

Management of Irritable Bowel Syndrome (IBS) in Adults: Conventional and Complementary/Alternative Approaches

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Abstract

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder with a range of symptoms that significantly affect quality of life for patients. The difficulty of differential diagnosis and its treatment may significantly delay initiation of optimal therapy. Hence, persons with IBS often self-treat symptoms with non-prescribed pharmacological regimens and/or complementary and alternative medicines (CAM) and by modifying diet and daily activities. In addition, most common pharmacological approaches target IBS symptom management rather than treatment, and prescribed medications often result in significant side effects. The purposes of this review article are to: (1) address current issues related to IBS, including symptom presentation, diagnosis, and current treatment options; (2) summarize benefits and side effects of currently available pharmacological regimens and other symptom management strategies, with an emphasis on commonly used CAM therapies and diet modification; and (3) outline recommendations and future directions of IBS management based on systematic reviews, meta-analyses, and research findings. (*Altern Med Rev* 2011;16(2):134-151)

Introduction

IBS is defined as “abdominal pain or discomfort that occurs in association with altered bowel habits over a period of at least three months.”¹ Symptoms of IBS include abdominal pain, change in bowel habits (diarrhea or constipation), bloating, and incomplete defecation.² However, symptom presentation and severity vary.³ Since current diagnostic criteria are based on symptoms,¹ definitive diagnosis of IBS presents challenges due to overlap in symptom presentations with other diseases or associated conditions (e.g., lactose intolerance, inflammatory bowel disease, celiac sprue, small intestinal bacterial overgrowth). More than 75 percent of patients suffering from IBS in

the United States go undiagnosed; 75 percent of those diagnosed suffered at least two years or more, and one-third of these suffered for over 10 years prior to diagnosis.^{4,5} Lack of definitive diagnosis and treatment and the chronic, debilitating nature of IBS often compel patients to change or limit their diets,² seek non-prescribed pharmacological regimens (complementary and alternative medicine [CAM] therapies in particular),^{6,7} and modify routine daily activities⁸⁻¹⁰ in order to manage symptoms.

The purposes of this review article are to: (1) address current issues related to IBS including symptom presentation, diagnosis, and current treatment guidelines; (2) summarize benefits and side effects of currently available pharmacological regimens and other symptom management strategies, with an emphasis on commonly used CAM therapies and diet modification; and (3) recommend future directions of IBS management based on systematic reviews, meta-analyses, and research findings.

IBS: Prevalence and Diagnosis

Depending on how IBS criteria are defined, overall prevalence rates range from 2.1-22 percent. Women are about 1.5-2 times more likely to develop IBS than men.^{1,5,11,12} Although it is present in all age groups, prevalence of IBS seems to decline with advanced age.⁵ According to Rome III criteria, an IBS diagnosis can be made if recurrent abdominal pain has been present for at least three days per month during the preceding three months, accompanied by two of the following three symptoms: relief with defecation, onset of symptoms with a change of stool consistency, and stool frequency without any obvious biochemical abnormalities or morphological changes.¹³ Since

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current differential diagnosis of IBS is not based on morphological changes or characterized by biochemical dysregulation, the only way to differentiate IBS from other functional bowel disorders (FBD) is by exclusion. Despite the advocated use of Rome II and III criteria to diagnose IBS (Table 1), a recent systematic review published by the American College of Gastroenterology (ACG) Task Force reported that the accuracy of this criteria has not been well established.¹ This has been reflected in this review by referring to IBS as a symptom complex, where individual symptoms have limited diagnostic accuracy.

Impact on Quality of Life (QOL)

The most frequently reported symptoms negatively impacting QOL in persons with IBS are abdominal pain, bowel difficulties, bloating, and limitations in eating/diet restrictions.^{4,14} While constipation-predominant IBS and diarrhea-predominant IBS similarly impact QOL,^{2,14} bloating and diarrhea have the most negative impact on patient self-confidence and often lead to avoidance of social settings.¹⁵ IBS affects daily functioning, work and lifestyle,⁴ and interrupts sleep, which leads to increased fatigue.¹⁶ For example, many persons with IBS are forced to stay close to a toilet (>50%), are distressed by symptoms (69%),

experience lack of control over their lives (57%), and are emotionally disturbed (upset, depressed, less confident, or worried). The degree of interruption of daily life is also related to co-existing or co-occurring conditions such as depression and anxiety. Relationships between stress and IBS have been reported by researchers,¹⁷⁻²¹ and most patients suffering from IBS identify stress and anxiety as symptom aggravators.² Psychological stress can increase severity of IBS symptoms,¹⁷ and a correlation between slow onset of IBS symptoms and common stress disorders such as depression and anxiety was noted by Mayer et al.²¹ It is therefore important to consider each individual's lifestyle, medical history, and co-existing conditions (e.g., diet, physical activity, recent bowel infection, family history of colon cancer) when diagnosing patients.^{22,23}

Health Care Costs Associated with IBS

The direct and indirect costs associated with IBS are estimated at \$200 billion worldwide.²⁴ This is related to the high incidence (approximately 250-300 cases of IBS diagnosed per 100,000 people) and prevalence of IBS compared to other FBDs, such as inflammatory bowel disease (IBD). Moreover, the costs of IBS in the United States have significantly increased during recent

Table 1. Rome II and III IBS Diagnostic Criteria

Rome III criteria	Rome II criteria
Diagnostic criterion [†] Recurrent abdominal pain or discomfort [‡] at least three days/month in last three months associated with two or more of the following:	At least 12 weeks of abdominal discomfort or pain that has two out of three features, which need not be consecutive, in the preceding 12 months:
<ol style="list-style-type: none"> 1. Improvement with defecation. 2. Onset associated with a change in frequency of stool. 3. Onset associated with a change in form (appearance) of stool. 	<ol style="list-style-type: none"> 1. Relieved with defecation; and/or 2. Onset associated with a change in frequency of stool; and/or 3. Onset associated with a change in form (appearance) of stool.
In pathophysiology research and clinical trials, a pain/discomfort frequency of at least two days a week during the screening evaluation is recommended for subject eligibility.	Symptoms that cumulatively support the diagnosis of IBS: <ul style="list-style-type: none"> – Abnormal stool frequency (for research purposes “abnormal” may be defined as greater than three bowel movements per day and less than three bowel movements per week); – Abnormal stool form (lumpy/hard or loose/watery stool); – Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation); – Passage of mucus; – Bloating or feeling of abdominal distension.

[†] Criterion fulfilled for the last three months with symptom onset at least six months prior to diagnosis.

[‡] “Discomfort” means an uncomfortable sensation not described as pain.

Adapted from: Drossman DA, Douglas A, eds. *Rome III: The Functional Gastrointestinal Disorder*. 3rd edition ed: Degnon Associates; 2006.

years. In 1998, direct costs (e.g., medical services, hospitalizations) were estimated to be \$1.4 billion. Indirect costs (e.g., loss of work hours/productivity due to time spent in medical services/treatment, lost future earnings if job was lost) were estimated to be \$205 million, adding up to a total cost burden of \$1.6 billion. By 2000, this number increased to \$1.8 billion.²⁵

Pathogenesis and Pathophysiology

The pathophysiology of IBS is distinguishable from celiac disease and inflammatory bowel diseases (e.g., ulcerative colitis, Crohn's disease) since IBS does not present with gross organic or biochemical abnormalities.²⁶⁻²⁸

Although the pathogenesis of IBS is not known, a multi-factorial involvement of diet, gene mutations, psychosocial factors, and immune-mediated processes is hypothesized.²⁹ The contribution of these factors varies and in many cases no single cause can be determined.

One theory regarding the pathophysiology of IBS involves interference of neurotransmission between the central nervous system (CNS) and the intestines. A number of structures in the CNS are connected with the gut via serotonergic and cholinergic nerves – referred to as the enteric nervous system (ENS).^{30,31} Independent of the afferent connections, the intestine uses serotonin itself to regulate gut motility. Serotonin binds to 5-HT₄ and 5-HT₃ receptors, and its signaling activity is terminated by binding to the specific serotonin reuptake transporter.^{32,33} It has been shown that the activity of this transporter is reduced in several GI disorders (including IBS) that present with common symptoms of dysregulated intestinal motility caused by persistent serotonin release at its respective receptors.³³ Based on this theory, a variety of treatment approaches have been suggested that temporarily treat the symptoms rather than the cause of IBS, since there is still considerable lack of knowledge about IBS pathogenesis and pathophysiology.

Conventional Pharmacological Treatments

IBS can be classified as either diarrhea predominant (IBS-D), constipation predominant (IBS-C), or a mixed form (IBS-M).²² The diagnosis leads to treatment recommendations with limited effectiveness for IBS management. Due to the wide range of symptoms that may be experienced, the available pharmacological treatments are mainly targeted at symptom reduction. In addition, some patients may have coexisting conditions that contribute to the severity of IBS symptoms, requiring further consideration when choosing treatment options.^{34,35} Based on predominant GI motility

Table 2. Conventional Pharmacological Treatments for IBS

Indication	Drug Target	Physiological Effect	Drugs/Compounds Examples
IBS-M	serotonergic and adrenergic receptors	↑ compliance, ↔ motility	venlafaxine, fluoxetine
	intestinal flora	↔ motility, ↓ bloating, ↓ pain	probiotics
	cholinergic receptor antagonists	↓ intestinal motility, ↓ pain	cimetropium, pinaverium, hyoscine, otilonium, mebeverine
IBS-D	5-HT ₃ receptor antagonists	↓ intestinal motility, ↓ pain	ondansetron, alosetron, cilansetron
	selective M ₃ receptor antagonists	↓ intestinal motility	zamifenacin, darifenacin
	α ₂ agonist	↓ intestinal motility, ↓ pain sensation	clonidine
	μ-opioid receptor agonist	↓ intestinal motility, ↓ peripheral pain	loperamide
IBS-C	chloride channel modulator	↑ intestinal motility, ↑ water secretion	lubiprostone
	5-HT ₄ agonists	↑ intestinal motility, ↑ water secretion	tegaserod, metoclopramide, domperidone, cisapride

dysfunction, loperamide and codeine for the treatment of diarrhea in IBS-D, laxatives and prokinetics for the treatment of constipation in IBS-C, and antispasmodics for all types of IBS have been used extensively to reduce the respective symptoms. Current pharmacological treatments are summarized in Table 2.

IBS-D Treatments

Loperamide is an opioid receptor agonist that is not absorbed from the GI tract after oral administration, acting locally to reduce GI motility and spasms.³⁶ Similar to loperamide, codeine can reduce abdominal and visceral pain³⁷ as well as GI motility, but may affect the CNS, causing sedation and potential drug abuse.³⁸ Many patients with IBS-D also suffer from nausea and vomiting due to serotonin stimulation of 5-HT₃ receptors in the intestines. There are a number of 5-HT₃ antagonists that were originally prescribed for the treatment of chemotherapy-related nausea, but are now often used to reduce symptoms of IBS-D.³⁹ For instance, ondansetron, granisetron, alosetron, and cilansetron are all specific 5-HT₃ receptor antagonists that reduce nausea and vomiting and act as visceral analgesics in IBS-D.⁴⁰

IBS-C and IBS-M Treatments

Although it was more effective than a placebo, the use of the prokinetic tegaserod in IBS-C and IBS-M has been limited due to adverse ischemic cardiovascular events.^{1,41} Several other prokinetics such as metoclopramide, domperidone, and cisapride are used off-label, even without a specific indication for IBS treatment.⁴² Lubiprostone is another recently approved prokinetic drug that acts on chloride channels to increase water secretion into the intestines. Prokinetics increase GI motility and provide visceral analgesia by acting as dopamine antagonists, serotonin antagonists at the 5-HT₃ receptor, and serotonin agonists at the 5-HT₄ receptor.^{43,44}

Increasing dietary fiber intake is an important treatment option that should be considered before prescribing tegaserod or lubiprostone for patients with IBS-C. Fiber stimulates GI motility and loosens stool consistency.⁴⁵ Laxatives may also be considered as initial treatment if fiber intake alone does not alleviate constipation. Use of laxatives such as polyethylene glycol, or the stool softener docusate, should be monitored with care since electrolyte imbalances may occur. Overall, the effectiveness of laxatives and stool softeners in the treatment of IBS-C is limited.⁴⁶

Antispasmodics for Various Forms of IBS

Antispasmodics are the most common class of pharmacological drugs used for managing various forms of IBS. Antispasmodics predominantly act as antagonists at cholinergic receptors and thereby reduce contraction of the GI tract. Commonly used antispasmodics that have proven to be effective in the treatment of IBS spasms are cimetropium, pinaverium, hyoscine, and otilonium.⁴⁷ Depending on the symptoms, antispasmodics are administered up to three times daily in conjunction with prokinetics or laxatives to normalize GI motility without causing constipation.

Effect of Antidepressants on IBS Symptoms

In addition to normalization of GI motility with antispasmodics, tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have become a mainstay of supportive treatment for IBS.⁴⁸ Both drug classes were initially used to treat co-existing mental disorders such as depression and anxiety in patients with IBS, but clinical trials have shown that IBS patients without a depressive disorder can benefit from low-dose TCA therapy.⁴⁹ Surprisingly, both TCAs and SSRIs do not interfere with serotonin concentrations in the intestines, which would otherwise further increase IBS symptoms. Instead, they appear to normalize GI motility and reduce visceral pain.^{50,51} Long-term outcomes of these therapies are, however, not well understood and require more research.¹ In spite of currently available pharmacological treatments to reduce symptoms of IBS and improve QOL, the search for more effective therapies with fewer side effects continues.¹

Use of CAM for IBS

CAM is often used for chronic medical conditions, health promotion, and/or disease prevention.⁵²⁻⁵⁵ Currently available systematic reviews provide conflicting findings about the effectiveness of CAM therapies for IBS. The American College of Gastroenterology Task Force on IBS¹ reported that CAM therapies have not demonstrated any strong evidence-based support for positive outcomes. Other systematic reviews, however, indicate evidence of effectiveness.^{6,56,57}

In recent studies, up to 50 percent of individuals suffering from IBS reported using CAM,^{6,7} which is not surprising considering currently available pharmacological treatments for IBS have shown limited benefit and significant side effects. About 50 percent of self-prescribed herbal supplement users perceived benefits of using herbal

supplements for IBS, while the other half reported equivocal effects.⁷ Considering the chronic but variable nature of IBS, it is not surprising that many IBS patients using CAM are unsure of its effectiveness. Among various types of CAM, herbal products including Chinese herbal mixtures, hypnosis, relaxation technique, acupuncture, dietary changes, probiotics, and exercise have been studied for their potential benefits.⁶

Herbal Therapies

Although a limited number of well-designed studies are available, various herbal remedies have been tested for managing IBS, either as a single herb or herbal combination. Single herbs that have been studied include peppermint oil, turmeric

extract, and artichoke leaf. Common combinations of multiple herbs used for IBS include a variety of Chinese herbal formulas, the Tibetan herbal mixture Padma Lax[®], and a combination of nine herbs referred to as STW 5, marketed under the trade name Iberogast[®].⁵⁸

Enteric-coated Peppermint

Steam distillation oil extracts from the peppermint plant (*Mentha piperita*, Lamiaceae) are among the oldest remedies for treatment of GI problems. These extracts are believed to improve IBS symptoms by exerting a spasmolytic effect on the smooth muscles in the digestive tract.⁵⁹ In addition to a number of case reports and small, uncontrolled studies,⁶⁰⁻⁶⁴ two randomized, double-blind,

Table 3. Single Herbal Medicines for IBS

Reference	Sample size	Sample characteristics	Study design	Dose of active	Duration	Outcome
Enteric-coated peppermint oil capsules						
Capello et al (2007)	57	All IBS forms, IBS determined by Rome II criteria	R,D,P	225 mg peppermint oil per cap; 2 caps bid	4 weeks rx; 4 weeks follow-up	Significant reduction in IBS symptoms after 4 weeks in peppermint oil group vs. placebo group
Merat et al (2010)	90	All IBS forms, IBS determined by Rome II criteria	R,D,P	187 mg peppermint oil tid, 30 min before meals	8 weeks	Significant reduction in abdominal pain and severity in peppermint oil group vs. placebo, significant increase in QOL in peppermint oil group vs. placebo
Turmeric extract (standardized)						
Bundy et al (2004)	207	All IBS forms, IBS determined by Rome II criteria	R, non-D, non-P	2 doses, 72 mg (1 tablet) or 144 mg (2 tablets) daily	8 weeks	Significant improvement in IBS QOL at end of trial compared to baseline for both treatment groups
Artichoke leaf extract						
Walker et al (2001)	279	All IBS forms, meeting at least 3 out of 5 Rome II criteria	R, non-D, non-P	320 mg artichoke leaf extract per cap; 2 caps tid w/ meals	6 weeks	Significant reduction of IBS-related symptoms evaluated on a Likert scale at end of study compared to baseline
Bundy et al (2004)	208	All IBS forms, meeting at least 3 out of 5 Rome II criteria	R, non-D, non-P	320 mg (1 capsule) or 640 mg (2 capsules) of 1:5 artichoke leaf extract daily	8 weeks	Significant reduction in NDI QOL score at end of trial compared to baseline

R: Randomized, D: Double-blind, P: Placebo-controlled
 NDI=Nepean Dyspepsia Index

placebo-controlled trials report a beneficial effect of peppermint oil for the treatment of IBS symptoms.^{65,66}

In one study, after four weeks of treatment, a group receiving two enteric-coated capsules containing 225 mg of peppermint oil twice daily (n=28) showed a statistically significant improvement in overall IBS symptoms compared with a placebo group (n=29). The peppermint oil was effective in alleviating constipation, bloating, diarrhea, abdominal pain, passage of gas or mucus, urgency at defecation, pain during evacuation, and feelings of incomplete evacuation. Efficacy was evaluated via intensity and frequency score using a Likert scale (0-4) for each symptom.⁶⁵

A randomized, double-blind clinical trial with 90 IBS patients (45 subjects in each group) confirmed that both pain severity and general health improved after eight weeks of administration with an enteric-coated product (Colpermin®, containing 187 mg peppermint oil) three times daily compared to placebo. Outcomes were measured using the SF-36 questionnaire as well as an intensity and frequency score with a Likert scale (0-3).⁶⁶

The use of peppermint oil for the treatment of IBS in children has also received a positive

evaluation by the American Academy of Pediatrics, but with cautions due to potential side effects of heartburn or respiratory depression and lack of availability of standardized dosages. It is suggested to give 0.1-0.2 mL three times daily for no longer than two weeks under the guidance of a health care practitioner.⁶⁷

Turmeric

Turmeric (*Curcuma longa*, Zingiberaceae) has been traditionally used for managing abdominal pain, indigestion, and abdominal bloating. Effectiveness of turmeric on improvement of IBS symptoms and QOL was investigated in 207 IBS patients. Statistically significant improvements based on symptoms and quality of life (IBS-QOL questionnaire) were found after eight weeks of turmeric intervention at a dose of 72 or 144 mg daily, compared to screening and baseline phases (but no placebo group). There were no differences between the two groups, indicating a dose-independent or threshold effect.⁶⁸

Artichoke Leaf Extract

Two studies on artichoke (*Cynara scolymus*, Asteraceae) leaf extract (ALE) indicated IBS symptom improvement. According to a post-marketing surveillance study of 279 subjects, two capsules ALE three times daily with meals (320 mg ALE per capsule) relieved abdominal pain, cramps, bloating, flatulence, and constipation in subjects with dyspepsia and at least three of five commonly observed IBS symptoms (evaluated by physicians and patients using a Likert scale).⁶⁹

In another open, post-marketing study involving 208 subjects, the Nepean Dyspepsia Index (NDI) indicated that there was a significant decrease in overall IBS symptoms, including abdominal pain, diarrhea and/or constipation, urgency, straining, feeling of incomplete passage, and passage of mucus after two months of intervention with 320 mg or 640 mg ALE daily. In addition to normalization of bowel movements, an increased QOL was reported with use of ALE.⁷⁰

Although the two ALE studies were conducted by some of the same researchers with the same artichoke extract, it is not clear why the dosage was so different between the two studies^{69,70} (assuming the correct dosages were provided by the study authors).

Table 4. Herbs in Iberogast

Plant (Latin name)	Herb-Extract ratio (alcoholic extracts)	In 100 mL Iberogast
Bitter candytuft (<i>Iberis amara</i>)	1:1.5-2.5	15.0 mL
Angelica root (<i>Angelica archangelica</i>)	1:2.5-3.5	10.0 mL
Chamomile flowers (<i>Matricaria recutita</i>)	1:2.5-4.0	20.0 mL
Caraway fruits (<i>Carum carvi</i>)	1:2.5-3.5	10.0 mL
Milk thistle fruits (<i>Silybum marianum</i>)	1:2.5-3.5	10.0 mL
Lemon balm leaves (<i>Melissa officinalis</i>)	1:2.5-3.5	10.0 mL
Peppermint leaves (<i>Mentha x piperita</i>)	1:2.5-3.5	5.0 mL
Celandine (<i>Chelidonium majus</i>)	1:2.5-3.5	10.0 mL
Licorice root extract (<i>Glycyrrhiza glabra</i>)	1:2.5-3.5	10.0 mL

Adapted from: Vinson B. Development of Iberogast: Clinical evidence for multicomponent herbal mixtures. In: R. Cooper and F. Kronenberg, eds. *Botanical Medicine: From Bench to Bedside*. Mary Ann Liebert Inc. 2009.

Combination Herbal Formulas

Multiple herbal preparations such as Iberogast, Padma Lax, and Tong Xie Yao Fang (TXYF) have shown promising outcomes for managing IBS.

Iberogast, a combination of nine herbal extracts (Table 4), was shown in several clinical trials to improve symptoms of functional dyspepsia at a dose of 20 drops three times daily.⁷¹⁻⁷³ While symptoms of functional dyspepsia are often similar to IBS in terms of gastrointestinal disturbances, pain, and reduced quality of life, only limited clinical data are available regarding its effectiveness for specific IBS symptoms. The symptoms of functional dyspepsia are often predominantly related to food consumption, with resulting gastric acid secretion leading to gastrointestinal symptoms without detectable functional problems.

Iberogast has been shown to interact with several receptors in the GI tract that play an important role in regulation of motility and pain perception, including serotonin, muscarine, and opioid receptors. For example, the different extracts in Iberogast bind to the 5-HT₃ serotonin receptor as agonists, while antagonizing the 5-HT₄ and muscarine M₃ receptor in a similar manner to current synthetic drugs. Overall, the pharmacological effects of Iberogast are complex in nature, affecting acid secretion, inflammation, oxidative processes, as well as both hyper- and hypomotility to varying degrees (Table 5).⁷⁴

Although some case reports provide evidence for effectiveness of Iberogast in alleviating abdominal pain and normalizing gut motility,⁷⁵ only one clinical trial with a double-blind, placebo-controlled design has been conducted in 208 patients with IBS.⁷⁶ In this study, patients were randomly assigned to commercially available Iberogast (STW 5; n=51), a research preparation of some of the herbs in Iberogast (bitter candytuft, chamomile flower, peppermint leaves, caraway fruit, licorice root, and lemon balm leaves referred to as STW 5-II; n=52), bitter candytuft alone (n=53), or

Table 5. The Pharmacological Effects of Iberogast

Symptoms / Botanical	Acid secretion	Inflammation	Oxidative processes	Hypomotility	Hypermotility
Peppermint leaf extract	W	S	S	N	M
Chamomile flower extract	S	W	M	M	S
Licorice root extract	W	S	W	N	M
Angelica root extract	M	W	M	N	S
Caraway fruit extract	M	S	W	N	W
Milk thistle fruit extract	M	M	M	N	M
Melissa leaf extract	M	M	S	N	W
Celandine herb extract	N	M	M	M	N
Bitter candytuft extract	M	S	W	M	W

N=No effect, W=Weak effect, M=Moderate effect, S=Strong effect

From: Wagner H. Multitarget therapy – the future of treatment for more than just functional dyspepsia. *Phytomedicine* 2006;13 suppl 5:122-129.

placebo (n=52) (20 drops three times daily for four weeks). Both STW 5 and STW 5-II were found to be effective in reducing abdominal pain severity (evaluated via abdominal pain scale) and improving overall symptoms (using the IBS symptom scale) compared to placebo or bitter candytuft alone.

The complex Tibetan preparation, Padma Lax (herbs in formula are listed in Table 6), has been shown to be effective in alleviating symptoms of IBS-C.⁷⁷ In a three-month, double-blind, randomized observational trial, 482 mg twice daily (once daily in seven patients who got loose stool from the twice-daily dosage) was superior to a placebo for reducing constipation, abdominal pain, and flatulence.⁷⁸ Furthermore, rat studies demonstrate Padma Lax exerts part of its activity through cholinergic receptors by reducing contractility of smooth muscles in the colon as well as procontractile stimulation.⁷⁹

Traditional Chinese medicine (TCM), in the form of standardized combinations or formulas tailored specifically to the individual symptom presentations, improved common IBS symptoms compared to placebo as evaluated in a double-blind, placebo-controlled, randomized study.⁵⁶ The study was conducted on 116 patients who received placebo, a

Table 6. Botanicals in Padma Lax

Plant part (Latin name)
Ginger rhizome (<i>Zingiber officinalis</i>)
Chinese rhubarb root (<i>Rheum officinale</i>)
Frangula bark (<i>Rhamnus rubra</i>)
Cascara sagrada bark (<i>Rhamnus purshiana</i>)
Gentian root (<i>Gentiana lutea</i>)
Chebulic myrobalan fruit (<i>Terminalia chebula</i>)
Elecampane rhizome (<i>Inula helenium</i>)
Aloe extract (<i>Aloe vera</i> and/or <i>Aloe ferox</i>)
Calumba root (<i>Jateorhiza calumba</i>)
Condurango bark (<i>Gonolobus condurango</i>)
Long pepper fruit (<i>Piper longum</i>)
Nux vomica seed (<i>Strychnos nux vomica</i>)

(From <http://www.naturalhealthconsult.com/Monographs/padmaLax.html>)

Table 7. Modified TXYF Formula

Chinese name	Plant part (Latin name)	Dosage (g/day)
Bai zhu	Rhizome (<i>Atractylodes macrocephala</i>)	15
Huang qui	Root (<i>Astragalus membranaceus</i>)	15
Bai shao	Peeled root (<i>Paeonia lactiflora</i>)	15
Cang zhu	Rhizome (<i>Atractylodes chinensis</i>)	12
Chai hu	Root (<i>Bupleurum chinense</i>)	9
Chen pi	Peel (<i>Citrus reticulata</i>)	9
Fang feng	Root (<i>Saposhnikovia divaricata</i>)	9
Jiu li xiang	Twigs (<i>Murraya paniculata</i>)	9
Shi liu pi	Rind (<i>Punica grantum</i>)	9
Ma chi xian	Aerial parts (<i>Portulaca oleracea</i>)	30
Huang lian	Rhizome (<i>Coptis chinensis</i>)	6

standard mixture of 33 herbs, or an individualized mixture of herbs selected by a TCM specialist from a list of 81 herbs. After 16 weeks, patients in the active treatment groups showed significant improvements in bowel symptom scores (as evaluated by visual analog scales) and increased QOL compared to placebo.

A specific TCM herbal mixture, Shugan Jianpi, was found to reduce the number of serotonin-positive cells compared to a placebo in patients with IBS.⁸⁰ The 24 patients received standard care that included cognitive-behavioral therapy and a whey protein (lactein). The placebo group did not receive any additional medication, while the Shugan Jianpi groups took 24 g of the herbal mixture three times daily or 24 g of the herbal mixture plus 15 g Smecta® (a high viscosity muco-protective agent) three times daily for two weeks prior to biopsy to measure number of serotonin-positive cells. The authors did not evaluate any subjective or other objective clinical parameters.⁸⁰

Tong Xie Yao Fang (TXYF), a Chinese herbal preparation and a variation (TXYF-A) have the potential to improve global symptoms in IBS-D.^{57,81} Although a systematic review of TXYF-A indicated its potential effectiveness for reducing IBS symptoms, more studies with rigorous designs are warranted.⁸² The standard preparation of TXYF is composed of four traditional herbs – Cang zhu (*Atractylodes chinensis*), Bai shao (*Paeonia lactiflora*), mandarin orange (*Citrus reticulata*), and Fang feng (*Saposhnikovia divaricata*). Based on the individual symptoms, additional herbs may be added to the mixture, with the resultant formula referred to as TXYF-A. The review evaluated 12 randomized studies with 1,125 participants for the short- and long-term effects of TXYF-A in reducing clinical IBS symptoms. The heterogeneity of the study design and duration of the studies complicated the definition of end points. Overall, the preparations improved various IBS symptoms, including abdominal pain, distension, flatulence, and diarrhea for as long as six months after the intervention ended.

Leung and colleagues⁸³ compared a preparation of 11 herbal extracts (Table 7) comprising a modification of the traditional TXYF formula (n=60) with a placebo (n=59) in a controlled, randomized, blinded design. They found that global assessment scales and QOL did not differ between the TCM herbal preparation and placebo after eight weeks of treatment. Based on this study, TCM herbal preparations may not be beneficial to all IBS

patients but may show promise for specific IBS symptoms. More clinical data utilizing rigorous clinical trial designs are required to further support their use.

In summary, a number of single herbal remedies or herbal combinations (Table 8) are reportedly effective for relieving IBS symptoms. Further studies investigating the potential mechanisms of pharmacological action and symptom management

in rigorous clinical trial designs are warranted to confirm the observed treatment effects.

Mind-Body Therapies

Among mind-body therapies, hypnotherapy and cognitive-behavioral therapy (CBT) seem to be the most widely accepted by IBS patients.

Table 8. Summary of Studies on Herbal Combinations for IBS

Reference	Sample size	Sample characteristics	Study design	Dose	Duration	Outcome
Iberogast®						
Madisch et al (2004)	203	All IBS forms, IBS determined by Rome II criteria	R,D,P	STW 5, STW 5-II, or bitter candytuft extract, 20 drops tid	4 weeks	Significant reduction of IBS symptoms and abdominal pain in Iberogast and research solution compared to placebo
Padma Lax®						
Sallon et al (2002)	61	IBS-C, IBS determined by Rome I criteria	R,D,P	482 mg Padma Lax (n=34) or placebo (n=27), bid (once daily in subjects w/ loose stool)	12 weeks	Significant reduction in symptom severity scores and abdominal pain in Padma Lax compared to placebo
Traditional Chinese Herbal Medicine						
Bensoussan et al (1998)	116	All IBS forms, determined by Rome criteria (not specified)	R,D,P	Standard TCM mixture of 33 herbs (n=43), individualized formula (n=38), or placebo (n=35), 5 capsules tid	16 weeks	Significant reduction in bowel symptom scores and increase in QOL for individual preparation and standard TCM compared to placebo
Wang et al (2008)	24	All IBS forms, evaluation not specified	R,non-D,P	24 g Shugan Jianpi granules tid, 24 g Shugan Jianpi granules plus 15 g Smecta® tid, or cognitive therapy and lactein treatment as standard care	2 weeks	Significant reduction in serotonin positive cells in both Shugan Jianpi groups compared to standard care
Leung et al (2006)	119	IBS-D, IBS determined by Rome II criteria	R,D,P	See Table 7 for daily dose of each herb (n=60) or placebo (n=59)	8 weeks	No significant improvement in SF-36 or global symptoms compared to placebo

R: Randomized, D: Double-blind, P: Placebo-controlled

Hypnotherapy

According to several clinical trials hypnotherapy has the potential to be effective in managing IBS symptoms (Table 9).⁸⁴⁻⁸⁶ Hypnotherapy was effective in improving health-related QOL and anxiety, tiredness, and physical symptoms, but not depression, after 12 weeks of intervention without randomization,⁸⁶ while three systematic reviews⁸⁷⁻⁸⁹ reported that hypnotherapy can be used to treat abdominal pain and improve QOL, as well as reduce anxiety and depression. A nonsignificant reduction in depression scores was seen in the aforementioned study,⁸⁶ while systematic reviews of hypnotherapy for IBS provide evidence for a reduction in depressive symptoms.⁸⁷⁻⁸⁹ This difference in outcomes may be due to heterogeneity of study designs.

and improvement in visceral sensations.⁹⁰ It has therefore been proposed that GI symptom improvement is a result of central effects that modulate cortical brain circuits involved with pain and vigilance modulation.⁹¹ However, further well-designed studies should be conducted to conclusively establish efficacy of hypnotherapy as a supportive treatment for IBS.

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy is another potential alternative approach to managing IBS, although according to a recent Cochrane database review there does not seem to be concrete, reliable evidence to prove its efficacy.⁹² A primary concern with psychotherapeutic interventions is the influence of psychological factors on a patient's

Table 9. Studies of Hypnotherapy for IBS

Reference	Sample size	Sample characteristics	Study design	Number of sessions	Duration	Outcome
Gonsakorale et al (2002)	250	All IBS forms, IBS determined by Rome I criteria	non-R, non-D, non-P	12 hypnotherapy sessions followed by self-study	12 weeks	Significant improvements in HADS scores and IBS symptoms compared to baseline
Gonsakorale et al (2003)	204	All IBS forms, IBS determined by Rome I criteria	non-R, non-D, non-P	Retrospective analysis of IBS symptoms one year after hypnotherapy		Significant reduction in IBS symptoms and HADS scores as well as reduction in medication use in hypnotherapy-responsive patients compared to non-responsive patients
Smith (2006)	75	All IBS forms, IBS determined by Rome II criteria	non-R, non-D, non-P	5-7 hypnotherapy sessions over three months with follow-up	12 weeks	Significant improvement in IBSQOL scores, abdominal pain and distension, and anxiety compared to baseline

R: Randomized, D: Double-blind, P: Placebo-controlled

Although the precise mechanisms of action for hypnotherapy are not known, several psychological and physiological changes have been observed in many of the studies, including improvement in cognitive function, reductions in anxiety and depression scores, decreased colonic contractions,

perception of IBS symptoms.⁹³ Since IBS is diagnosed based on exclusion criteria and is associated with significant psychosomatic relations, patients who reject psychological interventions or whose symptoms are not severe enough are not considered potential candidates for CBT. In many cases, a

combination of CBT with pharmacological treatment provides the best outcome.¹ According to Van Dulmen and colleagues,⁹⁴ eight two-hour sessions of CBT intervention over a period of three months was effective in significantly decreasing abdominal discomfort, enhancing coping strategies, and diminishing avoidance behavior (impacting QOL) in IBS patients. The patients were asked to keep a daily record of the activities they avoided because of their IBS symptoms.⁹⁴

In a randomized, controlled trial with three arms (CBT, relaxation therapy [RT], or routine clinical care [RCC]) involving 105 subjects, individuals were treated weekly over an eight-week period with follow-up at 26 and 52 weeks. Although results showed significant improvement after eight weeks with all three interventions compared to baseline in all parameters measured, there were no significant differences among the three treatment groups during the follow-up period. It was concluded that RCC was as effective as CBT or RT.⁹⁵

A number of additional clinical trials and meta-analyses found similar results; CBT was as effective as current standard pharmacological treatments for IBS. A combination of both may provide additive symptom relief to patients.⁹⁶⁻¹⁰⁰ The ACG Task Force on Irritable Bowel Syndrome supports the use of CBT for the treatment of certain forms of IBS.¹

Relaxation Techniques

Relaxation techniques have been studied for their potential role in alleviating IBS symptoms. Multiple studies have indicated positive correlations among psychological distress, daily stress, and GI symptom aggravation^{17-20,101} that triggered IBS symptoms.^{2,102} Women with IBS tend to report a higher amount of psychological distress and lifetime psychopathology than those with no GI symptoms.¹⁰³ Relaxation training may be beneficial for symptom improvement and appears to be at least as effective as standard pharmacological treatment. The relaxation techniques used in this study included progressive muscle relaxation, release-only, cue-controlled, and applied relaxation, in addition to standard clinical care.⁹⁵ Inclusion of autogenic training, a relaxation technique that serves to increase self-directed awareness tension through conscious breathing, slowing of the heartbeat, and muscle relaxation, and other relaxation techniques improve IBS-related GI symptoms as well as QOL and increase symptom-free days compared to standard pharmacological

treatment.^{102,104-106} In addition, the self-administration of relaxation techniques provided long-term relief of most IBS symptoms as assessed by a one-year follow-up study.¹⁰⁴ The retrospective study reviewed 10 patients with IBS, who initially participated in a three-month study on the use of relaxation response meditation. After one year, participants were evaluated for abdominal pain, diarrhea, distension, and flatulence – all of which presented with significant reductions compared to baseline.¹⁰⁴

Acupuncture and Moxibustion

Acupuncture can cause physiological changes that affect various endogenous neurotransmitter systems. Of specific interest to the treatment of IBS is the influence of acupuncture and moxibustion on the serotonergic and cholinergic neurotransmission of the brain-gut axis. Both animal and human trials indicate specific targets for acupuncture on serotonergic, cholinergic, and glutamatergic pathways as well as reductions in blood cortisol levels.¹⁰⁷⁻¹¹⁰

In a controlled, randomized pilot study, 30 subjects received routine clinical care or acupuncture for IBS. After three months of treatment, outcomes of acupuncture intervention revealed statistically and clinically significant improvements in symptom severity, including pain, distension, bowel habits, and QOL compared to usual care only. In this study, however, the type of IBS was not defined for the sample population.¹¹¹

In a large, randomized, controlled study, 230 subjects with IBS were assigned to one of three groups. The two intervention groups were either three weeks of true or sham acupuncture following a three-week run-in period of sham acupuncture therapy with a “limited” (friendly, interactive) patient-practitioner relationship, while the third arm was a waitlist control group. Findings indicated no significant difference in global outcome measurements between real and sham acupuncture, but both interventions showed significant improvement over the waitlist control group.¹¹²

In another similar study, Schneider and colleagues randomized 43 subjects to receive either acupuncture or sham acupuncture for 10 sessions (an average of two per week).¹¹³ Although the Functional Diseases QOL questionnaire (FDDQL) in this study revealed that both groups improved significantly in overall QOL, there was no difference between the two groups, suggesting that the effect of acupuncture was primarily a placebo response.

According to Anastasi and colleagues, a combination of acupuncture and moxibustion (acu/moxa) can be highly effective in IBS treatment. Twenty-nine subjects who met Rome II criteria were randomized into either individualized acu/moxa treatments or sham/placebo acu/moxa treatments. Results indicated that acu/moxa reduced abdominal pain, significantly reduced gas and bloating, and improved stool consistency over a four-week, eight-session intervention period.¹¹⁴ A Cochrane meta-analysis suggests larger-scale studies are warranted to confirm the benefits of acu/moxa in alleviating IBS symptoms.¹¹⁵

Diet Modification

A primary goal of all IBS interventions is to provide the patient with relief of symptoms and improve the quality of life. Although the data from clinical trials may in some cases not provide strong evidence for benefits of dietary modification, it remains the primary non-pharmacological clinical intervention for IBS patients; exclusion diets are successfully used by many clinical practitioners.¹

Food intolerances or allergies are strong contributors to the exacerbation of IBS symptoms. Individuals with IBS often discover that certain foods aggravate symptoms,^{2,116-118} while others have found relief from IBS symptoms by modifying their daily diet and increasing exercise activities.^{2,8-10}

Symptoms of IBS may be associated with visceral hyperactivity, GI motility disturbances, sugar malabsorption, gas-handling disturbances, and abnormal intestinal permeability.^{13,22,119} Elimination diets are often employed that remove the most common allergens from the diet.¹²⁰ Although some patients reported that removing wheat, dairy products, eggs, coffee, yeast, potatoes, and citrus fruits from their diets is helpful, such restrictions may be difficult to follow.¹¹⁸ Dietary restrictions may provide patients with relief of IBS symptoms over time, while entirely skipping meals has been found to worsen IBS symptoms.^{118,121}

Macronutrients: Fat, Sugar, and Sugar Alcohols

IBS studies indicate a positive relationship between fat intake and increased stool number and diarrhea.^{9,121} Intake of carbohydrates can also aggravate IBS symptoms.¹¹⁸ Offending carbohydrates include fructose and fructose-containing products such as soft drinks, cereals, and packaged/baked goods. Sorbitol and other sugar-alcohols found in most sugar-free or reduced-sugar products are poorly absorbed in the GI tract and may cause increased flatulence, abdominal discomfort,

and diarrhea, thus exacerbating IBS symptoms.¹¹⁷ Other types of sugar-alcohols proposed to aggravate IBS symptoms include mannitol, xylitol, erythritol, lactitol, maltitol, and isomalt.¹¹⁷ Due to the multitude of variables related to IBS symptoms, study results are difficult to validate and challenging to interpret.

Fiber

Fiber intake from fruits and vegetables is inversely correlated to bloating.⁹ The addition of psyllium fiber, especially for persons with IBS-C, reduced IBS symptoms in some people,^{117,122,123} while either wheat bran or a low-fiber diet was found to be an ineffective management measure as evaluated by two meta-analyses of a total of 30 studies.¹²³ Because most of the evaluated studies had small sample sizes, the results are highly variable. Other widely variable factors included the amount of soluble (5-30 g) and insoluble (4.1-36 g) fiber added to the diet and the duration of study intervention (3-16 weeks). Overall, consumption of soluble fiber resulted in a decrease in global IBS symptoms and constipation, whereas insoluble fiber demonstrated a less significant effect. Neither intervention, however, decreased abdominal pain in IBS patients. Due to its moderate effectiveness, additional intake of soluble fiber maybe recommended for IBS-C patients. Studies also revealed that pain relief was not associated with increased fiber intake and that the addition of insoluble fiber such as nuts or whole grains to the diet had either no effect or exacerbated IBS symptoms.¹²²

Lactose Intolerance

Patients with IBS were found to have significantly more subjective lactose intolerance complaints (bloating, distention, and diarrhea) than those without IBS and to have increased likelihood of lactose malabsorption than the general population.¹²⁴ Thus, decreased intake of lactose can benefit some IBS patients.¹²⁵ It is hypothesized that, following ingestion of lactose, hydrogen gas is produced and gut distention is promoted due to bacterial fermentation of the unabsorbed lactose. Interestingly, the majority of IBS sufferers, however, failed to test positive for hydrogen breath tests that indicate lactose intolerance.¹²⁵

Probiotics

Probiotics have been extensively studied for the treatment of IBS. A thorough review of the research is beyond the scope of this article. A number of studies have examined the effect of single

organisms on IBS symptoms and/or quality of life. Most studies used various species of *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* strains given in concentrations of 10^8 - 10^{10} colony forming units per day (cfu/day). The primary endpoints of many studies are reductions in bloating, abdominal pain, and flatulence, as well as evaluation of global symptoms using the IBS severity scoring system.

In a randomized, controlled trial, 44 IBS patients were given either *Bacillus coagulans* strain GBI-30, 6086 or placebo for eight weeks. *B. coagulans* resulted in significant relief of abdominal pain and bloating from baseline during each of seven evaluation weeks; the placebo group experienced only significant relief in abdominal pain at the sixth and eighth week.¹²⁶ In another study, 52 patients with IBS-D were randomized to receive either this same strain of *B. coagulans* or placebo once daily for eight weeks. The average number of bowel movements daily significantly decreased in the treatment group compared to placebo.¹²⁷

There was a slight but statistically significant reduction in symptom severity observed in 60 patients with mild IBS randomly assigned to *Lactobacillus plantarum* in a rosehip tea or rosehip tea alone for four weeks. *L. plantarum* strain DSM 9843 at a dose of 2×10^{10} cfu/day was found to decrease pain and flatulence compared to those taking only rosehips.¹²⁸

At least two studies have evaluated the effects of *Bifidobacterium infantis* 35624. One randomized, controlled trial (n=362 women with IBS of all types) found a dose of 10^8 cfu/day for four weeks (but not 10^6 or 10^{10}) was effective in reduced bloating, abdominal pain, and flatulence, as well as global IBS symptoms compared to placebo.¹²⁹ In the second study, 77 IBS patients were randomly assigned to *B. infantis* 35624, *Lactobacillus salivarius* UCC4331, each (10^{10} cfu/day), or placebo for eight weeks. *B. infantis* resulted in significant reduction in symptom scores and inflammatory cytokines compared to either *L. salivarius* or placebo.¹³⁰

A beneficial yeast *Saccharomyces boulardii* has also been tested for IBS treatment. Subjects received either *S. boulardii* (n=34) or placebo (n=33) for four weeks. The *S. boulardii* group experienced significant improvement in IBS-QOL but not individual symptom scores compared to placebo.¹³¹

In addition to these individual organisms, more than a dozen studies, just in the last five years, have examined the effect of multiple probiotic strains on IBS.

Exercise

Exercise can help maintain GI function and reduce stress, which can help relieve some IBS symptoms. Studies of IBS indicate positive relationships between physical activity and symptom relief.^{10,121,132} Physical activity, such as pedaling a bicycle, protects against GI symptom aggravation and alleviates gas in several studies.^{10,121,132} Although one study revealed an inverse relationship between exercise and all GI symptoms except constipation,⁹ another study reported constipation improved with mild exercise, therefore, potentially benefiting IBS-C patients.⁸

The practice of yoga has also demonstrated reduction of IBS symptoms in both adult and adolescent populations.^{133,134} Pranayama yoga has been identified as an exercise regimen that increases sympathetic tone, which is decreased in IBS-D patients.¹³⁵ In a two-month study, a yoga intervention group practiced twice daily, while the conventional treatment group received 2-6 mg loperamide daily. Results indicated that yoga demonstrated improvement of IBS symptoms equivalent to conventional treatment.¹³⁵

Summary

The goal of current standard pharmacological treatment is to alleviate clinical symptoms of IBS. Because conventional treatments typically do not get to the root of the problem or provide anything but symptomatic relief, patients often seek CAM therapies, including cognitive-behavioral therapy, herbal therapies, probiotics, mind-body therapies, acupuncture, dietary changes, and exercise. Although most CAM therapies reviewed in this article seem to provide some benefit in alleviating IBS, it is apparent that the duration, dosages, and specifics of the intervention greatly affect the outcomes. More studies need to be conducted to establish the subtle nuances associated with these treatments (e.g., specific probiotics, standardization of herbal extracts, yoga style, etc.) to provide the most significant benefit for IBS.

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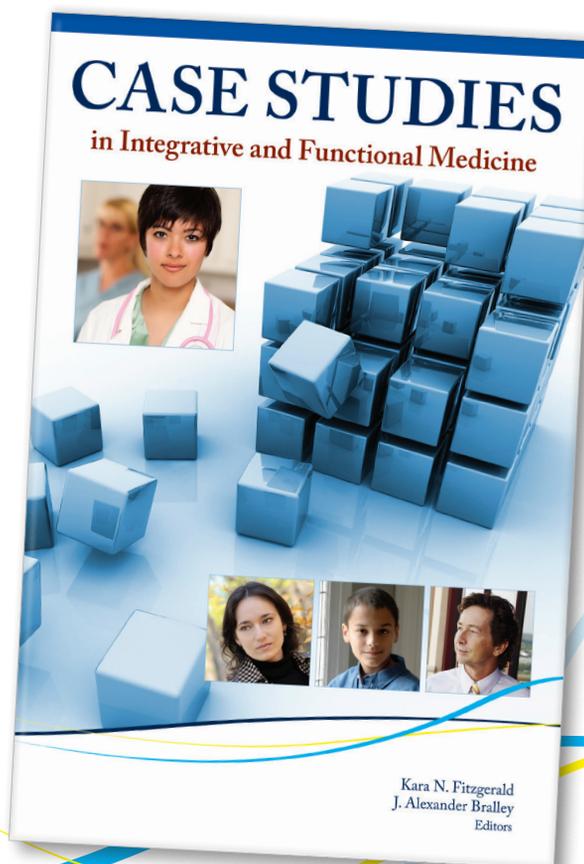
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