, the treatment arm showed a greater effect ( $p=0.001$ , 95% CI 0.11–0.47) on the subjects most inconvenient GI symptom (acid symptoms, epigastric pain, dysmotility-like symptoms, or functional vomiting). IBS patients also showed improved abdominal pain and IBS symptom scores after STW 5 treatment in a randomised, double blind, placebo controlled trial.<sup>12</sup>

### Single herb therapy

Single herb therapies have also been described for IBS and FD. Peppermint oil extract and artichoke leaf extract are two of the most common single herbs. Artichoke leaf extract has been studied in a randomised placebo controlled trial for FD and a postmarketing surveillance study for IBS.<sup>17,18</sup> The extract improved global symptoms and quality of life (QOL) in dyspeptic patients when compared to placebo. The mechanism of action is not clear, but the extract has been shown to have antimicrobial effects, to stimulate bile flow, and may also act as an antispasmodic.<sup>19–21</sup>

Peppermint oil has been studied in both IBS and FD with inconsistent results. Peppermint oil is widely available in capsule form and in some preparations is combined with caraway oil. It is thought to act via calcium channel blockade, as an intestinal antispasmodic with smooth muscle relaxant properties.<sup>22</sup> In combination, but not individually, peppermint and caraway oils decrease visceral hyperalgesia to colorectal distension in a post-inflammatory rat model, another possible reason for benefits seen in FGID patients.<sup>23</sup> In a study by Liu *et al*, IBS patients treated for one month with peppermint oil had improved abdominal pain, bowel movement frequency, abdominal distension, and flatulence over a placebo control group.<sup>24</sup> Several similar studies in IBS have shown benefit, but a meta-analysis of the randomised controlled trials was inconclusive due to methodological flaws among the analysed trials.<sup>25</sup> When studied in FD

in combination with caraway oil, peppermint oil has been shown to provide global symptom improvement,<sup>26</sup> and was shown elsewhere to provide benefit equivalent to cisapride.<sup>27</sup> Peppermint oil was well tolerated in multiple clinical trials, though theoretical concerns for worsening acid reflux exist due to lower oesophageal sphincter relaxation.

Single herb preparations have been available as constipation aids for many years. Increasingly, combinations of these herbs, with or without a fibre supplement, have been marketed as well. Aloe vera, senna, cascara sagrada, and rhubarb root are among the most common herbal laxatives. Despite hundreds of years of use, very little data is available about the long-term safety and efficacy of these herbs. It has long been a concern that herbal stimulant laxatives lead to worsening constipation or even colonic inertia, but this theory is not well supported and may merely reflect the natural history of chronic constipation in some patients.

In summary, there is considerable promise for several herbal agents in treating FGIDs based on both preclinical and clinical studies. Unfortunately many of the clinical trials are small or of suboptimal methodology. The contradictory results of some studies stem from the lack of standardisation for doses, ingredients and outcome measures. While knowledge of the available data may help us guide patients when they choose herbal treatments, clear recommendations are difficult to make at this point.

### Acupuncture

Acupuncture is an attractive modality for those patients who prefer not to take medications or supplements. Unfortunately, while many intriguing effects of acupuncture on GI and central nervous system physiology have been described, the current literature does little to support the use of acupuncture clinically in FGIDs, other than as a placebo. Several animal and human studies have shown acupuncture effects on GI motility, including improved gastric emptying and accommodation.<sup>28,29</sup> Acupuncture may also decrease visceral pain, via deactivation of descending nociceptive pathways and decreased limbic activity.<sup>30–32</sup> Decreased pain and decreased autonomic nervous system response to visceral stimulation are also seen when acupuncture is performed on dogs and rats undergoing colonic balloon inflation.<sup>33,34</sup> Studies of acupuncture effects on rectal sensitivity to balloon distension in humans have shown varied results, though decreased rectal hypersensitivity with acupuncture has been reported.<sup>35–37</sup>

With this encouraging preclinical data, it remains surprising that acupuncture trials for IBS have shown mostly a placebo effect. A number of issues make interpretation of the existing acupuncture data in IBS difficult. Some experts believe that acupuncture is only useful in the context of individualised point combinations (as in TCM), while others choose specific points based on the physiology gleaned from preclinical models. A wide variety of acupuncture styles use various acupoint combinations, needling techniques, depth of insertion, and use of electro-acupuncture which impairs standardisation across studies. It is also very difficult to choose a placebo control, as

some of the 'sham' techniques may have potential benefits themselves. Examples of these would include acupuncture at points not traditionally considered acupoints, and shallow-insertion acupuncture. The two studies with the best methodology available are randomised blinded sham controlled trials of acupuncture for IBS, both of which showed no benefit over the sham condition.<sup>38,39</sup> Acupuncture would theoretically appear useful for functional dyspepsia due to the described effects on gastric emptying, visceral sensitivity, and potential vagal nerve stimulation.<sup>28,29,40</sup> Unfortunately no high quality trials of acupuncture for FD are available in Western literature. In summary, despite observed effects on GI physiology, at this point acupuncture cannot be endorsed as efficacious for FGIDs. Continuing research in this area may determine why the expected effects have not been revealed in clinical trials.

### Hypnotherapy

The effectiveness of hypnotherapy for IBS has repeatedly been shown.<sup>41-45</sup> Hypnosis usually requires weekly individual sessions over several months, but has been used in groups and also successfully through self-instruction.<sup>46</sup> Hypnosis involves progressive relaxation, followed by suggestions of soothing imagery and sensations focused on the individual's symptoms. Improvements in overall well-being, QOL, abdominal pain, constipation, and bloating have been noted.<sup>43-45</sup> Physiological changes have also been observed. Simren *et al* have shown that hypnotherapy reduces both the sensory and motor component of the gastrocolonic response.<sup>47</sup> Emotional states of anger and relaxation induced by hypnosis can alter rectal sensitivity to balloon distension.<sup>48</sup> Symptoms of functional dyspepsia have also been successfully reduced following hypnotherapy.<sup>49</sup> One of the difficulties with hypnosis is that it is very dependent on the therapist, and it may be difficult to find one who is both trained in hypnosis and knowledgeable about FGIDs. Additionally, like many alternative therapies, it can be costly and often is not covered by insurance plans.

### CAM for inflammatory bowel disease

Few clinical trials have been published in the English literature on CAM treatment for ulcerative colitis (UC) and Crohn's disease, though surveys from multiple Western countries show frequent use of herbal and other alternative treatments in this patient population.<sup>4,50,51</sup> Ulcerative colitis is the focus of most studies, as it tends to have more homogeneous presentation than Crohn's disease. Most published trials are small, uncontrolled studies which can not reasonably guide therapy. Among the few randomised controlled trials is a study of aloe vera gel for mild to moderate UC.<sup>52</sup> The rationale for use of aloe vera in inflammatory bowel disease (IBD) includes historic claims of healing, anti-inflammatory effects, as well as supportive *in vitro* data.<sup>53</sup> After four weeks the treatment group had a greater decrease in histological colitis score and clinical activity index compared to placebo, though there was no difference in sigmoidoscopic score. Patients continued on a stable dose of their usual

disease-suppressing therapies during the study. Difficulties with the study, however, included a 20% drop-out rate, a small sample size, and relative small improvements in the primary outcome parameters. Thus it is suggested but not conclusive that aloe vera gel may be a reasonable adjunctive agent to standard UC medications. Other herbal treatments that appear to be worth further study include wheatgrass juice (an antioxidant)<sup>54</sup>, the Ayurvedic preparation of *Boswellia serrata*<sup>55</sup> and Chinese herbal medicine.<sup>56</sup>

### Other CAM modalities for inflammatory bowel disease

Two small studies in the English literature have examined the use of acupuncture for UC with the suggestion of benefit compared to sham acupuncture<sup>57</sup> or 5-aminosalicylic acid (5-ASA) agents<sup>58</sup> but neither had high quality methodology. An effect of acupuncture via the vagally mediated anti-inflammatory pathway has been suggested as a possible mechanism of potential benefit in IBD.<sup>59,60</sup> This pathway may similarly be benefited by mind-body therapies, though few specific IBD studies exist. A novel multi-component mind-body intervention was examined in UC patients by Elsenbruch *et al* including stress management, diet, exercise, and self-care training.<sup>61</sup> Outcome measures included QOL, perceived stress, IBD symptoms questionnaire (IBDQ), as well as laboratories for inflammatory and endocrine factors. While QOL and IBDQ improved in comparison to a waiting-list control group, no changes in inflammatory mediators were seen. Studies looking at single component mind-body therapies, such as yoga and meditation, which have traditionally been purported to have immunological benefits, are needed.

### CAM for liver disease

Herbal treatments are the most commonly reported CAM methodologies used for chronic liver disease. Viral hepatitis, alcoholic hepatitis, and cirrhosis have been the most studied liver disorders in trials using herbal products. Milk thistle, or silymarin, is one of the most well known of these herbal products and is widely available as a dietary supplement. Silymarin extracts have been shown to be hepato-protective in animal models against multiple toxins, including acetaminophen,<sup>62</sup> excess iron,<sup>63</sup> and carbon tetrachloride.<sup>64</sup> While numerous studies have been published using silymarin in a range of hepatic diseases, many of these studies have been uncontrolled, have small sample sizes, and lack useful outcomes such as histological improvement or improvements in mortality. A few studies have shown improvements in liver biochemistries,<sup>65,66</sup> but a meta-analysis limited to high quality studies of longer duration did not.<sup>67</sup> No improvement in all cause mortality was found with treatment of liver disease with silymarin in a recent systemic Cochrane review.<sup>68</sup> Despite the lack of efficacy data, silymarin ranked as the 10th most commonly purchased single herb supplement in 2005 by the American Botanical Council. While it is generally agreed that silymarin is well-tolerated and safe, proof of the benefits of the extract remain elusive.<sup>69</sup>

Liquorice root extract, phyllanthus, and multiple herb combinations are also used by patients for liver disorders, but with even less supportive evidence.<sup>69</sup> Acupuncture and mind-body approaches to liver disease remain largely unstudied in the English literature. Mind-body techniques such as mindfulness meditation, tai chi, or yoga are potential areas of interest for study in patients with chronic liver disease, as they have been shown to improve QOL and stress symptoms associated with other medical illnesses such as chronic heart failure, HIV, and cancer.<sup>70–74</sup> In summary, there are no CAM modalities for liver disease with adequate proof of efficacy to recommend them at this time. Particular caution should be taken with herbal treatments due to toxicity risks.

## Conclusions

Patients with GI disorders continue to use CAM therapies at considerable cost and with very little evidence of efficacy. As primary care physicians and gastroenterologists, it is in our best interests to know what alternative therapies our patients are using and make informed recommendations. Patients choose CAM therapies not only to feel better, but also to take control of their own healthcare decisions. In this setting, the patient-physician relationship can be harmed by overt dismissal of CAM modalities by the physician. When there is available literature on a specific treatment, a knowledgeable discussion of the pros and cons can be helpful in gaining patient trust. Discussing alternative therapies that appear to be benign and may have potential benefit (true or placebo), such as hypnotherapy, peppermint oil or acupuncture, is reasonable if they are not cost prohibitive to the patient. It is important to emphasise that, particularly in regards to herbal treatments, 'natural' or 'alternative' is not equivalent to safe. Herbal side effects, toxicities, and drug-herb interactions can occur and patients should be aware of this. Additionally, regulation of herb purity and dosage remains problematic.

Clearly we have much still to learn about CAM treatments in terms of efficacy, safety and cost-effectiveness. As interest in this area of research increases, the greatest barriers to moving forward are the lack of research funding and the continued use of less than rigorous methodologies in designing new clinical trials. A truly collaborative effort between CAM practitioners and conventional research physicians or scientists, along with continued support from governmental agencies will be needed if our knowledge has a chance of catching up with our patient's use of CAM modalities.

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