Natural Products for the Treatment of Irritable Bowel Syndrome

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Abstract: Irritable bowel syndrome (IBS) is a common disorder of gut-brain interaction that significantly impacts quality of life. Studies indicate that more than one-third of patients with IBS use nonpharmacologic therapies, which include natural products and mind-body therapies, with higher prevalence identified among women, younger individuals, and those with higher education levels. This article examines the efficacy and safety of various natural products for the treatment of IBS, including fiber supplements, probiotics, herbal remedies (including Aloe vera and peppermint oil), and dietary supplements. Although some therapies show promise in symptom management, the evidence remains mixed for many of these interventions. Further high-quality research is needed to establish the role of many of these therapies in IBS treatment.

Keywords
Irritable bowel syndrome, natural products, fiber, herbal supplements, diet

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction (DGBI) and is defined by the Rome IV criteria as recurrent abdominal pain associated with disordered defecation. IBS can present as diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), mixed (IBS-M), or unsubtyped (IBS-U). IBS has an estimated prevalence of 4.7% to 6% in the United States.[1-3] This condition is more prevalent in women than in men and is more commonly seen in younger individuals.[3,4] IBS has a significant negative impact on quality of life (QoL). One study found that patients with IBS would give up 25% of their remaining life (average, 15 years) to receive a treatment that would make them symptom free.[1] There have been a number of advances in treatment options for IBS, with many patients seeking nonpharmacologic treatments as initial interventions (Table 1).

Nonpharmacologic therapies include both natural products (eg, fibers, probiotics, herbs, and dietary supplements) and mind-body therapies (eg, hypnosis, cognitive behavioral therapy, yoga, and acupuncture).[2,3] These therapies can be used as adjuncts to or in lieu of conventional medicine and are sought out by patients for many reasons. Patients turn to nonpharmacologic therapies not only because of a preference for natural treatments, but also to improve general wellness, energy, or immunity.[4,5] Some patients believe that nonpharmacologic therapies can be used independently, without assistance from a medical professional. Other patients

Table 1. Overview of Nonpharmacologic Therapies for IBS

What are nonpharmacologic therapies?
• Set of therapies used as adjunct or alternative to traditional medicine
• Can be divided into 2 buckets: (1) natural products (eg, herbs, dietary supplements) and (2) mind-body therapies (eg, hypnosis, cognitive behavioral therapy, yoga, acupuncture)
Use of nonpharmacologic therapies by patients with IBS
• Estimated to be used by >1/3 of patients with IBS
• More likely to be used in patients who are female, are younger, have higher BMI, or have higher level of education
Potential drawbacks of nonpharmacologic therapies
• Potential side effects include headaches, GI symptoms, liver injury
• Financial burden to patient
• Many patients reluctant to share with provider that they are using nonpharmacologic therapies
• Physicians may underestimate how many of their patients use nonpharmacologic therapies
• Physicians may be uncomfortable discussing such therapies with their patients

BMI, body mass index; GI, gastrointestinal; IBS, irritable bowel syndrome.

already incorporate these therapies into their well-being as part of their upbringing or culture. Nonpharmacologic treatments may also be used when conventional medicine has not yielded desired results.[6]

The term *complementary and alternative medicine* (CAM) was renamed *complementary and integrative health* by the National Institutes of Health in 2014, but CAM is still considered and used as the common colloquialism. CAM has historically referred to many of these nonpharmacologic therapies but does not include fiber. Recent articles exploring nonpharmacologic treatments for IBS have focused on CAM therapies across different DGBIs or have examined both natural products and mind-body therapies for IBS.[3,7] This article provides an updated and comprehensive review focusing specifically on natural products for IBS (including fiber) in order to offer clinicians nuanced and evidence-based guidance (Table 2).

Prevalence of CAM Usage in Irritable Bowel Syndrome

Multiple studies have shown that CAM use is prevalent in patients with IBS. In 2008, a 6-month study from a health maintenance organization (HMO) that included more than 1000 DGBI patients found that 38% of those with IBS used at least 1 CAM therapy to treat gastrointestinal (GI) symptoms.[6] Of those patients with IBS, the most commonly used CAM therapies were ginger root/tea (14.8%), massage therapy (12.6%), and yoga (10.0%). The 2012 National Health Interview Survey (NHIS) evaluated use of CAM in patients with any GI conditions and found that 42% had used CAM therapy within the prior year; however, only 3% had specifically used CAM to address a GI condition, and of those, 45% had used CAM to address abdominal pain.[4] Single-center studies have found similar rates of CAM use among patients with IBS. A 2015 study that included patients attending GI or hepatology clinics at a single academic center found that 44% of patients had used CAM therapy. The most common symptoms targeted were constipation (44%), diarrhea (47%), and bloating (59%).[5] A single-center study from Italy found that 45% of patients with IBS who were surveyed reported CAM use.[8] Certain demographics are associated with increased use of CAM therapy. Female sex, younger age, higher body mass index, and higher levels of education have been associated with expanded use in patients with IBS.[6,8-10]

Potential Drawbacks of Nonpharmacologic Therapies

Although generally considered safe, dietary and herbal supplements have been associated with adverse events, including headaches, GI symptoms, and elevated liver enzymes.[11] These supplements may interact with medications. The financial burden of such therapies for IBS remains unclear. A 2008 HMO study found that the median out-of-pocket cost for CAM therapy was $200 per year, which was roughly one-third of the median pharmacy cost.[6] Updated analyses are needed to determine the current cost in 2025.

Multiple studies show that patients are reluctant to share their CAM use with providers.[5,12] A single-center study of 269 GI clinic patients found that only 70% discussed CAM use with physicians. Of those who did not discuss CAM therapy, 82% cited that their doctor did not ask them about it, and 68% said they did not know that it was something they should discuss.[5] Similar results were identified in a study by Dossett and colleagues using NHIS data in which the most common reasons patients did not disclose CAM use were because the provider did not ask (51%) or because they did not think the provider needed to know (44%).[4]

Provider factors also impact how CAM therapy is discussed. A Canadian survey-based study of practicing gastroenterologists found that only 18% had discussed CAM therapy in the majority of their patient encounters.[13] Only 51% said they felt comfortable discussing CAM with patients (mostly owing to lack of knowledge of

Table 2. Natural Products for IBS

Treatment	Mechanism of action	Dose and administration	Evidence	Notes
Soluble fiber (psyllium, *Plantago ispaghula*)	Increases water in small bowel and colon and decreases bowel transit time	Total daily fiber intake recommendation is 25-35 g daily. Can be titrated as needed based upon initial response. Supplemental soluble fiber 8-12 g/day	2015 meta-analysis of 22 RCTs comparing fiber with placebo for IBS found improvement in global symptoms with soluble fiber (RR, 1.49; 95% CI, 1.09-2.03).[15]	May cause gas and bloating. No benefit seen with insoluble fiber. ACG 2021 guideline for IBS recommends use of soluble fiber for global IBS symptoms.[17]
Probiotics	Live micro-organisms that are thought to impact the host microbiome	Dosing depends on strain of bacteria. Many exist	Meta-analyses evaluating probiotics in patients with IBS vs placebo have found some potential for improvement of global symptoms, abdominal pain, bloating, and distension with certain strains of bacteria.[24-27] Certainty in the evidence has remained low.	2020 AGA guideline recommends probiotics only be used under the auspices of a clinical trial.[29] 2021 ACG guideline recommends against probiotics for IBS.[17] 2021 British IBS guideline recommends trial of probiotics can be used for IBS.[28]
Herbal supplements				
Aloe vera (*Aloe barbadensis* Mill.)	Thought to have anti-inflammatory and immuno-modulatory properties. May have prebiotic effects	1-2 tbsp daily (liquid formulation)	2018 meta-analysis (3 RCTs, 151 patients) found greater improvement in IBS symptom scores with Aloe vera vs placebo (standardized mean difference, 0.41; 95% CI, 0.07-0.75; *P*=.020).[35] 2020 RCT (160 patients) found no difference in number of responders between Aloe vera and control groups (30% vs 38%, respectively; *P*=.26).[33]	Rare side effects reported, including diarrhea and hepatitis
Cannabis	May impact intestinal motility by acting at G protein–coupled cannabinoid receptors in enteric nervous system	No recommended dosing	Dronabinol 5 mg decreased the fasting left colonic motility index compared with placebo and increased colonic compliance in patients with IBS.[39] Cannabis use was associated with reduced 30-day all-cause hospital readmission rates in patients with IBS.[41]	Can cause anxiety, psychogenic effects, drowsiness. Can induce cyclic vomiting and cannabis hyperemesis syndrome
Ginger (*Zingiber officinale roscoe*)	May impact intestinal motility and intestinal hypersensitivity	No recommended dosing	2020 study found ginger could improve intestinal hypersensitivity in rats with IBS-D via modulation of proinflammatory cytokines, including TNF-α and IL-6.[44] A double-blind RCT with 45 IBS-D patients receiving placebo or 1 or 2 g of ginger for 28 days showed that patients taking ginger did not have significant improvement in IBS severity scale compared with placebo.[45]	Well tolerated with rare side effects, including GI upset

(Table continues on next page)

Table 2. *(Continued)* Natural Products for IBS

Treatment	Mechanism of action	Dose and administration	Evidence	Notes
Herbal supplements				
Peppermint oil (*Mentha piperita*)	Active ingredient, L-menthol, relaxes smooth muscle by blocking calcium channels. May also have anti-inflammatory properties and serotonergic effects[48-50]	Varies by formulation	2019 meta-analysis (835 patients) found, compared with placebo, peppermint oil resulted in significant improvement in symptoms (RR, 2.39; 95% CI, 1.93-2.97; *P*<.00001) and abdominal pain (RR, 1.78; 95% CI, 1.43-2.20; *P*<.00001).[48] In 2021 RCT (133 patients) of peppermint oil vs placebo, both groups showed significant improvements in symptoms, but there was no significant difference between peppermint oil and placebo groups.[53]	Side effects include reflux/heartburn, belching, and abdominal pain.[54]
STW-5 and STW-5II	Product made from combination of 6 (STW-5II) or 9 herbal extracts (STW-5). Thought to impact gut motility, inflammation, microbiome, intestinal permeability[55]	STW-5: 1 mL taken 3 times daily STW-5II: available in 20 mL and 50 mL liquid drops as well as softgels	2004 RCT found patients taking STW-5 had a significantly improved reduction in abdominal pain scores (*P*=.0009) and the IBS symptom score (*P*=.001) at 4 weeks.[55] In 2024 crossover RCT of STW-5 on colonic gas in patients with IBS vs placebo, gas filling was associated with a greater rise in abdominal symptoms for placebo (score increment, 4.0 ± 0.3) vs patients taking STW-5 (score increment, 3.2 ± 0.4; *P*=.035).[56]	Case reports of liver injury (in particular from celandine herbs) and 1 case requiring liver transplantation.[57] The 6 extracts: candy tuft, caraway fruit, licorice root, chamomile flower, lemon balm leaf, peppermint leaf (+ Angelica root, milk thistle, and celandine herb for 9 extracts)
Turmeric (*Curcuma longa*)	Active ingredient is curcumin. Increases GI motility and impacts inflammation and molecular signaling	Typically dosed in 500-2000 mg in 1-2 doses divided daily	Meta-analysis evaluating use of curcumin for IBS (326 patients from 3 studies) found curcumin resulted in improved IBS symptoms. This was not statistically significant (−0.466, 95% CI, −1.113 to 0.182; *P*=.158), and there was heterogeneity across the studies, including lack of consistent IBS definition and different curcumin formulations.[62]	Case reports of liver injury from turmeric supplements (this may have been related to contaminants in the products)[63]
Dietary supplements				
L-glutamine	Amino acid thought to alter tight junction proteins, impact inflammatory signaling, and thus impact intestinal permeability	5 g by mouth up to 3 times daily	2019 trial randomized 115 patients to L-glutamine or placebo for 8 weeks. 79.6% of L-glutamine vs 5.8% of placebo group had a reduction in IBS-SSS at 8 weeks (*P*<.0001). L-glutamine also reduced daily bowel movement frequency, improved stool form, and reduced intestinal permeability.[65]	L-glutamine has been well tolerated with no significant adverse effects.
Melatonin (5-methoxy-N-acetyltryptamine)	Hormone secreted by pineal gland regulating sleep-wake cycle. Also released by enterochromaffin cells in GI tract with impact on gut motility	1-5 mg taken prior to sleep	Small studies evaluating melatonin in patients with IBS have found improvement in bowel symptoms and abdominal pain scores.[70-73]	Melatonin is well tolerated with side effects, including daytime sleepiness and fatigue.

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-D, diarrhea-predominant IBS; IBS-SSS, IBS Symptom Severity Scale; IL, interleukin; RCT, randomized controlled trial; RR, risk ratio; TNF, tumor necrosis factor.

CAM). This may be reflective of the fact that most medical schools do not include CAM education as part of their curricula. Gastroenterologists may underestimate how many of their patients use CAM therapy. A 2013 Italian study revealed that 44% of gastroenterologists thought that less than 10% of patients with IBS use CAM therapy, which was significantly different from reported CAM use by IBS patients (close to 40%).[14] Thus, practitioners should consider addressing the use of natural interventions with their patients and develop better knowledge of the risks and benefits of these therapies.

Fiber

Dietary fibers refer to those that are neither digested nor absorbed in the small intestine. Fiber acts as an osmotic bulking agent and decreases bowel transit time. It is categorized as insoluble and soluble. Insoluble fiber is found in certain vegetables, whole grains, and wheat bran. Soluble fiber is found in products such as oat bran, beans, and psyllium.

Data support positive benefits for soluble, but not insoluble, fiber for IBS. A 2015 European meta-analysis that included 22 studies comparing fiber with placebo for IBS found improvements in global symptoms in patients receiving soluble fiber (risk ratio, 1.49; 95% CI, 1.09-2.03). However, there was no improvement in global symptoms for insoluble fiber (risk ratio, 1.08; 95% CI, 0.89-1.31). There was significant improvement in abdominal pain scores for patients receiving soluble fiber (mean difference, −1.84; 95% CI, −2.72 to −0.97) vs no improvement for insoluble fiber.[15] A meta-analysis that included 14 randomized controlled trials (RCTs) evaluating the effect of fiber in 906 patients with IBS found there was a significant benefit for only soluble fiber (risk ratio, 0.83; 95% CI, 0.73-0.94; *P*=.005) with a number needed to treat of 7. No effect was seen with bran (insoluble) fiber (risk ratio, 0.90; 95% CI, 0.79-1.03; *P*=.14).[16] The American College of Gastroenterology (ACG) 2021 guideline on IBS recommends the use of soluble fiber to treat global IBS symptoms, with recommended fiber intake of 20 to 35 g/day.[17] However, typical dietary fiber intake in the United States is only 15 g/day.[18]

Psyllium

Psyllium husk (*Plantago ispaghula*) is a soluble fiber commonly recommended for IBS. Psyllium increases water content in the small bowel and ascending and descending colon via its polymers.[19] One of the major drawbacks of fiber is its propensity to increase gas and bloating in a population already experiencing these symptoms. Psyllium may minimize this effect. In a study evaluating the effects of inulin (rapidly fermented in the colon causing an increase in colonic gas and breath hydrogen) alone vs inulin with psyllium in 19 patients with IBS-D or IBS-C, combining inulin with 20 g of psyllium reduced colonic gas as measured by breath hydrogen (*P*=.02 and *P*=.007, respectively). However, adding psyllium to inulin did not decrease gas production in this in-vitro study.[20] Psyllium may reduce colonic gas symptoms by decreasing the rate of delivery of inulin (or other poorly absorbed dietary polysaccharides) to the colon. Psyllium is inexpensive, available in multiple over-the-counter formulations, and has been shown to be safe and well tolerated with minimal adverse effects.

Probiotics

Probiotics are live microorganisms that provide a health benefit when given in adequate amounts.[21] Probiotics are increasingly used by patients despite limited evidence of their efficacy. The global probiotics market was projected to be worth more than $70 billion by 2024.[22] A survey-based study from a center in the Northeast United States queried 479 general GI patients undergoing endoscopy about their probiotic use. Approximately 27% reported probiotic use, with most (18.2%) using probiotics sporadically and 9% using probiotics daily. The most common reasons listed for using probiotics were to improve health and longevity (54%) and to improve GI symptoms (45%).[22]

Given validation that the gut microbiome plays a role in the pathogenesis of IBS, probiotics have been repeatedly studied.[23] However, inconsistencies in the organisms (types and concentrations) used, dosing, small sample sizes, and high placebo rates have resulted in ambiguous results. Meta-analyses evaluating the impact of probiotics on patients with IBS vs placebo have found potential benefit with probiotics for improvement of global symptoms, abdominal pain, bloating, and distension with certain strains of bacteria.[24-27] However, certainty in the evidence remains low, and further studies are needed.

Inconsistent results of probiotic studies have also led to discordant guidelines. The 2021 British guideline recommends probiotics be used as effective treatments for both global symptoms and abdominal pain for IBS. A 12-week trial of therapy is recommended, but recommendations regarding specific species or strains are not provided.[28] The 2020 American Gastroenterological Association (AGA) clinical practice guidelines for probiotics make no recommendations regarding the use of probiotics in patients with IBS, citing issues with heterogeneity in the strains of probiotics used and study design.[29] Probiotics are recommended only under the auspices of a clinical trial. The 2021 ACG IBS guideline recommends against the use of probiotics for the treatment of IBS; however,

this is a conditional recommendation based on very low levels of evidence.[17]

Herbal Supplements

Aloe vera

Aloe vera (AV; *Aloe barbadensis* Mill.) has been used for many therapeutic purposes, including as a topical salve, oral supplement, and even for cosmetics. AV is thought to have anti-inflammatory and immunomodulatory properties, as well as possible prebiotic effects (as it is used by microbiota in the GI tract to support the microbiome) owing to its beta polysaccharides and short-chain fatty acids.[30-33] AV has been used as a laxative to improve GI motility and therefore has been postulated to have benefit for patients with IBS, particularly IBS-C.

Individual RCTs have not identified improvements in symptoms or QoL. A randomized crossover, placebo-controlled study of 47 IBS patients who received AV found no difference between cohorts in any QoL parameters.[31] A 2015 study randomized 68 patients with IBS of any subtype to receive AV or placebo for 4 weeks. The patients were assessed using IBS symptom severity scales (IBS-SSS). Overall, 55% of patients receiving AV were responders (defined as reduction in IBS-SSS by ≥50 points) compared with 31% in the placebo group (P=.09). There was improvement in secondary endpoints of pain severity, pain frequency, and bloating in the AV group, but the study was not powered to measure these effects.[34] A 2020 RCT assigned 160 IBS patients (all subtypes) to receive either AV or control (inulin) for 4 weeks. There was no difference in responders between groups (30% vs 38%, respectively; P=.26).[32] A meta-analysis from 2018 that included 3 RCTs and 151 patients with IBS of all subtypes found greater improvement in symptom scores with AV vs placebo (standardized mean difference, 0.41; 95% CI, 0.07-0.75; P=.020). However, this meta-analysis could not evaluate efficacy of AV by IBS subtype and predated the more recent RCTs.[35] A subsequent analysis that added data from the aforementioned 2020 RCT to the 2018 meta-analysis made the response to treatment outcome no longer significant (risk ratio, 1.12; 95% CI, 0.84-1.48; P=.45).[33]

Overall, there are inconsistent data to suggest whether AV is effective in improving IBS symptoms, and further high-quality studies are needed. AV is considered a safe supplement. Rare reported side effects include diarrhea, although there have been some case reports of acute hepatitis.[3,36]

Cannabis

Cannabis can originate from 3 major plants—*Cannabis sativa, indica, and ruderalis*—and has been used as a natural remedy for centuries. Multiple hydrocarbon compounds known as cannabinoids can be extracted. The 2 most well-known are Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the main psychotropic cannabinoid, whereas CBD is nonpsychogenic.[37]

Cannabinoids can be plant-derived (phytocannabinoids), endogenously generated (endocannabinoids), or synthetic. They bind 2 different types of G protein–coupled receptors: CB1, which is located in the enteric and central nervous systems, and CB2, which is found in the immune system.[2,38] Cannabinoids are thought to reduce gastric, small intestinal, and colonic motility.[38]

Cannabis is increasingly used in the United States as a medicinal or recreational therapy, particularly in states where it has been decriminalized. However, there are limited studies evaluating its efficacy in IBS. Dronabinol is currently the only cannabinoid medication approved by the US Food and Drug Administration. Dronabinol is a nonselective synthetic cannabinoid receptor agonist, which slows both gastric emptying and colonic motility. In a 2011 study, 72 patients were randomized to receive 2.5 mg or 5 mg of dronabinol or placebo. Results showed that 5 mg of dronabinol decreased the fasting left colonic motility index compared with placebo (P=.46) and increased colonic compliance (P=.058). These effects were greatest in patients with IBS-D and IBS-U.[39]

A 2019 population-based study that included 31,272 patients hospitalized for IBS from the Nationwide Inpatient Survey found that cannabis use disorder was associated with increased odds of IBS (adjusted odds ratio, 2.03; 95% CI, 1.53-2.71). This was postulated to be a result of cannabis-induced stress and anxiety on the brain, as well as an increased arousal state in patients using cannabis in excess.[40] A retrospective cohort study that included 7163 patients with IBS from the 2016 Nationwide Readmissions Database found that there was no significant difference in 30-day readmission rates for IBS-specific causes in patients who reported cannabis use vs those who did not (P=.53). However, cannabis use was associated with reduced 30-day all-cause hospital readmission rates.[41] A 2023 RCT evaluating the cannabinoid 2 receptor agonist olorinab at 3 different doses in patients with IBS-D and IBS-C found reductions in abdominal pain scores at 12 weeks in all 3 of the olorinab cohorts. However, there were no differences in average abdominal pain scores at week 12 between the placebo and olorinab groups.[42]

Cannabis can be taken in multiple formulations. Side effects are dependent on the dose and ratio of CBD to THC and include anxiety, psychogenic symptoms, drowsiness, and dizziness.[37,39] Cyclic vomiting syndrome and cannabis hyperemesis syndrome can also be triggered.

In summary, cannabinoids have been validated to play a role in gut motility. The sensitive nature of their

use and lack of high-quality studies leave their therapeutic implications unclear. Further research is needed to determine whether cannabis should be used for IBS.

Ginger

Ginger root (*Zingiber officinale roscoe*) has historically been used for multiple symptoms, including nausea, pain, and inflammation. It is one of the most commonly used natural products for IBS, with up to 14% of IBS patients reporting use in a 2008 study of 1012 patients with DGBIs.[6] The mechanism of action requires further elucidation, although there is some evidence that ginger may have prokinetic effects on gut motility.[43] One study found that ginger could improve intestinal hypersensitivity in rats with IBS-D via modulation of proinflammatory cytokines, including tumor necrosis factor-α and interleukin-6.[44] However, a double-blind RCT that included 45 IBS-D patients receiving placebo or 1 or 2 g of ginger for 28 days showed that patients receiving ginger did not have better response (as measured via IBS severity scale) compared with placebo.[45] The AGA does not include ginger in its guidelines for the management of IBS, and there is no standard recommended dosage. Ginger is generally thought to be well tolerated.[46]

Peppermint Oil

Peppermint oil (*Mentha piperita*) has been used for centuries as a remedy for GI symptoms.[47] The active ingredient, L-menthol, causes smooth muscle relaxation by blocking calcium channels. It has been postulated that peppermint oil has anti-inflammatory effects and impacts kappa opioid receptors, serotonergic receptors, and the microbiome.[48-50] Peppermint oil is marketed as a treatment for IBS and comes in multiple over-the-counter formulations, including a triple-coated microspherical intestinal-release formulation containing 90 mg of purified peppermint oil. In a 4-week study, 72 patients with IBS-D or IBS-M were randomized to receive either placebo or 2 caplets of this formulation 3 times daily. Peppermint oil was associated with a 40% decrease in total IBS symptom score compared with placebo (24.3%) (P=.02246).[49]

Subsequent data regarding peppermint oil's efficacy in treating IBS symptoms have been mixed. A 2019 meta-analysis evaluating peppermint oil in 835 IBS patients (any subtype) found that, compared with placebo, peppermint oil resulted in significant improvement in symptoms (risk ratio, 2.39; 95% CI, 1.93-2.97; P<.00001) and abdominal pain (risk ratio, 1.78; 95% CI, 1.43-2.20; P<.00001).[48] The number needed to treat was 3 for global symptom improvement and 4 for abdominal pain improvement. However, a subsequent 8-week trial from the Netherlands examining 2 formulations (182 mg small intestinal release and 182 mg ileocolonic release) vs placebo found no difference in worst abdominal pain response between the cohorts. The small-intestinal release formulation did have greater improvement in abdominal pain (P=.16) and IBS severity (P=.20) compared with placebo.[51,52] A 2021 placebo-controlled trial from a center in the Northeast United States randomized 133 patients with IBS (any subtype) to receive placebo vs 180 mg of enteric-coated, small-intestinal release peppermint oil 3 times daily (part of a larger open-label placebo vs double-blind placebo study). Both groups showed improvements in symptoms; however, there were no significant differences between groups in IBS-SSS, global improvement in IBS symptoms, or adequate relief of symptom scores. It was noted that the lack of a more robust separation may have been owing to a high placebo response rate.[53]

The ACG IBS guidelines recommend using peppermint oil for relief of global IBS symptoms based on low-quality evidence.[17] Peppermint oil has been well tolerated, but rare side effects have been reported, including reflux/heartburn, belching, and abdominal pain.[53]

STW-5 and STW-5II

STW-5 is made from 9 herbal extracts: candy tuft (*Iberis amara*), lemon balm leaf (*Melissa officinalis*), chamomile flower (*Matricaria chamomilla*), caraway fruit (*Carum carvi*), peppermint leaf (*Mentha piperita*), licorice root (*Glycyrrhiza glabra*), Angelica root (*Angelica archangelica*), milk thistle (*Silybum marianum*), and celandine herb (*Chelidonium majus*). Its mechanism of action results from the combined effects of the 9 compounds, which play a role in gut motility, inflammation, neuronal signaling, the gut microbiome, and intestinal permeability.[54]

STW-5 has been used for more than 20 years for functional dyspepsia and other DGBIs, although it has not been commercially available in the United States. A 2004 RCT that included 208 patients with IBS who were randomized to receive 1 of 3 herbal preparations (one of which was STW-5) vs placebo found that patients receiving STW-5 experienced a significant reduction in abdominal pain scores (P=.0009) and IBS symptom score (P=.001) at 4 weeks.[55] A 2024 crossover RCT evaluated the impact of STW-5 on colonic gas in patients with IBS. After 2 weeks of STW-5 or placebo, 10 patients underwent gas challenge tests in which gas was continuously infused into the colon. Gas filling was associated with a rise in abdominal symptoms to a greater extent in patients receiving placebo (score increment, 4.0 ± 0.3) vs those receiving STW-5 (score increment, 3.2 ± 0.4; P=.035).[56] This study suggested that STW-5 may improve colonic gas tolerance in patients with IBS who have bloating. STW-5 is well tolerated. However, there have been case reports of liver injury (in particular from celandine herbs), with 1 individual requiring liver transplantation.[57]

Recently, a 6-herb formulation (STW-5II) has been released that includes *Iberis amara, Carum carvi, Glycyrrhiza glabra, Matricaria chamomilla, Melissa officinalis,* and *Mentha piperita*. Limited data on this newer formulation have focused on functional dyspepsia, where it has been shown to improve symptoms compared with placebo.[58,59] STW-5II is available as liquid drops and softgels and can be purchased in the United States.

Turmeric

Turmeric is a flowering plant in the ginger family that has been used as a dye and a spice and is used to treat many GI symptoms. Its active ingredient is curcumin. It is thought to increase motility, have anti-inflammatory properties, and play a role in molecular signaling.[60] There is a paucity of data evaluating the impact of turmeric on IBS. A 2004 study from the United Kingdom that included 207 IBS patients who took turmeric daily for 8 weeks found improvement in abdominal pain/discomfort.[61] A more recent meta-analysis evaluating use of curcumin for IBS included 326 patients from 3 studies and found that curcumin resulted in improved IBS symptoms, although this was not statistically significant (–0.466; 95% CI, –1.113 to 0.182; *P*=.158), and there was heterogeneity across the studies, including lack of consistent IBS definition and different curcumin formulations.[62] Turmeric is considered safe with minimal side effects, although there have been case reports of liver injury from turmeric supplements that may be related to contaminants in the products.[63]

Dietary Supplements

L-Glutamine

Some patients with IBS-D show increased small bowel and colonic intestinal permeability related to reduced expression of tight junctions.[64] L-glutamine, an essential amino acid, has been postulated to alter tight junction proteins, impact inflammatory signaling, and reduce intestinal permeability. A 2019 study randomized 115 patients with postinfectious IBS-D to receive L-glutamine 5 g 3 times daily or placebo for 8 weeks. A greater than 50-point reduction in IBS-SSS scores was experienced by 79.6% of glutamine recipients vs 5.8% of placebo recipients (*P*<.0001), correlating with reduced intestinal permeability (r=0.72).[65] L-glutamine also reduced daily bowel movements and improved stool form.[66] Another study randomized 50 IBS patients (any subtype) to receive a low–fermentable oligo-, di-, monosaccharide, and polyol diet either with L-glutamine 15 g/day or placebo for 6 weeks. The L-glutamine group showed significant reduction in total IBS-SSS compared with placebo (*P*<.0001).[67] L-glutamine is well tolerated without significant adverse effects. Further studies should explore L-glutamine's effects in different IBS populations.

Melatonin

Melatonin (5-methoxy-N-acetyltryptamine) is a hormone secreted by the pineal gland in the brain that is involved in regulation of the sleep-wake cycle. However, melatonin is also made by enterochromaffin cells in the GI tract and is thought to impact gut motility.[68] Patients with IBS are prone to sleep disturbances, and it has been proposed that melatonin deficiency may be involved in the pathogenesis of IBS.[69] Thus, melatonin has been postulated to improve IBS symptoms either via sleep regulation or by direct impact on the gut.[70] A 2005 study randomized 17 female patients with IBS to receive either melatonin 3 mg or placebo nightly for 8 weeks followed by washout and crossover. Patients had improvements in their mean IBS scores, as measured by the IBS Symptoms Evaluation Score Questionnaire, after melatonin compared with placebo (3.9 +/- 2.6 and 1.3 +/-4.0, respectively; *P*=.037).[71] In a recent RCT from Iran evaluating the impact of melatonin in patients with IBS (subtype agnostic) with or without sleep disorders, 136 patients were randomized to receive either melatonin 6 mg daily (3 mg fasting and 3 mg at bedtime) or placebo for 8 weeks. There was an improvement in IBS-SSS in patients receiving melatonin compared with placebo, both for those with sleep disorders (*P*=.022) and those without (*P*=.025). There were also improvements in abdominal pain.[72] Earlier small studies evaluating melatonin similarly found improvement in bowel symptoms and abdominal pain scores.[71,73] Melatonin is well tolerated with side effects including daytime sleepiness.

Conclusion

Nonpharmacologic therapies represent a developing class of treatment options that may have some benefit for patients with IBS. However, evidence for many of these interventions remains limited or mixed. There is a demonstrated need for more rigorous, multicenter RCTs to evaluate the efficacy, safety, and long-term outcomes of these natural products. The prevalence of nonpharmacologic treatment use by patients with IBS highlights the need for gastroenterologists to actively discuss both the potential benefits and risks. Integrating evidence-based treatments into conventional therapies may offer a more personalized and thorough approach to IBS management.

Disclosures

Dr Brigstocke has no relevant conflicts of interest to disclose. Dr Brenner serves as a consultant, advisor, and/or speaker for Anji, Ardelyx, AbbVie, Ironwood, Salix, Bayer, Gemelli, Laborie, Vibrant, Mahana, Owlstone, CinPhloro, Dr.

Reddy, and Blueprint Pharmaceuticals. He owns stock in Owlstone and sits on the board of directors for the nonprofit International Foundation for Gastrointestinal Disorders.

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