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Antibiotics: Evidence for Probiotics, Nutraceuticals, Herbal Therapies, and Diet in Small Intestinal Bacterial Overgrowth. A Narrative Review

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Abstract

Small intestinal bacterial overgrowth (SIBO) is a heterogeneous disorder in which excessive or altered microbial populations in the small intestine coexist with disturbances in motility, anatomy, host defenses, and luminal ecology. Although antibiotics remain the best-studied pharmacological treatment, incomplete response, recurrence, adverse effects, and repeated antimicrobial exposure have stimulated interest in non-antibiotic strategies. This narrative review evaluates clinical evidence for probiotics, *Saccharomyces boulardii*, berberine, herbal therapies, elemental and conventional dietary interventions, prebiotics/synbiotics, and fermented foods. Evidence syntheses and clinically informative trials were prioritized, with objective breath-test resolution considered separately from symptom improvement. Probiotics have the largest body of direct non-antibiotic clinical evidence, although results are heterogeneous and formulation-specific. *Saccharomyces boulardii* has shown promising results as monotherapy and as an adjunct to metronidazole in systemic sclerosis-associated SIBO. Berberine has emerged prominently in recent network-level comparisons, while standardized herbal combinations and elemental diets have produced clinically relevant signals but are supported by less robust direct evidence. Low-FODMAP and other dietary strategies may reduce fermentation-related symptoms, but evidence for SIBO eradication is limited. Kefir and kombucha are biologically plausible microbiome-modulating foods, yet SIBO-specific controlled therapeutic trials remain lacking. Overall, non-antibiotic management should be interpreted within a broader pathophysiological framework targeting microbial burden, substrate availability, intestinal motility, mucosal integrity, and underlying predisposing conditions. Symptom improvement, microbiome modification, and objective SIBO eradication should be regarded as related but non-equivalent outcomes.

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1. Introduction

Small intestinal bacterial overgrowth (SIBO) is a heterogeneous gastrointestinal disorder characterized by an abnormal increase in the number and/or composition of microorganisms within the small intestine, resulting in excessive fermentation and a broad spectrum of gastrointestinal manifestations. Abdominal bloating, distension, abdominal pain, diarrhea, altered bowel habits, flatulence, and nutritional abnormalities are among the most commonly reported manifestations. The clinical phenotype is influenced by the underlying disorder, intestinal transit, microbial composition, and the predominant gases generated during fermentation.^[1,2]

SIBO should also be distinguished from intestinal methanogen overgrowth (IMO). Although the two conditions frequently coexist in the clinical literature, methane is produced predominantly by archaea rather than bacteria, and methane-positive patients may exhibit different clinical characteristics and therapeutic responses. This distinction has become increasingly important when interpreting studies that combine hydrogen- and methane-positive breath tests within a single therapeutic outcome.^[1, 3]

The pathophysiology of SIBO is multifactorial. Normal defenses against excessive microbial colonization of the small intestine include gastric acidity, pancreaticobiliary secretions, an intact ileocecal valve, intestinal immune mechanisms, and, particularly, coordinated small-bowel motility and the migrating motor complex. Structural abnormalities, impaired motility, systemic diseases, previous gastrointestinal surgery, medications, and other conditions that disturb these protective mechanisms may predispose to microbial overgrowth. Consequently, eradication of excessive microorganisms without correction of the underlying predisposing factor may be followed by recurrence.^[1, 2]

Antibiotics, particularly poorly absorbed agents such as rifaximin, remain the most extensively studied pharmacological approach to SIBO. Nevertheless, antibiotic therapy has several limitations, including incomplete response, recurrence after initially successful treatment, adverse effects, cost, and concerns regarding repeated antimicrobial exposure. These limitations have stimulated considerable interest in non-antibiotic and complementary approaches aimed not only at reducing microbial overgrowth but also at modifying the intestinal ecosystem, luminal fermentation, intestinal barrier function, and gastrointestinal motility.^[1]

Among these strategies, probiotics have accumulated the largest body of direct clinical evidence. Other approaches include berberine and botanical therapies, elemental diets, prebiotics and synbiotics, conventional dietary interventions, and increasingly popular fermented foods such as kefir and kombucha. Importantly, biological plausibility and widespread use should not be conflated with demonstrated therapeutic efficacy.^[4-6]

Accordingly, the objective of this narrative review was to critically evaluate the clinical evidence supporting non-antibiotic and adjunctive approaches to SIBO, with particular emphasis on probiotics, berberine and other nutraceuticals, herbal therapies, elemental and dietary interventions, prebiotics and synbiotics, and fermented foods. Particular attention was given to the hierarchy of available evidence and to the important distinction between objective resolution of SIBO and improvement in gastrointestinal symptoms.

2. Methods

This evidence-based narrative review was designed to critically examine non-antibiotic, complementary, and adjunctive interventions evaluated for the management of SIBO. Because the purpose was to integrate a heterogeneous literature encompassing evidence syntheses, randomized and non-randomized clinical trials, dietary interventions, and emerging microbiome-directed approaches rather than to perform a new quantitative synthesis, a narrative review

framework was adopted.

Relevant literature was identified through searches of major biomedical databases and reference lists of key reviews and clinical studies. Priority was given to network meta-analyses, conventional meta-analyses, systematic reviews, randomized controlled trials, controlled clinical studies, and clinically informative prospective or retrospective studies. Recent evidence syntheses were additionally used to identify earlier primary studies.

Search concepts combined terms related to small intestinal bacterial overgrowth, SIBO, and intestinal methanogen overgrowth with probiotics, *Saccharomyces boulardii*, *Bacillus clausii*, *Lactobacillus*, *Bifidobacterium*, prebiotics, synbiotics, berberine, herbal therapy, botanical therapy, nutraceuticals, elemental diet, diet, low-FODMAP, fermented foods, kefir, and kombucha. Reference lists of relevant reviews and clinical trials were examined for additional studies.

Evidence was interpreted according to study design, with evidence syntheses followed by randomized controlled trials, controlled non-randomized studies, uncontrolled clinical studies, and indirect or mechanistic evidence. This hierarchy was used descriptively and was not intended as a formal certainty-of-evidence grading system.

Studies were evaluated according to population, diagnostic method, intervention, comparator, duration, objective breath-test outcomes, gastrointestinal symptom outcomes, adverse events, and major methodological limitations. Whenever possible, objective SIBO resolution or breath-test normalization was considered separately from symptomatic response, because improvement in bloating, abdominal pain, diarrhea, or other gastrointestinal symptoms does not necessarily indicate eradication of small-intestinal microbial overgrowth.

Studies enrolling methane-positive participants were interpreted cautiously because methane positivity may represent IMO rather than bacterial overgrowth. Results involving hydrogen- and methane-predominant populations were distinguished whenever sufficient information was available. For emerging interventions such as kefir, kombucha, and other fermented foods, the absence of controlled SIBO-specific trials was considered an evidence gap rather than evidence of ineffectiveness.

3. Results

3.1. Overall Landscape and Hierarchy of Evidence

The clinical literature evaluating non-antibiotic SIBO treatment was heterogeneous with respect to patient population, definition of SIBO, breath-test substrate and positivity threshold, treatment duration, comparator, and outcome definition. Earlier systematic evaluation of alternative therapies demonstrated a relatively small evidence base, principally involving probiotics, herbal preparations, and dietary therapy. More recent evidence syntheses have expanded this literature, particularly for probiotics and through network comparisons incorporating berberine and other interventions.^[4] The overall hierarchy of evidence supporting non-antibiotic and adjunctive approaches to SIBO, ranging from evidence syntheses and controlled clinical studies to preliminary, indirect, and mechanistic evidence, is summarized in Figure 1.

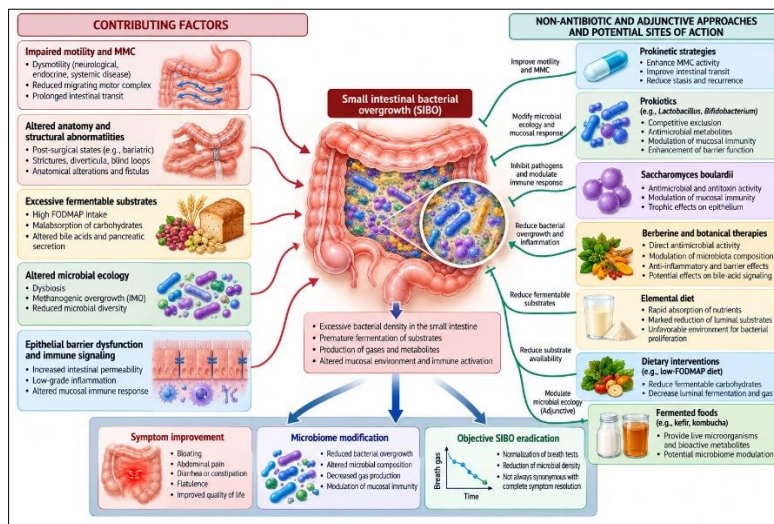


Fig 1

The hierarchy of available evidence is summarized in Table 1. Probiotics currently represent the non-antibiotic intervention with the broadest body of direct clinical evidence. Berberine has recently gained prominence through network-level comparisons and emerging direct comparative evidence. Specific probiotic preparations, particularly *Saccharomyces boulardii*, have additional controlled clinical evidence. Herbal combinations and elemental diets have generated clinically relevant signals, although their supporting study designs are less robust. Evidence for low-FODMAP diets, kefir, kombucha, and several other nutraceutical or fermented-food strategies remains largely indirect or insufficient for establishing SIBO eradication.

3.2. Probiotics: The Largest Body of Direct Non-Antibiotic Evidence

Probiotics have been studied more extensively than other non-antibiotic approaches, although the literature is characterized by considerable heterogeneity in species, strains, doses, duration, and study populations.

The earlier meta-analysis by Zhong *et al.* reported a pooled SIBO decontamination rate of 62.8% (95% CI 51.5–72.8). In comparisons with non-probiotic controls, probiotics were associated with a higher decontamination rate (RR 1.61, 95% CI 1.19–2.17). Probiotic therapy was also associated with a reduction in hydrogen concentration (weighted mean difference –36.35 ppm, 95% CI –44.23 to –28.47) and a modest improvement in abdominal pain.^[5]

The more recent review by Niño *et al.* identified 18 clinical trials; 14 had control groups and nine were randomized, encompassing 496 probiotic-treated patients and 480 controls. Six trials compared probiotics with placebo (122 vs 104 participants), but only three were sufficiently comparable for quantitative pooling. The individual studies further illustrate why probiotics should not be regarded as a homogeneous therapeutic class. Trials involved *Bacillus clausii*, *Saccharomyces boulardii*, *Lactobacillus* species, *Bifidobacterium* species, and multispecies preparations, with markedly different populations and comparators.^[6]

For example, Scarpellini *et al.* reported improvement in 17/30 (56.6%) patients receiving *B. clausii* compared with 12/30 (40%) receiving metronidazole. Soifer *et al.* reported clinical improvement in 20/25 (82%) probiotic-treated patients compared with 13/25 (52%) receiving

metronidazole. Conversely, other probiotic trials did not demonstrate significant benefit. In a placebo-controlled study in chronic liver disease, a multispecies probiotic produced SIBO resolution in 24% compared with 0% in the placebo group after four weeks. Taken together, probiotics have the largest clinical evidence base among non-antibiotic interventions, but efficacy observed with one formulation cannot automatically be extrapolated to another.^[7, 8, 9]

3.3. Saccharomyces Boulardii

Among individual probiotic organisms, *S. boulardii* deserves particular attention because it has been evaluated as monotherapy and in combination with antibiotics. García-Collinot *et al.* conducted an open randomized pilot clinical trial in patients with systemic sclerosis and hydrogen-positive SIBO. Forty patients were randomized to metronidazole plus *S. boulardii* (n=13), metronidazole alone (n=13), or *S. boulardii* alone (n=14).^[10] After treatment, SIBO eradication was reported in 55% of patients receiving combination therapy, 33% receiving *S. boulardii* alone, and 25% receiving metronidazole alone. Reductions in expired hydrogen and improvements in gastrointestinal symptoms were also observed in the *S. boulardii*-containing groups. These results should nevertheless be interpreted cautiously: only 29 of the 40 randomized participants completed two months of follow-up. The study therefore provides a clinically interesting signal rather than definitive evidence of superiority.^[10]

3.4. Berberine

More recent randomized pilot evidence in diarrhea-predominant irritable bowel syndrome (IBS) also supports continued investigation of *S. boulardii* CNCM I-745. Bustos Fernández *et al.* randomized patients to *S. boulardii* plus dietary advice or dietary advice alone; among 48 evaluable participants, hydrogen excretion decreased by 41% versus 29%, respectively, with greater symptom-score reduction in the probiotic group.^[15]

Berberine represents one of the most interesting emerging non-antibiotic interventions. A recent Bayesian network meta-analysis included 30 randomized controlled trials comprising 1,552 participants and 12 therapeutic interventions. Berberine achieved a favorable probabilistic ranking for SIBO eradication.^[11]

This finding is important but requires careful interpretation.

Network rankings integrate direct and indirect comparisons and can be influenced by the amount and quality of available evidence and the structure of the treatment network. Accordingly, berberine is best regarded as a promising emerging intervention for which additional direct comparative trials remain desirable.

3.5. Herbal and Botanical Therapies

Herbal combinations constitute another frequently discussed alternative to conventional antibiotic therapy. In the comparative study by Chedid *et al.*, patients selected either rifaximin or one of two multi-ingredient botanical regimens (Dysbiocide plus FC Cidal or Candibactin-AR plus Candibactin-BR). Among patients with follow-up testing, 17/37 (46%) receiving herbal therapy achieved a negative lactulose breath test compared with 23/67 (34%) receiving rifaximin ($P=0.24$); the adjusted odds ratio was 1.85 (95% CI 0.77–4.41; $P=0.17$)^[12].

Importantly, the herbal intervention evaluated by Chedid *et al.*^[12] did not consist of a single botanical compound, but rather one of two multi-ingredient commercial regimens: Dysbiocide plus FC Cidal or Candibactin-AR plus Candibactin-BR, administered for four weeks. The formulations contained multiple botanicals with putative antimicrobial or microbiome-modulating properties. FC Cidal included *Tinospora cordifolia*, *Equisetum arvense*, pau d'arco, *Thymus vulgaris*, *Artemisia dracunculus*, *Sida cordifolia*, and *Olea europaea*, whereas Dysbiocide contained, among other ingredients, dill seed, *Stemona sessilifolia*, *Artemisia absinthium*, *Pulsatilla chinensis*, *Brucea javanica*, *Picrasma excelsa*, *Acacia catechu*, *Hedyotis diffusa*, and *Achillea millefolium*. The alternative regimen combined Candibactin-AR, containing thyme and oregano oils together with sage and lemon balm extracts, with Candibactin-BR, a berberine-rich preparation containing *Coptis chinensis*, *Berberis aristata*, berberine sulfate, *Scutellaria baicalensis*, *Phellodendron chinense*, ginger, Chinese licorice, and Chinese rhubarb. Because these were complex multi-ingredient formulations, the observed clinical response cannot be attributed to any individual botanical constituent.

Because treatment allocation was not randomized, these findings cannot establish equivalence between botanical therapy and rifaximin. Nevertheless, the observed response provides a meaningful signal supporting prospective randomized evaluation of standardized botanical preparations.

3.6. Elemental Diet

The elemental diet represents a different therapeutic concept because it profoundly modifies the luminal nutritional environment rather than primarily introducing beneficial microorganisms or directly suppressing selected microbial populations. In the study by Pimentel *et al.*, approximately 80% of evaluable participants normalized their breath test after 14 days, increasing to approximately 85% after extension to 21 days.^[13]

The magnitude of this response is notable, but the absence of a randomized comparator, together with issues of adherence, tolerability, patient selection, and interpretation of lactulose breath testing, limits causal inference. The elemental diet

therefore provides a strong preliminary efficacy signal rather than definitive comparative evidence.

3.7. Prebiotics, Synbiotics, And Adjunctive Microbiome-Directed Therapy

Evidence for prebiotics and synbiotics is substantially less developed than that for probiotics. Much of the available literature evaluates these agents following or concurrently with antibiotic treatment rather than as independent therapies. Rosania *et al.*, for example, compared sequential rifaximin followed by *Lactobacillus casei* with rifaximin followed by short-chain fructooligosaccharides. Symptomatic improvement favored the probiotic sequence numerically (83.3% vs 66.6%), but the difference was not statistically significant ($P=0.57$). Such studies are clinically relevant but are best classified as adjunctive microbiome-directed strategies.^[14, 14,16]

3.8. Dietary Interventions and Low-Fodmap Approaches

Dietary modification is widely used in patients with SIBO because fermentable carbohydrates can influence luminal fermentation, gas production, bloating, and abdominal discomfort. Nevertheless, evidence supporting symptom management should be distinguished from evidence demonstrating eradication of SIBO. Low-FODMAP strategies may reduce rapidly fermentable substrates and improve symptoms in selected patients, but direct controlled evidence demonstrating sustained normalization of SIBO through a low-FODMAP diet alone remains insufficient. Thus, these approaches are better viewed primarily as symptom- and substrate-modifying strategies.

3.9. Kefir, Kombucha, and Fermented Foods

Kefir and kombucha warrant inclusion because they are increasingly used as food-based approaches to microbiome modulation. Both contain complex microbial communities and fermentation-derived metabolites and therefore have biological plausibility. However, their composition may vary considerably according to starter culture, substrate, fermentation conditions, storage, and commercial processing.^[4]

Adequately controlled SIBO-specific clinical trials demonstrating eradication with kefir or kombucha have not been identified. Their position at the lower end of the evidence hierarchy should therefore not be interpreted as evidence that they are ineffective. Rather, it reflects an absence of direct clinical investigation. Efficacy demonstrated for a standardized probiotic strain cannot automatically be extrapolated to kefir, kombucha, or fermented foods as a class.

3.10. Integration of The Evidence

The available evidence reveals a mismatch between the popularity of several non-antibiotic SIBO therapies and the strength of their clinical evaluation. Probiotics have the broadest direct clinical literature, but effects appear formulation-specific. Berberine has emerged prominently from network-level evidence, while herbal combinations and elemental diets show clinically relevant signals supported by less robust direct study designs. Low-FODMAP diets and fermented foods occupy a different evidentiary position: their

biological rationale and potential symptomatic effects are clinically relevant, but evidence of SIBO eradication is presently insufficient.

Collectively, these findings support a central distinction: improvement in gastrointestinal symptoms, modification of fermentation, alteration of the microbiome, and objective eradication of SIBO are related but non-equivalent therapeutic outcomes.

4. Discussion

The growing interest in non-antibiotic approaches to SIBO reflects both the limitations of conventional antimicrobial therapy and an evolving understanding of SIBO as more than a simple infectious disorder. Although excessive microbial colonization is central to its definition, the development and recurrence of SIBO frequently result from disturbances in intestinal motility, anatomy, luminal environment, host defenses, and microbial ecology. From this perspective, repeated antimicrobial eradication alone may not adequately address the mechanisms responsible for persistence or recurrence.

Among non-antibiotic strategies, probiotics have the most extensive direct clinical literature. This is biologically plausible because probiotics may influence the intestinal ecosystem through competitive exclusion, production of antimicrobial compounds, modification of luminal conditions, enhancement of epithelial barrier function, and modulation of mucosal immune responses. However, “probiotic” encompasses highly heterogeneous interventions. *Saccharomyces boulardii*, *Bacillus clausii*, *Lactobacillus* species, *Bifidobacterium* species, and multispecies preparations cannot reasonably be assumed to have identical biological or clinical effects. Future studies should therefore identify organisms at the strain level and standardize doses and treatment duration.

Saccharomyces boulardii is particularly interesting because it is a yeast rather than a bacterial probiotic and may be administered alongside antibacterial agents. The García-Collinot trial raises the possibility that microbiome-directed therapies may complement rather than necessarily replace antibiotics. Nevertheless, its small size, open-label design, systemic-sclerosis-specific population, and attrition preclude broad conclusions.^[10]

Berberine and botanical therapies represent another promising direction. Their proposed activity extends beyond direct antimicrobial effects and may include modulation of microbial composition, intestinal barrier function, inflammation, and host-microbial signaling. The favorable position of berberine in recent network analyses is noteworthy, but network ranking should not be equated with repeated direct demonstrations of superiority. Similarly, the Chedid study provides a useful signal for herbal combinations, but its non-randomized design does not establish equivalence with rifaximin. Standardization is also essential because “herbal therapy” is not a single reproducible pharmacological intervention.^[11, 12]

The elemental diet provides a different conceptual model. By altering nutrient delivery and reducing substrate available for microbial fermentation, it may change the luminal environment sufficiently to influence breath-test abnormalities. The high normalization rates reported in the historical study are striking, but the lack of a randomized comparator and practical issues of tolerability limit its routine interpretation. Nevertheless, these findings emphasize substrate availability as a potentially important therapeutic target.^[13]

Conventional dietary interventions require particular nuance. Low-FODMAP diets may reduce fermentation, gas production, and bloating without necessarily eliminating microbial overgrowth. This distinction may explain why some patients improve clinically despite persistent breath-test abnormalities, whereas normalization of a breath test does not guarantee complete symptom resolution in the presence of IBS, dysmotility, visceral hypersensitivity, or another underlying disorder. Symptom control is clinically meaningful, but claims that a diet “treats SIBO” should distinguish symptom modification from objective eradication.

Kefir and kombucha occupy an especially interesting position because their popularity exceeds the amount of SIBO-specific evidence. Their microbial communities and fermentation-derived metabolites provide biological plausibility, but product composition can vary substantially. The current lack of controlled SIBO trials should not be interpreted as evidence of ineffectiveness. It is more appropriately regarded as an evidence gap and a potential field for future clinical investigation.

Another important issue is the historical tendency to combine hydrogen-positive SIBO and methane-positive breath tests. Methane is produced predominantly by methanogenic archaea, and intestinal methanogen overgrowth may differ biologically and therapeutically from bacterial overgrowth. Future trials should therefore report hydrogen- and methane-predominant phenotypes separately whenever possible.^[1, 3] Taken together, the available evidence suggests that the future of SIBO management may involve a broader therapeutic model than microbial eradication alone. Probiotics may modify microbial competition and host-microbial interactions; botanical compounds may combine antimicrobial and microbiome-modulating properties; elemental diets alter fermentable substrate availability; conventional diets modify fermentation; and interventions directed at gastrointestinal motility may address an important mechanism of recurrence. These mechanisms are not mutually exclusive. Future approaches may ultimately combine interventions directed at microbial burden, intestinal motility, luminal substrate availability, mucosal integrity, and the underlying predisposing disorder. This integrated pathophysiological framework, linking the major factors contributing to SIBO with the potential sites of action of non-antibiotic and adjunctive interventions, is illustrated in Figure 2.

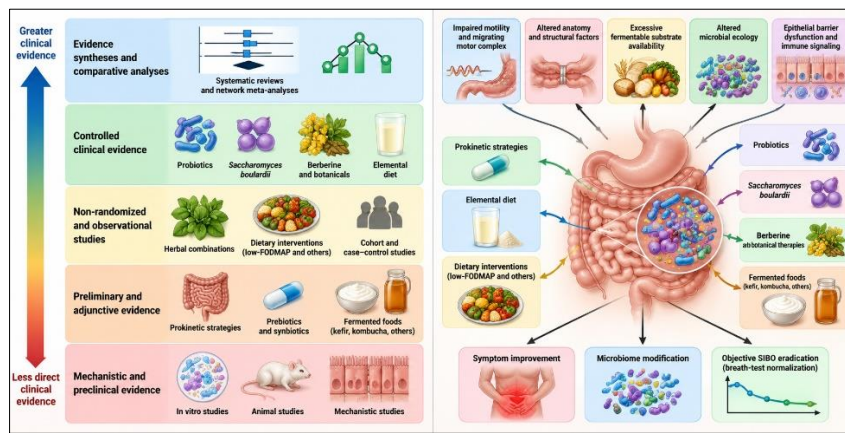


Fig 2

This framework also helps explain recurrence. If dysmotility, altered anatomy, medication exposure, or another predisposing condition persists after microbial suppression, recolonization is biologically plausible. Long-term management should therefore include identification and, whenever possible, correction of factors responsible for SIBO development.

The current literature does not support replacing all conventional SIBO treatment with a single “natural” therapy. Rather, it suggests a spectrum of interventions with different degrees of clinical investigation. Importantly, a lower position within the evidence hierarchy should not automatically be interpreted as lack of efficacy. In several instances—particularly kefir and kombucha—the appropriate conclusion is insufficient evidence rather than evidence of ineffectiveness.

Several limitations recur throughout the literature. Diagnostic definitions have changed over time, and studies use different substrates, sampling intervals, and thresholds for breath-test positivity. Populations include patients with IBS, systemic sclerosis, chronic liver disease, previous bariatric surgery, and other conditions. Therapeutic interventions are similarly heterogeneous, and several studies combine non-antibiotic approaches with antibiotics. Many studies are small and evaluate short-term outcomes, whereas recurrence is a central feature of SIBO. Future studies should assess not only breath-test normalization but also durability of response, recurrence, gastrointestinal symptoms, nutritional outcomes, quality of life, tolerability, and safety.

5. Conclusions

Non-antibiotic approaches to SIBO constitute a promising but heterogeneous therapeutic field. Probiotics currently have the largest body of direct clinical evidence, with *Saccharomyces boulardii* and selected multispecies preparations showing particularly interesting results. Berberine has emerged as a promising botanical therapy, while herbal combinations and elemental diets have also demonstrated clinically relevant signals. Dietary interventions may provide meaningful symptom relief, although evidence for eradication of SIBO remains limited. Kefir, kombucha, and other fermented foods represent an important evidence gap. Their biological plausibility and widespread use justify clinical investigation, but current evidence is insufficient to establish therapeutic efficacy

specifically for SIBO. Lack of evidence should not be interpreted as evidence of lack of effect.

Overall, available findings suggest that non-antibiotic therapy should be understood within a broader pathophysiological framework. Rather than focusing exclusively on eradication of microorganisms, future management strategies may increasingly target the intestinal ecosystem, including microbial composition, fermentable substrate availability, motility, epithelial barrier function, and the underlying factors that predispose to recurrent overgrowth.

Declarations

Ethics Approval and Consent to Participate

Not applicable. This article is a narrative review of previously published literature and did not involve new research with human participants or animals.

Consent for Publication

Not applicable.

Availability of Data and Materials

No new datasets were generated or analyzed for this narrative review. All information discussed in the article derives from previously published sources.

Competing Interests

The author declares that they have no competing interests.

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Table 1: Hierarchy of evidence for non-antibiotic and adjunctive therapies in small intestinal bacterial overgrowth.

Evidence hierarchy	Intervention	Highest evidence / key study	Main quantitative findings	Current interpretation / major limitations
Level I – evidence synthesis	Probiotics – overall	Zhong <i>et al.</i> ; Niño <i>et al.</i> (18 trials; 14 controlled; 9 randomized; 496 probiotic-treated and 480 controls)	Zhong: pooled decontamination 62.8% (95% CI 51.5–72.8); RR 1.61 (95% CI 1.19–2.17); H ₂ WMD –36.35 ppm (95% CI –44.23 to –28.47).	Largest direct non-antibiotic evidence base, but marked heterogeneity in strains, doses, populations, diagnostic criteria, and outcomes.
Level I – evidence synthesis	Berberine	Bayesian network meta-analysis: 30 RCTs; 1,552 participants; 12 interventions [11]	Favorable probabilistic ranking for SIBO eradication; emerging direct comparative evidence.	Promising; network ranking should not be interpreted as definitive direct superiority.
Level II – controlled clinical evidence	Saccharomyces boulardii	García-Collinot <i>et al.</i> [10]; randomized open-label pilot; systemic sclerosis; n=40	Eradication: 55% metronidazole+SB; 33% SB; 25% metronidazole. H ₂ reductions and symptom improvement also reported.	Interesting monotherapy and adjunctive signal; small disease-specific trial with substantial attrition.
Level II – controlled clinical evidence	Multispecies probiotics	Kwak <i>et al.</i> [9]; chronic liver disease + SIBO	SIBO resolution 24% with probiotics vs 0% placebo (P<0.05).	Supports formulation-specific benefit; small disease-specific population.
Level II – controlled clinical evidence	Bacillus clausii	Scarpellini <i>et al.</i> [7]; 30 vs 30	17/30 (56.6%) vs 12/30 (40%) with metronidazole.	Possible benefit; small older study and reporting limitations.
Level II/III – heterogeneous controlled evidence	Other probiotic combinations	Soifer <i>et al.</i> [8], Stotzer <i>et al.</i> [17], and other probiotic studies summarized in Niño <i>et al.</i> [6]	Soifer: clinical improvement 20/25 (82%) vs 13/25 (52%) with metronidazole; other studies were neutral.	Inconsistent; effects should not be generalized across probiotic formulations.
Level III – comparative non-randomized evidence	Herbal/botanical combinations	Chedid <i>et al.</i> [12]	Negative LBT 17/37 (46%) herbal vs 23/67 (34%) rifaximin; P=0.24; adjusted OR 1.85 (95% CI 0.77–4.41).	Potential benefit; non-randomized treatment selection. Lack of difference does not establish equivalence.
Level IV – uncontrolled clinical evidence	Elemental diet	Pimentel <i>et al.</i> [13]; 93 evaluable participants	Breath-test normalization ≈80% after 14 days and ≈85% after 21 days.	Large preliminary signal, but uncontrolled design and practical tolerability limitations.
Level III – adjunctive comparative evidence	Probiotic after rifaximin	Rosania <i>et al.</i> [14]; n=40	Symptom response 83.3% with rifaximin→L. casei vs 66.6% with rifaximin→short-chain FOS; P=0.57.	Adjunctive/sequential evidence; does not establish probiotic monotherapy efficacy.
Level III/IV – adjunctive evidence	Herbal + probiotic/prebiotic supplementation	Redondo-Cuevas <i>et al.</i> [16]; randomized adjunctive study; n=179	No significant overall reduction in breath-test gas concentrations; some symptom/remission signals reported in subgroups.	Multiple simultaneous interventions; difficult to attribute effects to an individual component.
Level V – indirect/insufficient direct evidence	Low-FODMAP / dietary substrate restriction	Narrative/systematic literature; direct eradication evidence remains limited [1, 4]	No convincing controlled evidence establishing SIBO eradication.	May improve fermentation-related symptoms; should not be equated with eradication.
Level V – indirect/insufficient direct evidence	Kefir	No adequate SIBO-specific controlled therapeutic trial identified in the reviewed clinical literature [4, 6]	No reliable SIBO-specific effect estimate.	Evidence gap, not evidence of ineffectiveness; biologically plausible microbiome-modulating fermented food.
Level V – indirect/insufficient direct evidence	Kombucha	No adequate SIBO-specific controlled therapeutic trial identified in the reviewed clinical literature [4, 6]	No reliable SIBO-specific effect estimate.	Evidence gap, not evidence of ineffectiveness; composition and biological effects may vary.
Level V – indirect/insufficient direct evidence	Other fermented foods / nutraceuticals	Mechanistic or limited clinical literature; no established SIBO-specific efficacy [4]	Insufficient direct controlled SIBO data.	Exploratory; product-specific effects require direct clinical evaluation.

Note: The evidence hierarchy is descriptive and reflects the design of the available literature; it is not a formal certainty-of-evidence grading system. A low position in the hierarchy, particularly for kefir and kombucha, indicates insufficient direct SIBO-specific investigation and should not be interpreted as evidence of ineffectiveness.

Table 2: Key clinical studies evaluating non-antibiotic and adjunctive interventions for small intestinal bacterial overgrowth.

Study	Population / design	Intervention	Comparator	Duration	Main objective outcome	Main clinical findings	Main limitations
Pimentel <i>et al.</i> , 2004	93 evaluable patients with IBS and abnormal LBT; uncontrolled study	Exclusive elemental diet (Vivonex Plus)	None	14 days; additional 7 days if LBT remained abnormal	LBT normalization	74/93 (80%) normalized LBT by day 15; five additional patients normalized by day 21, for an overall rate of 85%. Patients achieving normalization had greater symptom improvement than nonresponders	No randomized comparator; selected IBS population; historical LBT criteria; tolerability/adherence considerations
Scarpellini <i>et al.</i> , 2006	Patients with IBS and SIBO; comparative study	<i>Bacillus clausii</i>	Metronidazole	As reported in original study	Breath-test improvement	17/30 (56.6%) improved with <i>B. clausii</i> vs 12/30 (40%) with metronidazole	Published as supplement abstract; limited methodological information available
Gabrielli <i>et al.</i> , 2009	Patients with SIBO; clinical study/letter	<i>Bacillus clausii</i>	—	—	Breath-test response	Subsequent publication supporting evaluation of <i>B. clausii</i> for SIBO	Brief publication; limited reporting of methodological details
Soifer <i>et al.</i> , 2010	SIBO; randomized comparative study	Multispecies probiotic including <i>Lactobacillus casei</i> , <i>L. plantarum</i> , <i>Streptococcus faecalis</i> and <i>Bifidobacterium brevis</i>	Metronidazole	As reported in original study	Clinical response	Symptom improvement reported in 20/25 (82%) probiotic-treated patients vs 13/25 (52%) receiving metronidazole	Small sample; symptom-centered outcome; formulation-specific findings
Rosania <i>et al.</i> , 2013	40 patients receiving sequential treatment	Rifaximin followed by <i>Lactobacillus casei</i>	Rifaximin followed by short-chain FOS	Sequential therapy	Clinical response	Symptom improvement 83.3% vs 66.6%, respectively (P=0.57)	Adjunctive/sequential design prevents assessment of probiotic monotherapy
Kwak <i>et al.</i> , 2014	Chronic liver disease with SIBO; randomized placebo-controlled trial	Six-species probiotic preparation	Placebo	4 weeks	SIBO resolution by breath testing	SIBO resolution 24% vs 0% with placebo (P<0.05)	Disease-specific population; relatively small SIBO subgroup
Chedid <i>et al.</i> , 2014	Newly diagnosed SIBO by LBT; non-randomized comparative study	Commercial herbal combinations	Rifaximin 1,200 mg/day	4 weeks	Negative follow-up LBT	17/37 (46%) herbal vs 23/67 (34%) rifaximin, P=0.24; adjusted OR 1.85 (95% CI 0.77–4.41; P=0.17)	Patients selected therapy; non-randomized; study does not establish formal equivalence
García-Collinot <i>et al.</i> , 2020	40 patients with systemic sclerosis and SIBO; randomized open pilot trial	<i>S. boulardii</i> 200 mg BID; or metronidazole + <i>S. boulardii</i>	Metronidazole 500 mg BID	Cyclic treatment over 2 months	SIBO eradication by HBT	Eradication: 55% combination, 33% <i>S. boulardii</i> , 25% metronidazole; gastrointestinal symptom improvement in <i>S. boulardii</i> -containing groups	Small sample; open label; systemic-sclerosis-specific population; only 29/40 completed 2 months
Bustos Fernández <i>et al.</i> , 2023	IBS-D with bacterial overgrowth; randomized pilot study	<i>S. boulardii</i> CNCM I-745	Control	As reported in trial	Bacterial overgrowth and microbiota outcomes	Study provides additional contemporary direct evidence for <i>S. boulardii</i> in patients with IBS-D and bacterial overgrowth	Pilot study; population not necessarily representative of all SIBO phenotypes
Redondo-Cuevas <i>et al.</i> , 2024	179 participants with hydrogen- or methane-positive breath testing; randomized study	Botanical supplements combined with probiotic/prebiotic strategies	Study-specific comparator groups	According to protocol	Breath-gas concentrations and clinical response	No clear overall superiority for reducing gas concentrations; clinical response signals were reported in selected analyses	Multicomponent interventions; heterogeneous hydrogen/methane phenotypes; difficult to isolate effects of individual components

Abbreviations: BID, twice daily; FOS, fructooligosaccharides; HBT, hydrogen breath test; IBS, irritable bowel syndrome; IBS-D, diarrhea-predominant irritable bowel syndrome; LBT, lactulose breath test; OR, odds ratio; SIBO, small intestinal bacterial overgrowth.

Table 3: Proposed mechanisms, potential clinical benefits, safety considerations, and limitations of non-antibiotic interventions for SIBO.

Intervention	Proposed mechanisms relevant to SIBO	Potential clinical benefit	Main safety / tolerability considerations	Principal clinical limitation
Probiotics	Competitive exclusion; production of antimicrobial metabolites; modification of luminal environment; modulation of microbial composition; potential enhancement of epithelial barrier and mucosal immune responses	May reduce microbial overgrowth and fermentation and improve bloating, abdominal pain, diarrhea, and other gastrointestinal symptoms	Generally well tolerated; effects and safety depend on organism, host, and clinical setting	Major strain, dose, formulation, population, and outcome heterogeneity; “probiotics” should not be considered a single intervention
<i>Saccharomyces boulardii</i>	Yeast-based microbial competition; antimicrobial and antitoxin activity; modulation of mucosal immunity; potential trophic effects on intestinal epithelium	Direct SIBO evidence as monotherapy and potential adjunct to antibacterial treatment	Usually well tolerated in studied populations; patient-specific clinical context remains important	Evidence derives from relatively small studies and selected populations
<i>Bacillus clausii</i>	Spore-forming probiotic; potential competitive and microbiota-modulating effects	Breath-test improvement reported in SIBO studies	Generally reported as well tolerated	Evidence base is small; important early study was published as a supplement abstract
Multispecies probiotics	Multiple potentially complementary microbial effects; competitive exclusion; metabolite production; microbiome modulation	Some controlled trials demonstrate improved breath testing and/or symptoms	Product-specific tolerability	Results from one mixture cannot be extrapolated to another
Berberine	Potential direct antimicrobial activity; modulation of intestinal microbiota; possible effects on epithelial barrier, inflammation, bile-acid signaling, and gastrointestinal physiology	Promising eradication signal in network-level evidence	Gastrointestinal tolerability and potential interactions require consideration	Strong network-level signal but comparatively limited confirmatory direct SIBO evidence
Herbal/botanical combinations	Multiple botanical compounds with potential antimicrobial, antifungal, anti-inflammatory, and microbiome-modulating activities	Breath-test normalization observed in comparative clinical studies	Safety depends on specific constituents, dose, formulation, and concomitant therapies	Formulations are heterogeneous and difficult to generalize; strongest comparative study was non-randomized
Elemental diet	Rapid proximal absorption of nutrients; marked reduction of fermentable substrate reaching distal small bowel; alteration of luminal conditions supporting microbial proliferation	High breath-test normalization signal and associated symptom improvement	Palatability, adherence, nutritional supervision, and practicality are major considerations	Strong uncontrolled signal but lack of randomized comparative evidence
Low-FODMAP / fermentable-substrate restriction	Reduced delivery of rapidly fermentable carbohydrates; reduced fermentation, gas generation, and luminal distension	Potential improvement in bloating, pain, flatulence, and related symptoms	Excessive or prolonged restriction may impair dietary variety and nutritional adequacy	Symptom improvement should not be interpreted as demonstrated SIBO eradication
Prebiotics	Selective provision of substrates intended to influence microbial composition and metabolic activity	Potential microbiome modulation, particularly following antimicrobial treatment	Some fermentable prebiotics may increase gas or bloating in susceptible patients	Very limited evidence as stand-alone SIBO treatment
Synbiotics	Combination of probiotic organisms and substrates intended to support their activity	Theoretical complementary microbiome-directed effect	Formulation dependent	Few SIBO-specific controlled studies; difficult to separate probiotic and prebiotic effects
Kefir	Complex bacteria/yeast community; fermentation-derived metabolites; possible microbial competition, barrier, and immune effects	Plausible microbiome-modulating and gastrointestinal effects	Composition varies by preparation; individual tolerance may differ	No adequate controlled SIBO-specific therapeutic evidence identified; evidence gap rather than evidence of ineffectiveness
Kombucha	Fermentation-derived microorganisms, organic acids, and metabolites with potential microbiome effects	Biological plausibility for microbiome modulation	Highly product- and preparation-dependent	No adequate controlled SIBO-specific therapeutic evidence identified; clinical efficacy remains undetermined
Other fermented foods	Delivery of live microorganisms and fermentation products; potential modification of microbial ecology	Possible dietary microbiome support	Considerable variation among foods and preparations	Cannot extrapolate efficacy from defined probiotic strains to fermented foods as a class
Prokinetic strategies*	Enhancement of intestinal transit and migrating motor complex activity; reduction of intestinal stasis	May theoretically reduce conditions favoring recurrence rather than directly eradicate microorganisms	Agent-specific	Primarily relevant to recurrence prevention and correction of underlying dysmotility; outside the principal “natural therapy” focus of this review

Abbreviations: FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; IMO, intestinal methanogen overgrowth; MMC, migrating motor complex; SIBO, small intestinal bacterial overgrowth.

Prokinetic strategies are included for pathophysiological treatment category. context rather than as a principal non-antibiotic “natural”

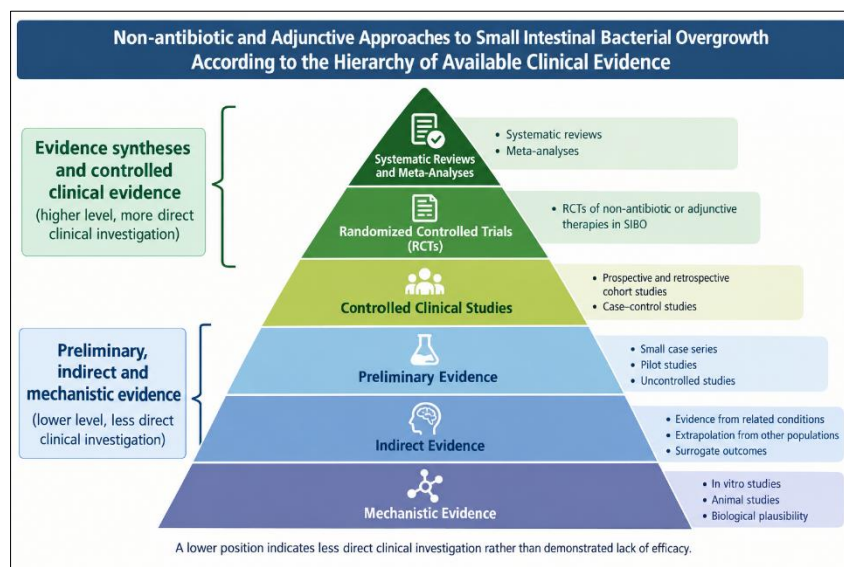


Fig 1: Non-antibiotic and adjunctive approaches to small intestinal bacterial overgrowth according to the hierarchy of available clinical evidence. The figure should distinguish evidence syntheses and controlled clinical evidence from preliminary, indirect, and mechanistic evidence. A lower position indicates less direct clinical investigation rather than demonstrated lack of efficacy.

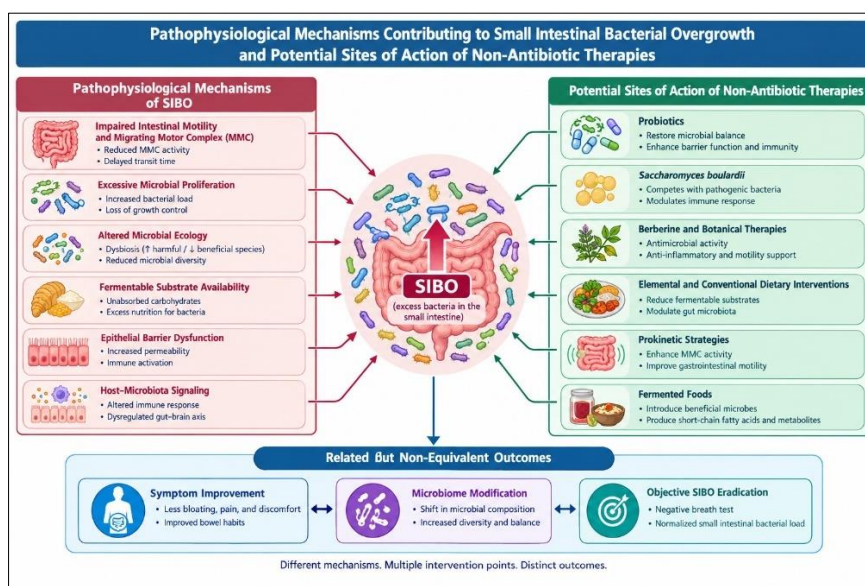


Fig 2: Pathophysiological mechanisms contributing to small intestinal bacterial overgrowth and potential sites of action of non-antibiotic therapies. The proposed framework integrates impaired intestinal motility and migrating motor complex activity, excessive microbial proliferation, altered microbial ecology, fermentable substrate availability, epithelial barrier dysfunction, and host–microbiota signaling with probiotics, *Saccharomyces boulardii*, berberine and botanical therapies, elemental and conventional dietary interventions, prokinetic strategies, and fermented foods. Symptom improvement, microbiome modification, and objective SIBO eradication should be depicted as related but non-equivalent outcomes.

References

- Pimentel M, Saad RJ, Long MD, Rao SSC. ACG clinical guideline: small intestinal bacterial overgrowth. *Am J Gastroenterol*. 2020;115(2):165-178. doi:10.14309/ajg.0000000000000501.
- Bures J, Cyrany J, Kohoutova D, Förstl M, Rejchrt S, Kvetina J, *et al*. Small intestinal bacterial overgrowth syndrome. *World J Gastroenterol*. 2010;16(24):2978-2990. doi:10.3748/wjg.v16.i24.2978.
- Rezaie A, Buresi M, Lembo A, Lin H, McCallum R, Rao S, *et al*. Hydrogen and methane-based breath testing in gastrointestinal disorders: the North American Consensus. *Am J Gastroenterol*. 2017;112(5):775-784. doi:10.1038/ajg.2017.46.
- Nickles MA, Hasan A, Shakhbazova A, Wright S, Chambers CJ, Sivamani RK. Alternative treatment approaches to small intestinal bacterial overgrowth: a systematic review. *J Altern Complement Med*. 2021;27(2):108-119. doi:10.1089/acm.2020.0275.
- Zhong C, Qu C, Wang B, Liang S, Zeng B. Probiotics for preventing and treating small intestinal bacterial overgrowth: a meta-analysis and systematic review of current evidence. *J Clin Gastroenterol*. 2017;51(4):300-311. doi:10.1097/MCG.0000000000000814.
- Fernando Niño S, Santiesteban M, Muñoz Valencia G. Eficacia de probióticos en el manejo de sobrecrecimiento bacteriano del intestino delgado. Revisión sistemática y metaanálisis [Efficacy of probiotics in the treatment of small intestinal bacterial overgrowth: systematic review and meta-analysis]. *Rev Gastroenterol Peru*.

- 2024;44(3):245-251.
7. Scarpellini E, Lauritano EC, Lupascu A, Novi M, Gabrielli M, Nucera G, *et al.* Bacillus clausii treatment of small intestinal bacterial overgrowth in patients with irritable bowel syndrome. *Dig Liver Dis.* 2006;38 Suppl 1. doi:10.1016/S1590-8658(06)80082-4.
 8. Soifer LO, Peralta D, Dima G, Besasso H. Eficacia comparativa de un probiótico vs un antibiótico en la respuesta clínica de pacientes con sobrecrecimiento bacteriano del intestino y distensión abdominal crónica funcional: un estudio piloto [Comparative clinical efficacy of a probiotic vs. an antibiotic in the treatment of patients with intestinal bacterial overgrowth and chronic abdominal functional distension: a pilot study]. *Acta Gastroenterol Latinoam.* 2010;40(4):323-327.
 9. Kwak DS, Jun DW, Seo JG, Chung WS, Park SE, Lee KN, *et al.* Short-term probiotic therapy alleviates small intestinal bacterial overgrowth, but does not improve intestinal permeability in chronic liver disease. *Eur J Gastroenterol Hepatol.* 2014;26(12):1353-1359. doi:10.1097/MEG.0000000000000214.
 10. García-Collinot G, Madrigal-Santillán EO, Martínez-Bencomo MA, Carranza-Muleiro RA, Jara LJ, Vera-Lastra O, *et al.* Effectiveness of *Saccharomyces boulardii* and metronidazole for small intestinal bacterial overgrowth in systemic sclerosis. *Dig Dis Sci.* 2020;65(4):1134-1143. doi:10.1007/s10620-019-05830-0.
 11. Zhang Q, Li H, Chen C, Li M, Song J, Pan S, *et al.* Comparative efficacy of diverse therapeutic regimens for small intestinal bacterial overgrowth: a systematic network meta-analysis. *Ther Adv Gastroenterol.* 2025;18:17562848251399033. doi:10.1177/17562848251399033.
 12. Chedid V, Dhalla S, Clarke JO, Roland BC, Dunbar KB, Koh J, *et al.* Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth. *Glob Adv Health Med.* 2014;3(3):16-24. doi:10.7453/gahmj.2014.019.
 13. Pimentel M, Constantino T, Kong Y, Bajwa M, Rezaei A, Park S. A 14-day elemental diet is highly effective in normalizing the lactulose breath test. *Dig Dis Sci.* 2004;49(1):73-77. doi:10.1023/B.0000011605.43979.E1.
 14. Rosania R, Giorgio F, Principi M, Amoroso A, Monno R, Di Leo A, *et al.* Effect of probiotic or prebiotic supplementation on antibiotic therapy in the small intestinal bacterial overgrowth: a comparative evaluation. *Curr Clin Pharmacol.* 2013;8(2):169-172. doi:10.2174/15748847113089990048.
 15. Bustos Fernández LM, Man F, Lasa JS. Impact of *Saccharomyces boulardii* CNCM I-745 on bacterial overgrowth and composition of intestinal microbiota in diarrhea-predominant irritable bowel syndrome patients: results of a randomized pilot study. *Dig Dis.* 2023;41(5):798-809. doi:10.1159/000528954.
 16. Redondo-Cuevas L, Belloch L, Martín-Carbonell V, Nicolás A, Alexandra I, Sanchis L, *et al.* Do herbal supplements and probiotics complement antibiotics and diet in the management of SIBO? A randomized clinical trial. *Nutrients.* 2024;16(7):1083. doi:10.3390/nu16071083.
 17. Stotzer PO, Blomberg L, Conway PL, Henriksson A, Abrahamsson H. Probiotic treatment of small intestinal bacterial overgrowth by *Lactobacillus fermentum* KLD. *Scand J Infect Dis.* 1996;28(6):615-619. doi:10.3109/00365549609037970.
 18. Wagner NRF, Ramos MRZ, de Oliveira Carlos L, da Cruz MRR, Taconeli CA, Filho AJB, *et al.* Effects of probiotics supplementation on gastrointestinal symptoms and SIBO after Roux-en-Y gastric bypass: a prospective, randomized, double-blind, placebo-controlled trial. *Obes Surg.* 2021;31(1):143-150. doi:10.1007/s11695-020-04900-x.

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