Supplementation for IBS

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Erin Judge is a registered dietitian nutritionist, certified personal trainer, and founder of Gutivate, a virtual nutrition counseling practice for digestive disorders and gastrointestinal conditions.

Erin's expertise is in providing medical nutrition therapy for functional gut disorders with a patient-centered focus. She is proud of her work in education and advocacy for the IBS patient community through social media, as well as her work in providing resources for dietitians in the GI field.

Disclosures: financial partnerships with FODZYME, ModifyHealth, Gemelli Biotech, mBIOTA, Gourmend, Fody Foods

Supplements, foods, and whole-diet interventions in IBS in clinical practice

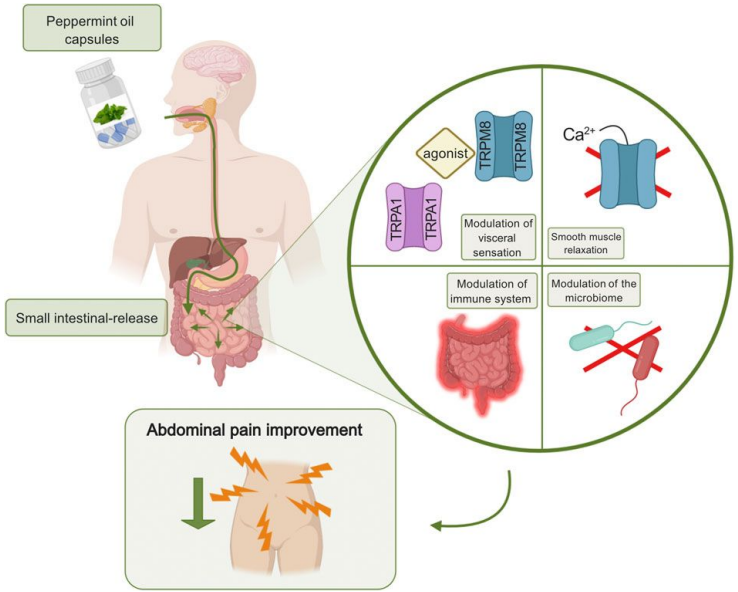
In general, data from meta-analyses in IBS suggest that effect sizes of benefit for some supplements (eg, wheat bran and prebiotics) are relatively small or non-existant, but for some whole-diet interventions (eg, low-FODMAP diet) are larger (table 1). Although there might be convincing mechanistic rationale for some whole-diet interventions, this pattern could be the result of fewer and sometimes smaller trials in whole-diet interventions, with greater difficulty in blinding meaning a tendency towards positive findings compared with control or comparator groups[41] and a greater potential for publication bias.

Whelan K, et al. Dietary management of irritable bowel syndrome: considerations, challenges, and solutions. Lancet Gastroenterol Hepatol. 2024 Dec;9(12):1147-1161. doi: 10.1016/S2468-1253(24)00238-3.

PAIN

Peppermint Oil Capsules

- L-menthol in peppermint oil acts as an antispasmodic agent, relaxing the smooth muscles of the intestinal wall, which helps reduce pain, cramping, bloating and motility-based symptoms
- Enteric-coated capsules are designed to release the oil in the small intestine (rather than the stomach), allowing it to reach the colon where IBS symptoms manifest, without causing heartburn



Colomier E, Algera J, Melchior C. Pharmacological Therapies and Their Clinical Targets in Irritable Bowel Syndrome With Diarrhea. Front Pharmacol. 2021 Feb 18;11:629026. doi: 10.3389/fphar.2020.629026.

Peppermint Oil Capsules

Meta-Analysis > J Clin Gastroenterol. 2014 Jul;48(6):505-12.
doi: 10.1097/MCG.0b013e3182a88357.

Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis

Reena Khanna [1], John K MacDonald, Barrett G Levesque

Affiliations + expand
PMID: 24100754 DOI: 10.1097/MCG.0b013e3182a88357

Clinical Trial > Gastroenterology. 2020 Jan;158(1):123-136. doi: 10.1053/j.gastro.2019.08.026.
Epub 2019 Aug 27.

Efficacy and Safety of Peppermint Oil in a Randomized, Double-Blind Trial of Patients With Irritable Bowel Syndrome

Zsa Zsa R M Weerts [1], Ad A M Masclee [2], Ben J M Witteman [3], Cees H M Clemens [4], Bjorn Winkens [5], Jacobus R B J Brouwers [6], Henderik W Frijlink [7], Jean W M Muris [8], Niek J De Wit [9], Brigitte A B Essers [10], Jan Tack [11], Johanna T W Snijkers [2], Andrea M H Bours [2], Annieke S de Ruiter-van der Ploeg [12], Daisy M A E Jonkers [2], Daniel Keszthelyi [2]

Affiliations + expand
PMID: 31470006 DOI: 10.1053/j.gastro.2019.08.026

- Some benefit in IBS symptoms with only mild side effects - mostly heartburn
- n=190, enteric coated peppermint capsules (small intestine released vs ileocolonic release) vs placebo
- no significant reductions in overall symptom relief, but the small intestine released capsules did reduce abdominal pain, discomfort, and IBS severity.

Khanna R, MacDonald JK, Levesque BG. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. J Clin Gastroenterol. 2014 Jul;48(6):505-12. doi: 10.1097/MCG.0b013e3182a88357.

Weerts ZZRM, et al. Efficacy and Safety of Peppermint Oil in a Randomized, Double-Blind Trial of Patients With Irritable Bowel Syndrome. Gastroenterology. 2020 Jan;158(1):123-136. doi: 10.1053/j.gastro.2019.08.026.

Peppermint Oil Capsules

› Biopsychosoc Med. 2024 Feb 8;18(1):3. doi: 10.1186/s13030-024-00302-y.

Efficacy and safety of peppermint oil for the treatment in Japanese patients with irritable bowel syndrome: a prospective, open-label, and single-arm study

Kei Matsueda [1], Shin Fukudo [2], Masayuki Ogishima [3], Yuki Naito [4], Soichiro Nakamura [3]

Affiliations + expand

PMID: 38331851 PMCID: PMC10854076 DOI: 10.1186/s13030-024-00302-y

- Tested ZO-Y60 peppermint oil capsules in IBS patients and found 71.6% symptom improvement in week 2 and 85.1% improvement in week 4
- Clarity on the specific product unknown

Matsueda K, Fukudo S, Ogishima M, Naito Y, Nakamura S. Efficacy and safety of peppermint oil for the treatment in Japanese patients with irritable bowel syndrome: a prospective, open-label, and single-arm study. Biopsychosoc Med. 2024 Feb 8;18(1):3. doi: 10.1186/s13030-024-00302-y.

Peppermint Oil Capsules

- Evidence = moderate
- Safety = high
- Go for enteric-coated, small intestinal release
- Typically dosed at 1-2 capsules 15-30 minutes before meals
- Can also be dosed with or after a meal if heartburn occurs

Peppermint Combo: STW5

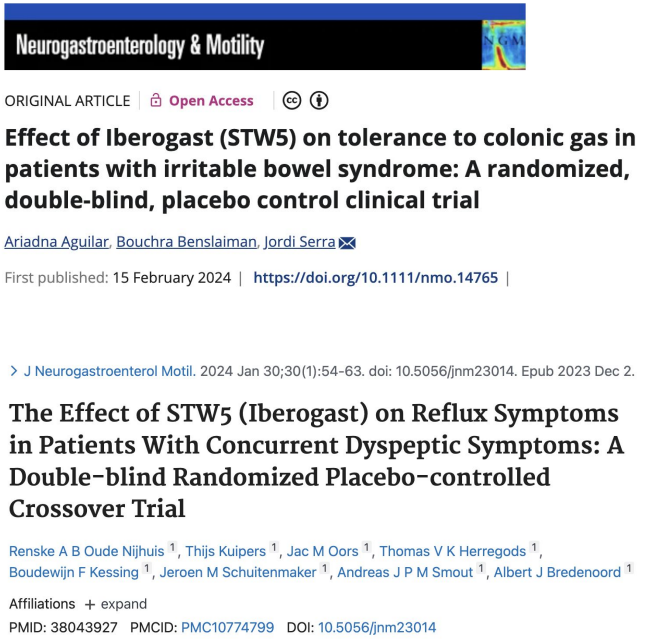
- Blend of Iberis amara (bitter candytuft), peppermint, chamomile, licorice, lemon balm, and caraway
- Designed to improve stomach acidity regulation for dyspepsia, relax gut muscles, improve GI motility, protect the mucus membrane of the gut, and offer anti-inflammatory properties
- Some research over time showing promising results in IBS and FD
- Used to be feared for liver injury due to some reported events - less now and research shows safety.
    - Removed in 2023: angelia root, milk thistle, and greater celandine (may have been the one linked with liver injury)

Ottillinger B, Storr M, Malfertheiner P, Allescher HD. STW 5 (Iberogast®)--a safe and effective standard in the treatment of functional gastrointestinal disorders. Wien Med Wochenschr. 2013 Feb;163(3-4):65-72. doi: 10.1007/s10354-012-0169-x.

Peppermint Combo: STW5

- IBS & gas: 2 weeks treatment vs placebo for 12 IBS pts
- Tolerance of gas significantly better in treatment arm

- Reflux: 4 weeks treatment vs placebo 18 patients with functional dyspepsia
- Benefit found in symptoms (reflux events) thoughts to be due to esophageal hypersensitivity



Neurogastroenterology & Motility

ORIGINAL ARTICLE | Open Access

Effect of Iberogast (STW5) on tolerance to colonic gas in patients with irritable bowel syndrome: A randomized, double-blind, placebo control clinical trial

Ariadna Aguilar, Bouchra Benslaiman, Jordi Serra

First published: 15 February 2024 | https://doi.org/10.1111/nmo.14765 |

> J Neurogastroenterol Motil. 2024 Jan 30;30(1):54-63. doi: 10.5056/jnm23014. Epub 2023 Dec 2.

The Effect of STW5 (Iberogast) on Reflux Symptoms in Patients With Concurrent Dyspeptic Symptoms: A Double-blind Randomized Placebo-controlled Crossover Trial

Renske A B Oude Nijhuis [1], Thijs Kuipers [1], Jac M Oors [1], Thomas V K Herregods [1], Boudewijn F Kessing [1], Jeroen M Schuitenmaker [1], Andreas J P M Smout [1], Albert J Bredenoord [1]

Affiliations + expand

PMID: 38043927 PMCID: PMC10774799 DOI: 10.5056/jnm23014

Aguilar A, Benslaiman B, Serra J. Effect of Iberogast (STW5) on tolerance to colonic gas in patients with irritable bowel syndrome: A randomized, double-blind, placebo control clinical trial. Neurogastroenterol Motil. 2024 Oct;36(10):e14765. doi: 10.1111/nmo.14765.

Oude Nijhuis RAB, Kuipers T, Oors JM, Herregods TVK, Kessing BF, Schuitenmaker JM, Smout AJPM, Bredenoord AJ. The Effect of STW5 (Iberogast) on Reflux Symptoms in Patients With Concurrent Dyspeptic Symptoms: A Double-blind Randomized Placebo-controlled Crossover Trial. J Neurogastroenterol Motil. 2024 Jan 30;30(1):54-63. doi: 10.5056/jnm23014.

Peppermint Combo: STW5

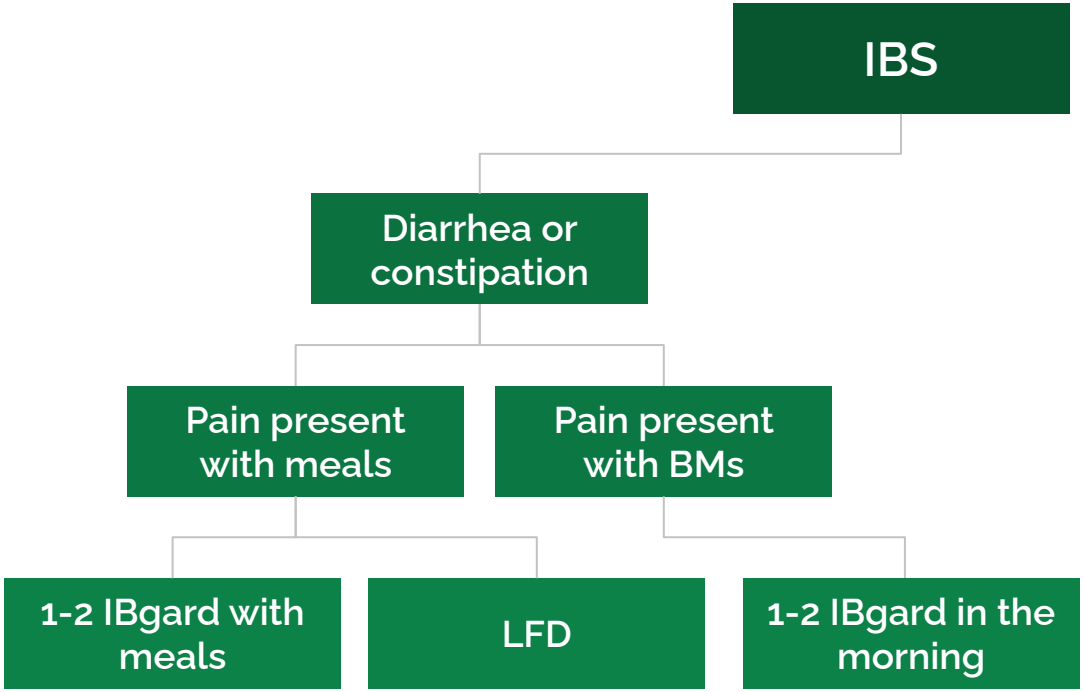
- In a liquid form so a dose is considered 20 drops - recommended up to 3/day before meals
- Bottle must be shaken and drops can be mixed with a small amount of liquid
- Softgel form is also now available in the US - not the form studied
- Should not be overdosed!

Peppermint Combo: Atrantil

- Quebrancho colorado to reduce gas, horse chestnut as an antimicrobial, and peppermint leaf to soothe gut muscles
- Marketed for SIBO because of the belief the combo can reduce hydrogen, reduce unwanted microbes, and support gut motility - all to improve bloating and potential for overgrowth
- 2016 2 week pilot study in 24 IBS-C patients = 88% had reduced symptom scores (pain, bloating, constipation) + improved QOL scores
- Larger study done in 2020-2022 but can't find results?

Brown K, Scott-Hoy B, Jennings LW. Response of irritable bowel syndrome with constipation patients administered a combined quebracho/conker tree/M. balsamea Willd extract. World J Gastrointest Pharmacol Ther. 2016 Aug 6;7(3):463-8. doi: 10.4292/wjgpt.v7.i3.463.

How I practice



BLOATING/GAS

Enzymes: α-Galactosidase

- Breaks down oligosaccharides (e.g., raffinose, stachyose) found in beans, cruciferous veggies, and other FODMAP-rich foods that can cause gas and bloating.
- 19 females with IBS with enzyme added to carb rich meals, measuring IBS symptoms + hydrogen/methane
- Did not significantly outperform placebo for immediate gas or symptom reduction, though some subjective improvements were noted including less bloating and pain the following day of the meal tested.
- Note: meals tested included other FODMAPs

Randomized Controlled Trial > Neurogastroenterol Motil. 2021 Jul;33(7):e14094.
doi: 10.1111/nmo.14094. Epub 2021 Feb 22.

A randomized double-blind placebo-controlled crossover pilot study: Acute effects of the enzyme α-galactosidase on gastrointestinal symptoms in irritable bowel syndrome patients

Lena Böhn [1], Hans Törnblom [1], Lukas Van Oudenhove [2], Magnus Simrén [1 3], Stine Störsrud [1]

Affiliations + expand

PMID: 33619835 DOI: 10.1111/nmo.14094

Böhn L, et al. A randomized double-blind placebo-controlled crossover pilot study: Acute effects of the enzyme α-galactosidase on gastrointestinal symptoms in irritable bowel syndrome patients. Neurogastroenterol Motil. 2021 Jul;33(7):e14094. doi: 10.1111/nmo.14094.

Enzymes: □-Galactosidase (Lactase)

- Breaks down lactose (sugar in milk/dairy)
- A very old and weak double-blind, cross-over trial of 12 IBS patients tested exogenous lactase supplementation in IBS patients who consumed milk.
- Result: In this small study, lactase did not significantly improve IBS symptoms overall. More results were present for those determined to be lactose maldigesters
- Lactose intolerance and lactase deficiency are commonly present in IBS populations and can worsen symptoms so addressing lactose digestion clinically often helps patients even if controlled trials are mixed.

Lisker R, Solomons NW, Pérez Briceño R, Ramírez Mata M. Lactase and placebo in the management of the irritable bowel syndrome: a double-blind, cross-over study. Am J Gastroenterol. 1989 Jul;84(7):756-62. P

Misselwitz B, Butter M, Verbeke K, Fox MR. Update on lactose malabsorption and intolerance: pathogenesis, diagnosis and clinical management. Gut. 2019 Nov;68(11):2080-2091. doi: 10.1136/gutjnl-2019-318404.

Enzymes: □-Galactosidase (Lactase)

- Most tolerate 12 g lactose (around 8.5 oz milk) - low FODMAP is considered <1 g
- Research on supplementation shows small benefit so can be used, but also reducing overall lactose intake may be most effective.
- If supplementing, dosing will be individualized so you could test tolerance first and then add 1 dose per 5-10 g above tolerance then work from there
- Enzymes should always be dosed with the food - typically at “first bite”

Lisker R, Solomons NW, Pérez Briceño R, Ramírez Mata M. Lactase and placebo in the management of the irritable bowel syndrome: a double-blind, cross-over study. Am J Gastroenterol. 1989 Jul;84(7):756-62. P

Misselwitz B, Butter M, Verbeke K, Fox MR. Update on lactose malabsorption and intolerance: pathogenesis, diagnosis and clinical management. Gut. 2019 Nov;68(11):2080-2091. doi: 10.1136/gutjnl-2019-318404.

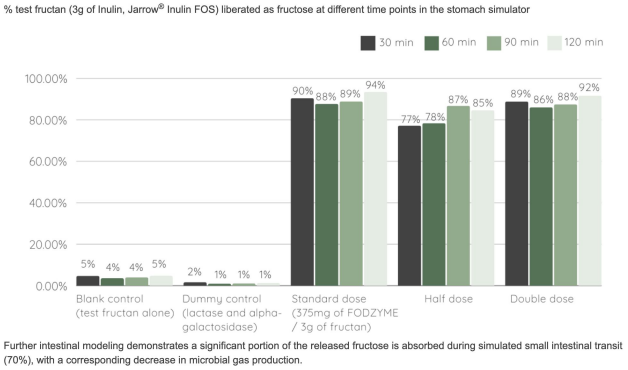
Enzymes: Brush Border Enzymes

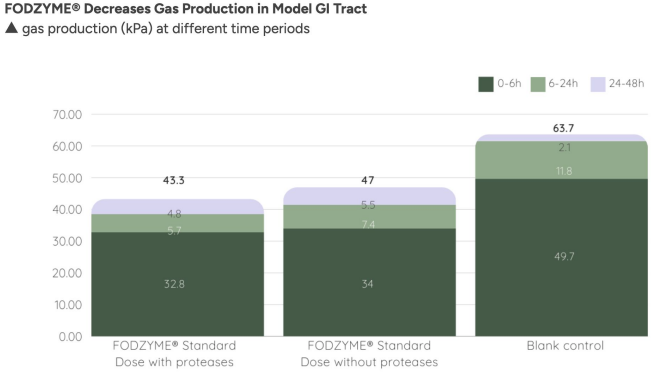
- Sucrase-Isomaltase, Maltase-Glucoamylase, Lactase, Trehalase, etc.
- Genes encoding these brush-border enzymes may influence carbohydrate digestion and symptom patterns in some IBS patients. Genetic variations are associated with symptoms and response to diets.
- Research measuring disaccharidase activity in biopsies has found deficiencies in some IBS patients, suggesting that enzyme deficiencies could contribute to symptoms or be therapeutic targets.
- Estimated that around 1 in 10 IBS-D patients may have sucrase-isomaltase deficiency

Kim SB, Calmet FH, Garrido J, Garcia-Buitrago MT, Moshiree B. Sucrase-Isomaltase Deficiency as a Potential Masquerader in Irritable Bowel Syndrome. Dig Dis Sci. 2020 Feb;65(2):534-540. doi: 10.1007/s10620-019-05780-7

Enzymes: Fructan Hydrolase (inulinase)

- Breaks apart the fructan molecule to pull out the fructose and allow for absorption to reduce fructan delivery in the colon
- In combo with lactase + α-galactosidase, shown in vitro to break down high-FODMAP fructans and potentially reduce symptoms via a SHIME GI model, but no peer-reviewed clinical trials in IBS yet.





https://providers.fodzyme.com/research-brief?_gl=1*c0he55*_up*MQ..*_gs*MQ..&gclid=CjwKCAiA3-3KBhBiEiwA2x7FdKk2cN9xuG7kXgREwrco5WpiFJ5MceN-3LXXIXsjjHbdgNUEiRMMnRoCDBIQAvD_BwE&gbraid=0AAAAABYBaddtUYL8PFxQhv_EsrEJYgwEa

Garvey SM, LeMoire A, Wang J, Lin L, Sharif B, Bier A, Boyd RC, Baisley J. Safety and Tolerability of Microbial Inulinase Supplementation in Healthy Adults: A Randomized, Placebo-Controlled Trial. Gastro Hep Adv. 2024 Jun 21;3(7):920-930. doi: 10.1016/j.gastha.2024.05.013.

Enzymes: Xylose Isomerase

- Not naturally produced in the body - found in bacteria, fungi, and plants
- Helps break down fructose for those who have fructose intolerance
- Not studied in IBS but shown to reduce hydrogen and symptoms in those with fructose intolerance

Randomized Controlled Trial > Aliment Pharmacol Ther. 2012 Nov;36(10):980-7.
doi: 10.1111/apt.12057. Epub 2012 Sep 24.

Oral xylose isomerase decreases breath hydrogen excretion and improves gastrointestinal symptoms in fructose malabsorption – a double-blind, placebo-controlled study

P Komericki [1], M Akkilic-Materna, T Strimitzer, K Weyermair, H F Hammer, W Aberer

Affiliations + expand

PMID: 23002720 DOI: 10.1111/apt.12057

Komericki P, Akkilic-Materna M, Strimitzer T, Weyermair K, Hammer HF, Aberer W. Oral xylose isomerase decreases breath hydrogen excretion and improves gastrointestinal symptoms in fructose malabsorption - a double-blind, placebo-controlled study. Aliment Pharmacol Ther. 2012 Nov;36(10):980-7. doi: 10.1111/apt.12057.

Enzymes: Pancreatic Enzymes

- An older review of alternative therapies noted that pancreatic enzyme therapy is widely used by patients but has limited and unproven clinical efficacy specifically in IBS, except in those with co-existing exocrine pancreatic insufficiency.
- Some IBS-D patients may have clinically relevant pancreatic insufficiency, and enzyme supplementation may improve symptoms in those subsets.

> Arch Intern Med. 2003 Feb 10;163(3):265-74. doi: 10.1001/archinte.163.3.265.

A systematic review of alternative therapies in the irritable bowel syndrome

Jennifer A Spanier [1], Colin W Howden, Michael P Jones

Affiliations + expand

PMID: 12578506 DOI: 10.1001/archinte.163.3.265

> Clin Gastroenterol Hepatol. 2010 May;8(5):433-8. doi: 10.1016/j.cgh.2009.09.032. Epub 2009 Oct 14.

Some patients with irritable bowel syndrome may have exocrine pancreatic insufficiency

John S Leeds [1], Andrew D Hopper, Reena Sidhu, Alison Simmonette, Narges Azadbakht, Nigel Hoggard, Stephen Morley, David S Sanders

Affiliations + expand

PMID: 19835990 DOI: 10.1016/j.cgh.2009.09.032

Spanier JA, Howden CW, Jones MP. A Systematic Review of Alternative Therapies in the Irritable Bowel Syndrome. Arch Intern Med. 2003;163(3):265–274. doi:10.1001/archinte.163.3.265

Leeds JS, Hopper AD, Sidhu R, Simmonette A, Azadbakht N, Hoggard N, Morley S, Sanders DS. Some patients with irritable bowel syndrome may have exocrine pancreatic insufficiency. Clin Gastroenterol Hepatol. 2010 May;8(5):433-8. doi: 10.1016/j.cgh.2009.09.032.

Herbs: Ginger

- Possesses carminative effect, decreases pressure on lower esophageal sphincter, reduces intestinal cramping, and prevents dyspepsia, flatulence, and bloating
- Giacosa, Morazzoni, et al., 2015 investigated the effects of ginger extract (100 mg = 2 g of rhizome twice a day) showed a significant increase in GI motility in the intervention group compared to placebo
- Micklefield et al., 1999 & Wu et al. 2008 showed that ginger accelerates gastric emptying and stimulates antral contractions in healthy individuals
- Hu et al., 2011 showed the same results in functional dyspepsia without changes in fundus dimension, GI symptoms, or serum gut peptides

van Tilburg MA, Palsson OS, Ringel Y, Whitehead WE. Is ginger effective for the treatment of irritable bowel syndrome? A double blind randomized controlled pilot trial. Complement Ther Med. 2014 Feb;22(1):17-20. doi: 10.1016/j.ctim.2013.12.015.

Herbs: Ginger

- 45 IBS patients 1 g/day ginger, 2 g/day ginger, or placebo for 28 days
- Ginger did not outperform placebo in overall IBS-SSS
- ~53% of participants reported "adequate relief" with placebo and similarly with ginger
- Well tolerated and seems safe (in the right dose + duration)

Complement Ther Med. Author manuscript; available in PMC: 2015 Feb 1.

Published in final edited form as: Complement Ther Med. 2014 Jan 8;22(1):17–20. doi: 10.1016/j.ctim.2013.12.015

Is ginger effective for the treatment of Irritable Bowel Syndrome? A double blind randomized controlled pilot trial

Miranda AL VAN TILBURG [1], Olafur S PALSSON [1], Yehuda RINGEL [1], William E WHITEHEAD [1]

Author information · Article notes · Copyright and License information

PMCID: PMC3958926 NIHMSID: NIHMS554318 PMID: 24559811

The publisher's version of this article is available at Complement Ther Med

Abstract

van Tilburg MA, Palsson OS, Ringel Y, Whitehead WE. Is ginger effective for the treatment of irritable bowel syndrome? A double blind randomized controlled pilot trial. Complement Ther Med. 2014 Feb;22(1):17-20. doi: 10.1016/j.ctim.2013.12.015.

Herbs: Ginger + Other Compounds

- Gingerol + menthol + limonene
- 56 IBS & IBS + FD patients
- Improved symptom scores more than placebo when added to standard therapy over 30 days
- No very clear if there was a difference in IBS and FD outcomes

Randomized Controlled Trial

> PLoS One. 2022 Jun 15;17(6):e0263880.
doi: 10.1371/journal.pone.0263880. eCollection 2022.

Efficacy and safety of a food supplement with standardized menthol, limonene, and gingerol content in patients with irritable bowel syndrome: A double-blind, randomized, placebo-controlled trial

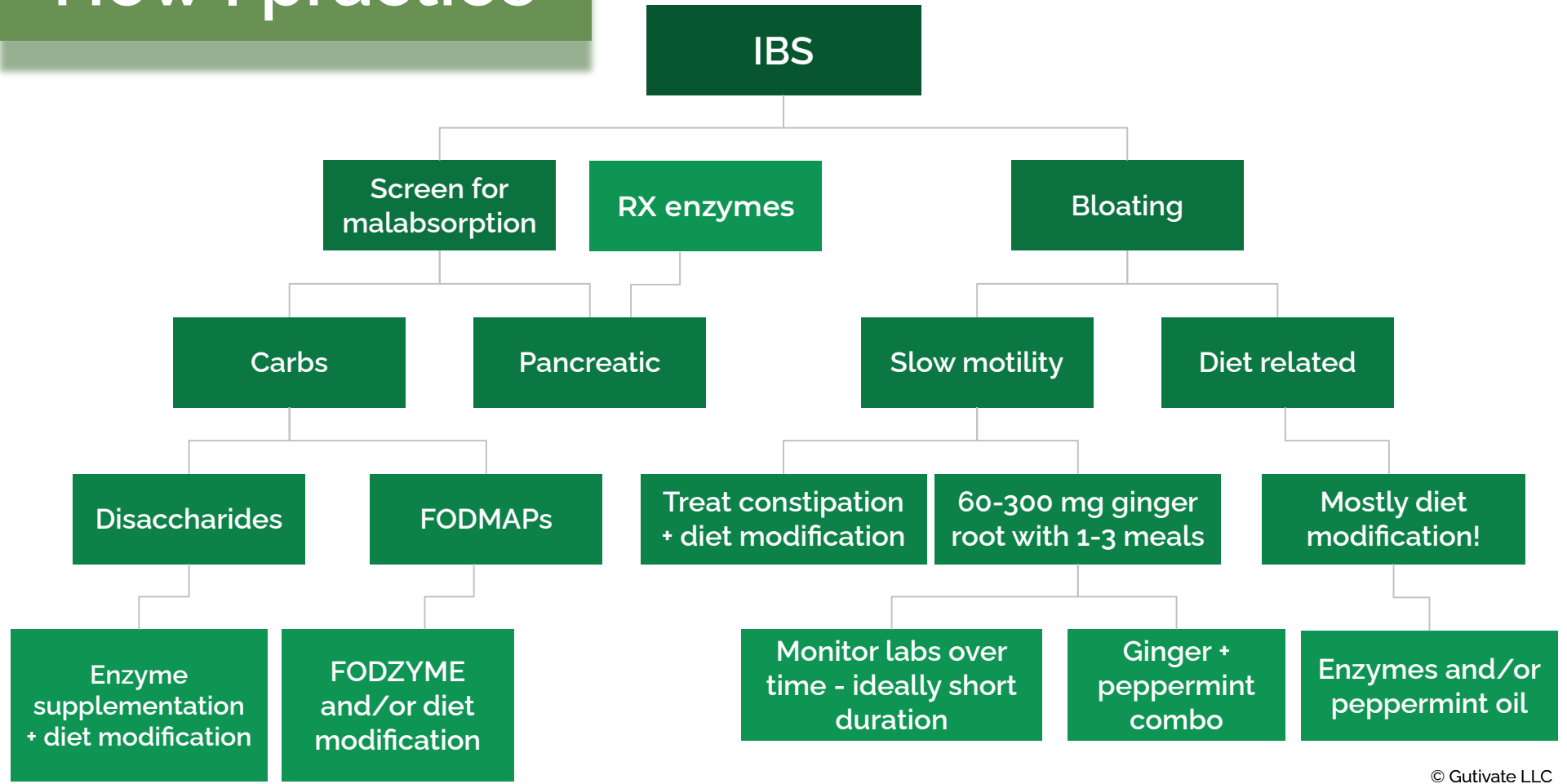
Vladimir T Ivashkin [1], Anna V Kudryavtseva [2], George S Krasnov [2], Yuri M Poluektov [2], Margarita A Morozova [3], Oleg S Shifrin [1], Allan G Beniashvili [2], Zarina A Mamieva [1], Alexandra L Kovaleva [1], Anatoly I Ulyanin [1], Elizaveta A Trush [1], Alexander G Erlykin [4], Elena A Poluektova [1]

Affiliations + expand

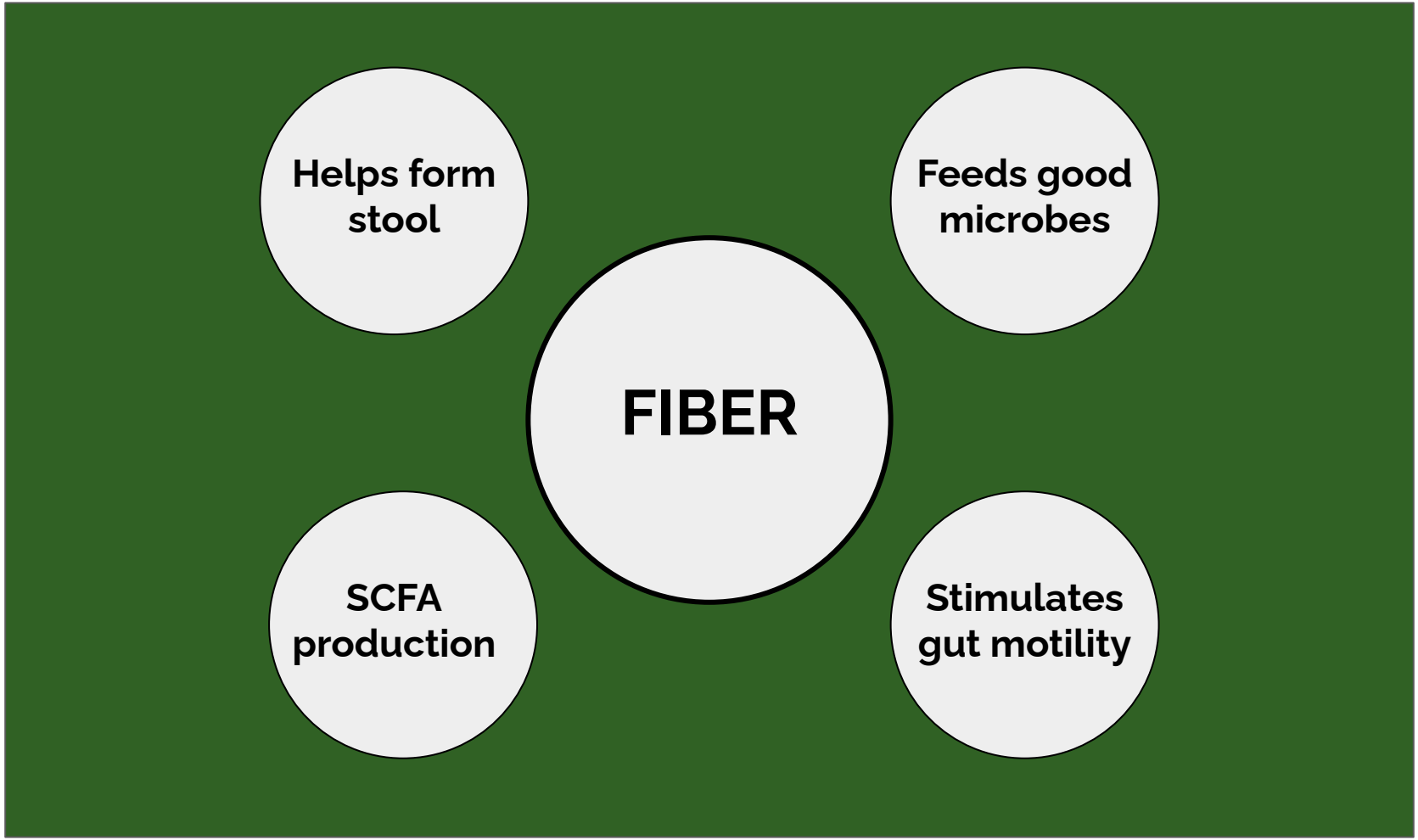
PMID: 35704960
PMCID: PMC9200470
DOI: 10.1371/journal.pone.0263880

Ivashkin VT, et al. Efficacy and safety of a food supplement with standardized menthol, limonene, and gingerol content in patients with irritable bowel syndrome: A double-blind, randomized, placebo-controlled trial. PLoS One. 2022 Jun 15;17(6):e0263880. doi: 10.1371/journal.pone.0263880.

How I practice



BOWEL MOVEMENTS



Fiber

- Solubility, fermentability, viscosity
- Non-fermented, soluble & viscous fibers can help reduce hypermobility and improve stool form
- Non-fermented, soluble fibers with some insolubility (viscous and non-viscous) may help improve motility and BM urgency
- Supplements offer isolated fibers to be strategic with their characteristics, without the complexity of food
- Can take a food first approach with fiber or a supplement first approach
- In IBS: goal is to use fiber to normalize bowel movements, reduce symptoms related to BMs, and improve microbial environment

Fiber - Psyllium

- Psyllium husk is a non-fermentable, viscous, soluble fiber that absorbs fluid and swells, forming a thicker, gel-like consistency to stool
- Helps with bowel regularity (both for diarrhea and constipation) and stool form
- 7 RCTs of 499 patients using up to 10 g/day compared to either placebo or low fiber diet found improved global IBS symptoms
- Some patients may improve with even higher doses - research is limited but some experts and researchers have had success increasing up to 20 g per day
- 7-9 grams dosed in around 8 oz water with adequate water intake throughout the day

https://www.health.com/psyllium-husk-benefits-7495040

Whelan K, Ford AC, Burton-Murray H, Staudacher HM. Dietary management of irritable bowel syndrome: considerations, challenges, and solutions. Lancet Gastroenterol Hepatol. 2024 Dec;9(12):1147-1161. doi: 10.1016/S2468-1253(24)00238-3.

Fiber - PHGG

- Partially hydrolyzed guar gum is a non-fermentable, soluble fiber that absorbs fluid without as much swelling, helping to soften stool without as much bulk
- Helps with bowel regularity (both for diarrhea and constipation) and softer stools - I find it helps constipation more
- 2014 study found accelerated colonic transit time with 4 weeks 5 mg PHGG in 49 chronic constipation adults
- 2002 study in 108 IBS patients compared 5 g to 30 g wheat bran for 4 weeks and found both improved pain and bowel habits, but PHGG was preferred by participants and many switched to the PHGG group from the bran

https://www.nexira.com/introduction-to-guar-gum/

Parisi GC, et al. High-fiber diet supplementation in patients with irritable bowel syndrome (IBS): a multicenter, randomized, open trial comparison between wheat bran diet and partially hydrolyzed guar gum (PHGG). Dig Dis Sci. 2002 Aug;47(8):1697-704. doi: 10.1023/a:1016419906546.

Polymeros D, Beintaris I, Gaglia A, Karamanolis G, Papanikolaou IS, Dimitriadis G, Triantafyllou K. Partially hydrolyzed guar gum accelerates colonic transit time and improves symptoms in adults with chronic constipation. Dig Dis Sci. 2014 Sep;59(9):2207-14. doi: 10.1007/s10620-014-3135-1.

Fiber - PHGG

- n=108 with IBS (all types)
- 6 g PHGG vs placebo for 12 weeks
- PHGG = improved bloating and bloating + gasses compared to placebo - continued 4 weeks after treatment ended
- No significant difference in pain, stool frequency, total SSS, and QOL
- BM frequency may be hard to measure - didn't isolate C or D results
- No side effects

Nutr Metab (Lond). 2016 Feb 6;13:10. doi: 10.1186/s12986-016-0070-5

Randomized clinical study: Partially hydrolyzed guar gum (PHGG) versus placebo in the treatment of patients with irritable bowel syndrome

E Niv [1,✉], A Halak [2], E Tiommny [2], H Yanai [2], H Strul [2], T Naftali [3], N Vaisman [1]

Author information Article notes Copyright and License information

PMCID: PMC4744437 PMID: 26855665

Niv E, Halak A, Tiommny E, Yanai H, Strul H, Naftali T, Vaisman N. Randomized clinical study: Partially hydrolyzed guar gum (PHGG) versus placebo in the treatment of patients with irritable bowel syndrome. Nutr Metab (Lond). 2016 Feb 6;13:10. doi: 10.1186/s12986-016-0070-5.

Fiber - PHGG

- Mixes into cold or hot liquids - can also be mixed into some foods, like yogurt
- 1 dose is typically 6-9 grams
- Start with 3 grams for 2-3 days then increase from there, individualized to the patient
- Can be used anytime of day, but evening may be ideal for increased BM urgency - anecdotal

Fiber - Acacia

https://www.verywellfit.com/the-benefits-of-acacia-fiber-89395

- Soluble fiber from the sap of acacia trees - aka gum arabic
- Only slightly viscous so still mixes well and may be tolerated better than psyllium for some bulking
- Is more fermentable but typically dosed lower than psyllium or PHGG
- Still considered low FODMAP

Fiber - Acacia

- n=18 IBS-C patients
- 10 g acacia vs BLa80 (*Bifidobacterium animalis* subsp. Lactis) probiotic vs 10 g maltodextrin placebo for 4 weeks
- Stool frequency improved in both fiber and probiotic groups compared to placebo with the probiotic showing higher reduction in IBS symptom severity and acacia showing more decreased constipation symptoms

Randomized Controlled Trial > Eur J Nutr. 2024 Aug;63(5):1983-1994.
doi: 10.1007/s00394-024-03398-8. Epub 2024 Apr 23.

Acacia fiber or probiotic supplements to relieve gastrointestinal complaints in patients with constipation-predominant IBS: a 4-week randomized double-blinded placebo-controlled intervention trial

Lonneke JanssenDuijghuijsen [# 1], Maartje van den Belt [# 2], Iris Rijnaarts [3], Paul Vos [1], Damien Guillemet [4], Ben Witteman [3 5], Nicole de Wit [1]

Affiliations + expand

PMID: 38653808
PMCID: PMC11329592
DOI: 10.1007/s00394-024-03398-8

JanssenDuijghuijsen L, et al. Acacia fiber or probiotic supplements to relieve gastrointestinal complaints in patients with constipation-predominant IBS: a 4-week randomized double-blinded placebo-controlled intervention trial. Eur J Nutr. 2024 Aug;63(5):1983-1994. doi: 10.1007/s00394-024-03398-8. Epub 2024 Apr 23. Erratum in: Eur J Nutr. 2025 Mar 22;64(3):135. doi: 10.1007/s00394-025-03586-0.

Fiber - GOS/FOS

- Found in prebiotic foods, but also isolated as supplements - inulin as an example
- 11 RCTs (including 8 in IBS and 3 in other DGBIs) of 729 patients compared to placebo found no benefit to global symptoms - very little heterogeneity between studies
- Older studies showed negative impact on IBS symptoms, but these were also higher doses
- There could be potential for lower doses but context in food may be most beneficial

Whelan K, Ford AC, Burton-Murray H, Staudacher HM. Dietary management of irritable bowel syndrome: considerations, challenges, and solutions. Lancet Gastroenterol Hepatol. 2024 Dec;9(12):1147-1161. doi: 10.1016/S2468-1253(24)00238-3.

Fiber - Others

Wheat bran	Insoluble & fermentable	Studied in 411 IBS patients over 6 RCTS = no improvement
Wheat dextrin	Soluble & fermentable	IBS research shows no benefit and possibility to worsen symptoms
Methylcellulose	Soluble, viscous & non-fermentable	Some research in IBS and constipation with some results - now being studied alongside inulin
Banana flakes	Resistant starch, soluble, fermentable & viscous	Great results in diarrhea, including with incontinence
Calcium polycarbophil	Insoluble, non-fermentable,	Some IBS trials show benefit with IBS-C or IBS-M

Whelan K, Ford AC, Burton-Murray H, Staudacher HM. Dietary management of irritable bowel syndrome: considerations, challenges, and solutions. Lancet Gastroenterol Hepatol. 2024 Dec;9(12):1147-1161. doi: 10.1016/S2468-1253(24)00238-3.

Lambeau KV, McRorie JW Jr. Fiber supplements and clinically proven health benefits: How to recognize and recommend an effective fiber therapy. J Am Assoc Nurse Pract. 2017 Apr;29(4):216-223. doi: 10.1002/2327-6924.12447.

Loperamide

- Works locally in the intestinal wall through several mechanisms:
  - Slows intestinal movement: it binds to the mu-opioid receptors in the gut wall, which decreases the contractions and peristalsis
  - Increases fluid absorption: by slowing down transit time, the intestines have more time to absorb water and electrolytes back into the body
  - Firms stool: the increased absorption of water results in stools that are firmer
  - Reduces urgency: it increases the tone of the anal sphincter, which helps improve bowel control and reduce the feeling of urgency

Lembo A, Sultan S, Chang L, Heidelbaugh JJ, Smalley W, Verne GN. AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea. Gastroenterology. 2022 Jul;163(1):137-151. doi: 10.1053/j.gastro.2022.04.017.

Loperamide

- Addresses BM frequency and consistency, but not pain in IBS-D
- AGA recommends against its use for overall symptoms due to lack of high-quality evidence
- But still used often due to a lower price than meds and patient acceptance
- Be mindful of “preventative” dosing that may lead to constipation

Practice Guideline > Gastroenterology. 2022 Jul;163(1):137-151.
doi: 10.1053/j.gastro.2022.04.017.

AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea

Anthony Lembo [1], Shahnaz Sultan [2], Lin Chang [3], Joel J Heidelbaugh [4], Walter Smalley [5], G Nicholas Verne [6]

Affiliations + expand

PMID: 35738725
DOI: 10.1053/j.gastro.2022.04.017

Full text links | Cite | ...

Abstract

Background & aims: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder associated with significant disease burden. This

Lembo A, Sultan S, Chang L, Heidelbaugh JJ, Smalley W, Verne GN. AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea. Gastroenterology. 2022 Jul;163(1):137-151. doi: 10.1053/j.gastro.2022.04.017.

Laxatives: Osmotics

- Draw water into the intestinal lumen to soften stool and increase bowel movement frequency by increasing transit
- Polyethylene Glycol (PEG)
  - In IBS: PEG has been used in a few RCTs for IBS-C, showing improved constipation symptoms but no reduction in abdominal pain or overall IBS symptom burden compared with placebo.
  - More efficacy for overall treatment in CIC starting at 17 g daily (electrolytes added may help), even compared to lactulose
  - Benefit remains over 6 months but often used more short term in practice
- Dosing: you can start with a half dose and then slowly work up to a full dose
- It can take a full 24-48 hours for BM improvement

Chang L, et al. American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Gastroenterology. 2023 Jun;164(7):1086-1106. doi: 10.1053/j.gastro.2023.03.214.

Papale AJ, Flattau R, Vithlani N, Mahajan D, Nadella S. A Review of Pharmacologic and Non-Pharmacologic Therapies in the Management of Irritable Bowel Syndrome: Current Recommendations and Evidence. J Clin Med. 2024 Nov 18;13(22):6948. doi: 10.3390/jcm13226948.

Laxatives: Osmotics

- Magnesium
  - Why? Some forms are less bioavailable leading to an osmotic effect in the colon
  - Magnesium oxide and citrate are used clinically, but there is limited high-quality IBS-specific studies. These can work but are more commonly studied in general chronic constipation.
  - Mg oxide 400-600 mg daily is recommended via AGA with potential to increase to 1000-1500 mg per day - caution with renal disease
  - Citrate form also works - I find this to be more gentle
  - Start low and work up slowly - similar to PEG

Chang L, et al. American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Gastroenterology. 2023 Jun;164(7):1086-1106. doi: 10.1053/j.gastro.2023.03.214.

Papale AJ, Flattau R, Vithlani N, Mahajan D, Nadella S. A Review of Pharmacologic and Non-Pharmacologic Therapies in the Management of Irritable Bowel Syndrome: Current Recommendations and Evidence. J Clin Med. 2024 Nov 18;13(22):6948. doi: 10.3390/jcm13226948.

Laxatives: Osmotics

- Lactulose
  - Not rigorously studied in IBS. Available evidence does not support strong benefits in IBS-C, and fermentation of lactulose can increase bloating and gas, which may worsen IBS symptoms.
  - May be recommended up to 15 g per day in CIC but no max dose has been identified in research. May cause hypernatremia and hypokalemia if patients experience significant diarrhea

Chang L, et al. American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Gastroenterology. 2023 Jun;164(7):1086-1106. doi: 10.1053/j.gastro.2023.03.214.

Papale AJ, Flattau R, Vithlani N, Mahajan D, Nadella S. A Review of Pharmacologic and Non-Pharmacologic Therapies in the Management of Irritable Bowel Syndrome: Current Recommendations and Evidence. J Clin Med. 2024 Nov 18;13(22):6948. doi: 10.3390/jcm13226948.

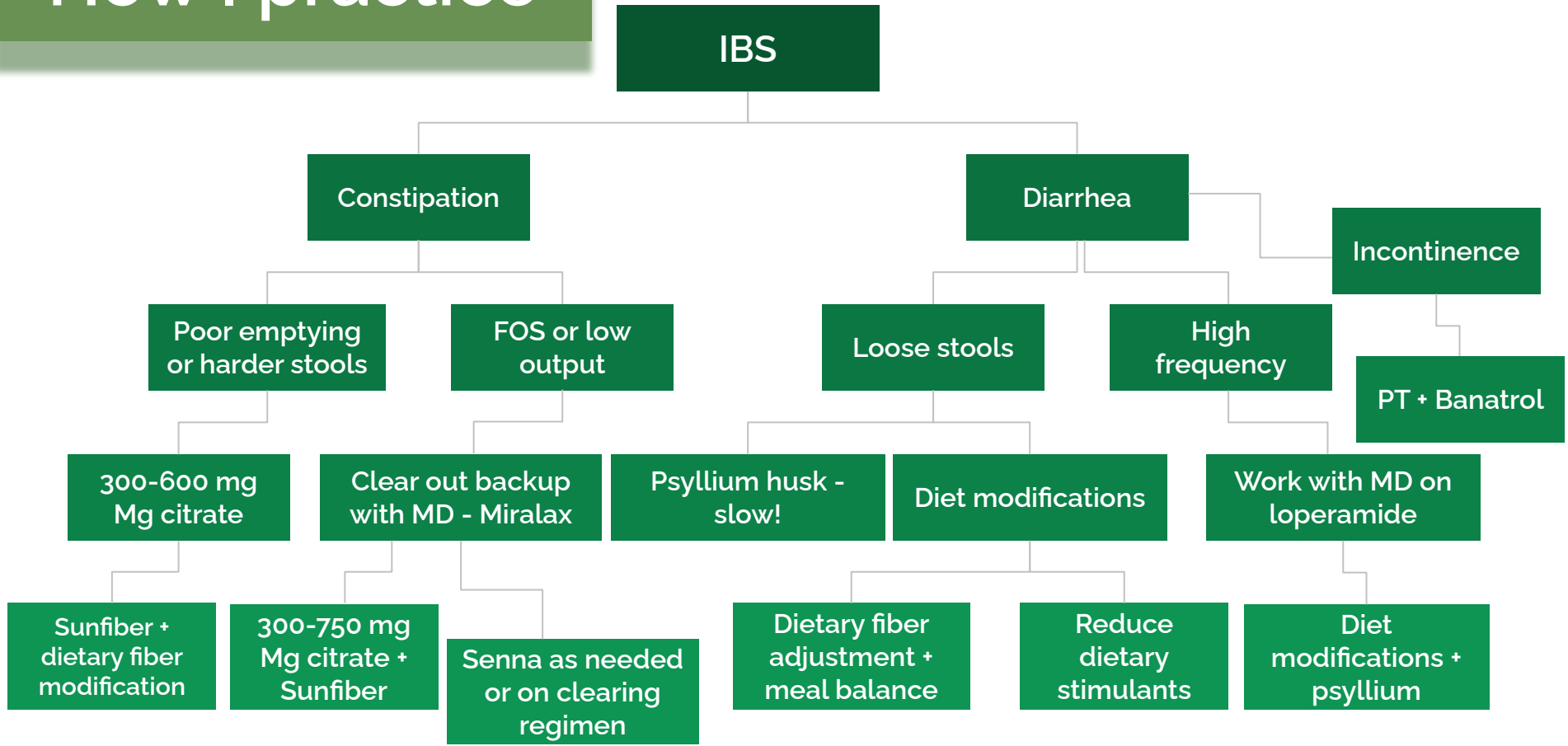
Laxatives: Stimulants

- Enhance intestinal motility by stimulating enteric nerves and promoting contractions
- Bisacodyl, Senna, Sodium Picosulfate
- While widely used in practice, no high-quality randomized trials in IBS-C
- Most evidence comes from chronic constipation studies
- Effective at increasing bowel movements, but may cause cramping, urgency, and diarrhea, which can be problematic for IBS symptoms
- Bisacodyl is used 5-10 mg short term per AGA
- Senna is used 8.6–17.2 mg daily per AGA
- Dependency - this has been debated and is an area to learn more in!

Chang L, et al. American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation. Gastroenterology. 2023 Jun;164(7):1086-1106. doi: 10.1053/j.gastro.2023.03.214.

Papale AJ, Flattau R, Vithlani N, Mahajan D, Nadella S. A Review of Pharmacologic and Non-Pharmacologic Therapies in the Management of Irritable Bowel Syndrome: Current Recommendations and Evidence. J Clin Med. 2024 Nov 18;13(22):6948. doi: 10.3390/jcm13226948.

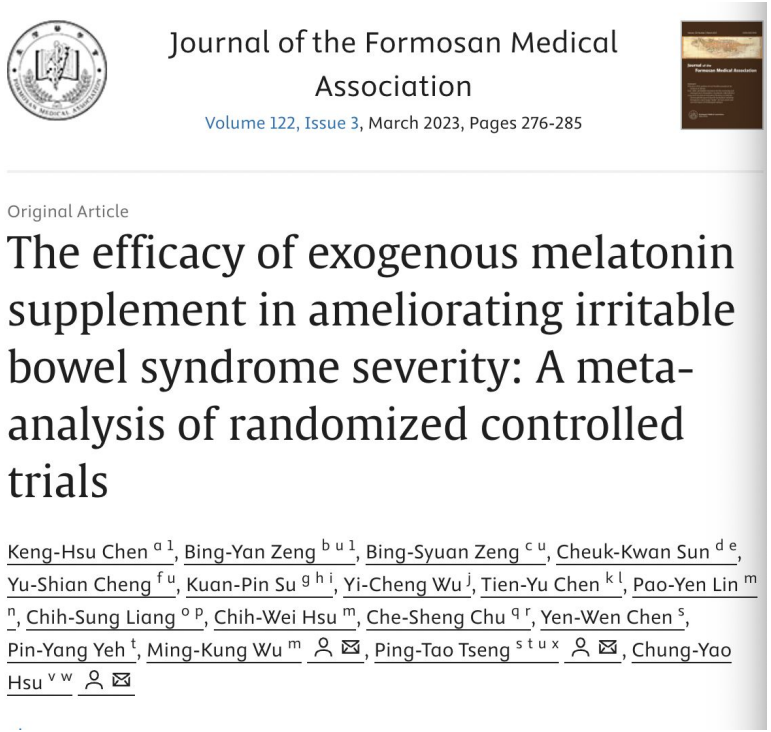
How I practice



GENERAL

Melatonin

- 4 RCTs and 115 participants revealed that 3 mg exogenous melatonin supplement was associated with significantly better improvement in overall IBS severity than placebo
- Supplementation was also associated with improved IBS pain severity and QOL, but not in distention



Journal of the Formosan Medical Association
Volume 122, Issue 3, March 2023, Pages 276-285

Original Article

The efficacy of exogenous melatonin supplement in ameliorating irritable bowel syndrome severity: A meta-analysis of randomized controlled trials

Keng-Hsu Chen [a l], Bing-Yan Zeng [b u l], Bing-Syuan Zeng [c u], Cheuk-Kwan Sun [d e], Yu-Shian Cheng [f u], Kuan-Pin Su [g h i], Yi-Cheng Wu [j], Tien-Yu Chen [k l], Pao-Yen Lin [m n], Chih-Sung Liang [o p], Chih-Wei Hsu [m], Che-Sheng Chu [q r], Yen-Wen Chen [s], Pin-Yang Yeh [t], Ming-Kung Wu [m], Ping-Tao Tseng [s t u x], Chung-Yao Hsu [v w]

Lembo A, Sultan S, Chang L, Heidelbaugh JJ, Smalley W, Verne GN. AGA Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea. Gastroenterology. 2022 Jul;163(1):137-151. doi: 10.1053/j.gastro.2022.04.017.

L-Glutamine

- Amino acid produced in the body that helps build proteins - also found in many protein-rich foods
- Thought to support immune cells during inflammation and to help repair the intestinal wall after injury or increased permeability
- Weak RCT in 2019 tested 15 g (5g TID) for 8 weeks in 54 PI-IBS patients vs 52 placebo - found significant reduction in IBS-SSS, daily bowel movement frequency, bristol stool scale, and intestinal permeability measured by urinary lactulose/mannitol ratios
- 2021 study compared LFD alone or with 15 g L-glutamine for 6 weeks - found higher IBS-SSS reduction in glutamine group

Zhou Q, Verne ML, Fields JZ, Lefante JJ, Basra S, Salameh H, Verne GN. Randomised placebo-controlled trial of dietary glutamine supplements for postinfectious irritable bowel syndrome. Gut. 2019 Jun;68(6):996-1002. doi: 10.1136/gutjnl-2017-315136.

Rastgoo S, Ebrahimi-Daryani N, Agah S, Karimi S, Taher M, Rashidkhani B, Hejazi E, Mohseni F, Ahmadzadeh M, Sadeghi A, Hekmatdoost A. Glutamine Supplementation Enhances the Effects of a Low FODMAP Diet in Irritable Bowel Syndrome Management. Front Nutr. 2021 Dec 16;8:746703. doi: 10.3389/fnut.2021.746703.

L-Glutamine

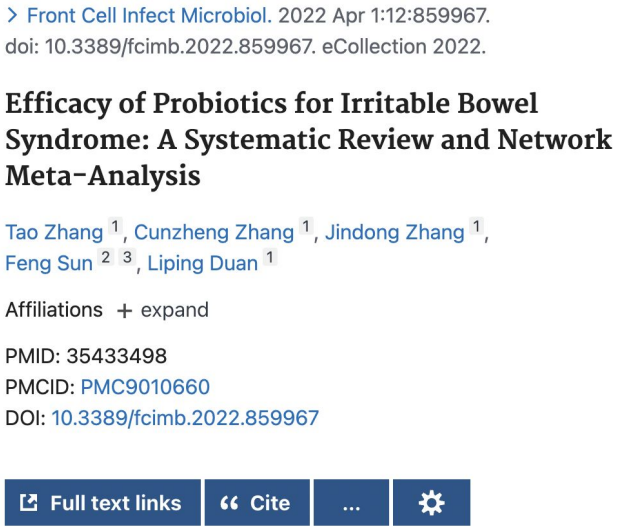
- No recommendation from AGA or ACG
- RDs do tend to use this with success in practice, especially in IBS-D and suspected PI-IBS
- Dosing: typically 15 g per day split into 3 5 g doses
- You can also build up dosing, testing a few weeks at a time
- 3 months of use to test seems to be a good option but we don't have great data on ideal dosing and monitoring
- May not be safe in those with liver and kidney disease
- Could increase mania in those with bipolar disorders, as well as increase seizures (also interacts with seizure meds)

Probiotics

- Why they could help (debated):
  - gut microbiota modulation by competition and inhibition of pathogens adhesion to the gut epithelia by the production of bacteriocins, SCFAs, and biosurfactants
  - improvement in the gut barrier function of the gut mucosa by downregulation of low-grade mucosal immune activation, increasing the mucus layer, and production of proteins of tight junctions
  - anti-inflammatory effects via suppression of proinflammatory cytokines; improvement of the gut immunity by stimulating secretory IgA production and enhancement of gut–brain communication

Probiotics

- 43 RCTs with 5531 IBS patients
- B.coagulans improved best in improving IBS symptoms, as well as global symptoms, abdominal pain, bloating, and straining scores.
- L.plantarum ranked first in ameliorating the QOL of IBS patients
- L.acidophilus had lowest incidence of adverse events
- No significant differences found between different doses of probiotics in all outcomes, while treatmen length can significantly influence the efficacy of probiotics in improving abdominal pain



> Front Cell Infect Microbiol. 2022 Apr 1:12:859967.
doi: 10.3389/fcimb.2022.859967. eCollection 2022.

Efficacy of Probiotics for Irritable Bowel Syndrome: A Systematic Review and Network Meta-Analysis

Tao Zhang [1], Cunzheng Zhang [1], Jindong Zhang [1], Feng Sun [2] [3], Liping Duan [1]

Affiliations + expand

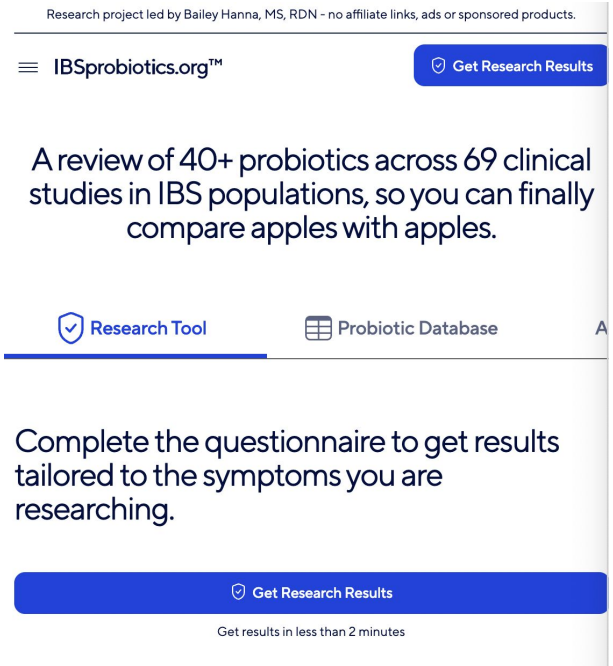
PMID: 35433498
PMCID: PMC9010660
DOI: 10.3389/fcimb.2022.859967

Full text links | Cite | ...

Zhang T, Zhang C, Zhang J, Sun F, Duan L. Efficacy of Probiotics for Irritable Bowel Syndrome: A Systematic Review and Network Meta-Analysis. Front Cell Infect Microbiol. 2022 Apr 1;12:859967. doi: 10.3389/fcimb.2022.859967.

Probiotics

- Research doesn't show consistent benefit and aren't replicated well
- Decent studies currently exist mostly in in vitro and mouse models vs human models
- Overall, evidence is too weak for a broad or first-line recommendation
- A lot of potential for personalized medicine in the future
- Can be a safe option for many patients but currently will be weak evidence-informed trial and error



Simon E, Călinoiu LF, Mitrea L, Vodnar DC. Probiotics, Prebiotics, and Synbiotics: Implications and Beneficial Effects against Irritable Bowel Syndrome. Nutrients. 2021 Jun 20;13(6):2112. doi: 10.3390/nu13062112.

Berberine

- Isoquinoline alkaloid found in a variety of plant species that has anti-inflammatory properties and may help reduce LPS-induced intestinal damage (increased permeability seen in some with IBS?)
- n=29 with IBS-D or functional diarrhea - 250 mg berberine paired with .5 mg melatonin and 750 mg guar gum every 12 hours for 90 days
- 30 days = reduction in symptom scores of approximately 50 and 70% is shown for IBS-D and FD, respectively.
- 90 days = a reduction of more than 70 and 80%, respectively.

> Minerva Gastroenterol Dietol. 2020 Mar;66(1):29-34.
doi: 10.23736/S1121-421X.19.02649-7.

Role of a berberine-based nutritional supplement in reducing diarrhea in subjects with functional gastrointestinal disorders

Francesco Di Pierro [1], Alexander Bertuccioli [2], Rosanna Giuberti [3], Mariella Saponara [4], Leandro Ivaldi [5]

Affiliations + expand

PMID: 32283882
DOI: 10.23736/S1121-421X.19.02649-7
Free article

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Abstract

Background: Berberine, an alkaloid obtained by extraction from Berberis spp., is a botanical that is widely used in the nutraceutical sector to control cholesterol and blood glucose levels. It is also a molecule that is effective in limiting diarrhea due to its multi-factorial properties, including its antimicrobial, gut eubiotic and antisecretive actions, and its ability to slow gut motility. In our routine clinical practice, we have suggested the use of a berberine-based nutraceutical, formulated with melatonin and depolymerized guar gum, to patients affected by functional diarrhea (FD) or by diarrhea-type irritable bowel syndrome (IBS-D).

Methods: We have therefore retrospectively analyzed the clinical effect of such a nutritional

Di Pierro F, Bertuccioli A, Giuberti R, Saponara M, Ivaldi L. Role of a berberine-based nutritional supplement in reducing diarrhea in subjects with functional gastrointestinal disorders. Minerva Gastroenterol Dietol. 2020 Mar;66(1):29-34. doi: 10.23736/S1121-421X.19.02649-7.

Izadparast F, Riahi-Zajani B, Yarmohammadi F, Hayes AW, Karimi G. Protective effect of berberine against LPS-induced injury in the intestine: a review. Cell Cycle. 2022 Nov;21(22):2365-2378. doi: 10.1080/15384101.2022.2100682.

Berberine

- Also believed to be anti-microbial so has been used to treat infections and bacterial overgrowth
- Was studied against rifaximin at 800 mg/day over 4 weeks and showed similar treatment outcomes but rifaximin dose studied was lower than what had been studied successfully (800 mg/day) for SIBO tx so a poor study to lean on
- While berberine is considered possibly safe for up to 6 months of use at recommended doses, there is a lack of high-quality long-term research (beyond 6-12 months) to definitively confirm its safety for prolonged period
- It can interact with DM meds, blood pressure meds, blood thinners and anti clotting drugs, immunosuppressants, and sedatives

Gao J, Guo H, Zhu L, et alIDDF2025-ABS-0189 New choice for small intestinal bacterial overgrowth: an RCT comparing berberine and rifaximinGut 2025;74:A328-A329.

Berberine

- Likely best used in patients with confirmed bacterial overgrowth or suspected impaired intestinal permeability - possibly used in diarrhea over constipation
- Can offer a lower cost alternative to Rifaximin for SIBO - but NOT FULLY VALIDATED AS TREATMENT
- Can trial between 250-800 mg (both doses studied) for 4-12 weeks
- Check meds first

Oregano

- Oregano oil is believed to improve IBS symptoms primarily through its antimicrobial, anti-inflammatory, and antioxidant properties - attributed to active compounds, mainly carvacrol and thymol
- No human trials in IBS
- 1 study in SIBO: n=19 Biocidin + olivirex + GI Detox+ for 14 weeks - most effective for hydrogen- and hydrogen sulfide-dominant SIBO, leading to negative breath test results at week 10 in 42.8% and 66.7% of participants, respectively
- Not enough info on dosing to have full confidence
- Should we be “treating” SIBO?

Clinical Trial > Nutrients. 2024 Sep 18;16(18):3149.
doi: 10.3390/nu16183149.

An Oral Botanical Supplement Improves Small Intestinal Bacterial Overgrowth (SIBO) and Facial Redness: Results of an Open-Label Clinical Study

Mildred Min [1 2], Dawnica Nadora [1 2], Mincy Chakkalakal [1], Nasima Afzal [1], Chaitra Subramanyam [1 3], Nimrit Gahoonia [1 4], Adrianne Pan [1 2], Shivani Thacker [1], Yvonne Nong [1 5], Cindy J Chambers [1 6], Raja K Sivamani [1 2 6 7]

Affiliations + expand

PMID: 39339748
PMCID: PMC11435404
DOI: 10.3390/nu16183149

Min M, et al. An Oral Botanical Supplement Improves Small Intestinal Bacterial Overgrowth (SIBO) and Facial Redness: Results of an Open-Label Clinical Study. Nutrients. 2024 Sep 18;16(18):3149. doi: 10.3390/nu16183149.

Oregano

- Long term safety not fully explored
- Can lower blood sugar levels - be mindful of DM meds
- Not ideal for pregnancy due to increased uterine contractions and risk of miscarriage
- Can also interact with blood thinners and may affect absorption of iron, zinc, and copper
- Essential oil vs food grade oil is more concentrated

Vitamin D

- n=36 IBS-D found that 44% had vitamin D deficiencies and in correcting those over 12 weeks, symptoms improved, specifically the regulation of BMs.
- Further testing showed improved intestinal barrier and decreased proinflammatory factors (IL-6 & IL-9)

- Review in IBS patients showed a positive correlation between vitamin D supplementation and improved symptoms + QOL - mechanism unknown in this review

Clinical Trial > Nutrients. 2021 Mar 21;13(3):1011.
doi: 10.3390/nu13031011.

The Relationship between Low Serum Vitamin D Levels and Altered Intestinal Barrier Function in Patients with IBS Diarrhoea Undergoing a Long-Term Low-FODMAP Diet: Novel Observations from a Clinical Trial

Michele Linsalata [1], Giuseppe Riezzo [1], Antonella Orlando [1], Benedetta D'Attoma [1], Laura Prospero [1], Valeria Tutino [2], Maria Notarnicola [2], Francesco Russo [1]

Nutr J. 2022 May 5;21:24. doi: 10.1186/s12937-022-00777-x

The efficacy of vitamin D supplementation for irritable bowel syndrome: a systematic review with meta-analysis

Hangkai Huang [1,#], Linjie Lu [1,2,#], Yishu Chen [1,#], Yan Zeng [1], Chengfu Xu [1,2,✉]

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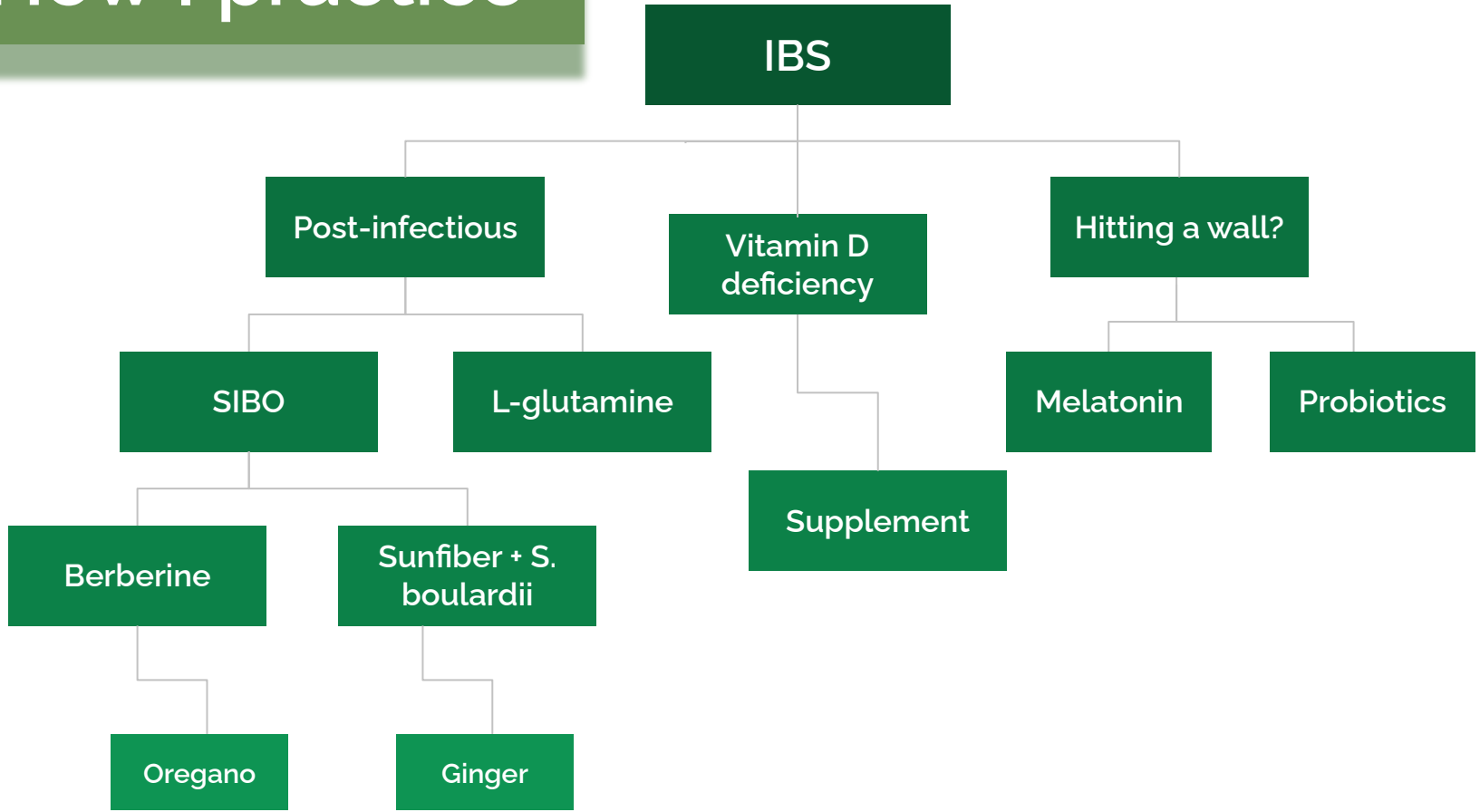
PMCID: PMC9069731 PMID: 35509010

Linsalata M., et al. The Relationship between Low Serum Vitamin D Levels and Altered Intestinal Barrier Function in Patients with IBS Diarrhoea Undergoing a Long-Term Low-FODMAP Diet: Novel Observations from a Clinical Trial. Nutrients. 2021;13:1011. doi: 10.3390/nu13031011

Huang H., Lu L., Chen Y., Zeng Y., Xu C. The efficacy of vitamin D supplementation for irritable bowel syndrome: A systematic review with meta-analysis. Nutr. J. 2022;21:24. doi: 10.1186/s12937-022-00777-x.

How I practice



Let’s discuss!