The Role of Yeast Probiotics in Gastrointestinal Conditions: An Overview

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Abstract

The human gut is home to a variety of microbes, including bacteria, viruses, fungi, eukaryotes, and archaea, which together form a complex structure. In general, the microbiota that colonizes the gastrointestinal (GI) tract plays a significant role in maintaining human health and has been implicated in the pathogenesis of a number of GI illnesses. The structural integrity and metabolic processes of the alimentary canal are physiologically influenced by the dynamic interactions between the gut and bacteria. GI dysbiosis is a result of an imbalance brought on by a decline in microbial diversity, the loss of helpful bacteria, and an increase in pathobions. It is crucial to restoring the gut microbiota. In order to regain the eubiotic state of the microbial flora, varied methods are being researched and implemented. The use of probiotics is one strategy for re-establishing healthy gut flora. Probiotics are "living microorganisms" that improve the health of the host when provided in adequate quantities. There are two types of probiotics—bacteria and yeast-based. The review will look at and summarize the information for yeast-based Saccharomyces probiotics regarding their effectiveness and safety in treating a variety of patient diseases, particularly irritable bowel syndrome (IBS), antibiotic-associated diarrhea, and Helicobacter pylori (HpSA) infection. The only commercially accessible yeast probiotic, the Saccharomyces strain, which consists of Saccharomyces cerevisiae (S. cerevisiae) and Saccharomyces boulardii (Sb), provides a number of benefits over bacterial probiotics. The significance of Sb as a potent biotherapeutic medication that may be utilized to prevent or treat a variety of GI disorders has been substantiated by several experimental studies and clinical trials.

Introduction

Many microbes, such as bacteria, fungi, viruses, archaea, and eukaryotes, contribute to the complicated structure of the human gut. The microbiota not only plays a major factor in the pathophysiology of various GI complications but also plays a critical role in healthy living. The internal structure and biochemical activities of the alimentary canal are physiologically influenced by the dynamic interplay between the microbial flora and gut. The gut microbiota is a dynamic ecological system shaped temporarily by physiological life events, namely the mode of delivery, dietary patterns, aging, and interactions with the surrounding environment. The balance could be shifted by exposure to various environmental factors, including dietary changes, toxins, drugs, antibiotics, stress, and pathogens. The imbalance caused by a reduction in microbial diversity and loss of beneficial bacteria with an increase in pathobions leads to GI dysbiosis. Dysbiosis can be both an effect or a contributor to the pathogenesis of several GI and extra-GI diseases. As a result, it is crucial to try to restore the gut microflora with therapeutic potential in conditions where intestinal microflora dysbiosis appears to be a cause.

Mechanism of Action of Yeast Probiotics

Many planned remedies are being researched and put out with the aim of regaining and/or maintaining the eubiotic condition of the microflora gut ecosystem. Probiotic usage is one method for re-establishing healthy gut flora. Live microorganisms that, when given in sufficient quantities, benefit the host's health are referred to as probiotics. Several probiotics are available for clinical use, out of which yeast-based probiotics appear to confer a specific additional advantage over bacteria-based probiotics. The review will examine and outline the available evidence for Saccharomyces probiotics concerning their efficacy and safety in treating different conditions in patients, specifically irritable bowel syndrome, antibiotic-associated diarrhea, and in HpSA Infection.

Methods/Search Strategy

We looked for English-language articles published between the years 2000 and 2021 using PubMed, Google Scholar, and Medline. However, certain relevant cross-references preceding the year 2000 were included to synthesize our review. Reviews, other studies that were cross-indexed by authors, secondary and manual searches of reference lists, and more were also carried out. IBS, diarrhea, probiotics, risk factors, randomized controlled trials, placebo-controlled, and bloating were among the search phrases used. Abstracts of all citations and full-text articles were retrieved and reviewed.

Yeast Probiotics

Although having genetic relatedness to S. cerevisiae, Sb is the most prevalent yeast with probiotic properties. The resilience of the two strains to temperature, acidity stimuli, and growth traits vary. In addition to the treatment of acute GI conditions like diarrhea or chronic conditions like inflammatory bowel disease and inflammatory bowel syndrome, S. cerevisiae is beneficial. The yeast cells of Sb, if compared to bacterial probiotics, have a few advantages, like antibiotic resilience due to its fungal nature, resistance to stomach and bile acids, survival at human body temperature, and inhibition of pathogenic growth. As seen in Table 1, Sb is more robust to temperature and acidic stimuli but less tolerant to bile salts. Sb differs from bacterial probiotics by its ability to improve the microbiota composition in the gut and promote humoral and innate immunity in healthy subjects. Based on these properties, chronic diseases like ulcerative colitis, IBS, Crohn's disease, human immunodeficiency virus related diarrhea, and parasitic infections, Sb, have been found to be beneficial.

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and thereby reducing the ability of the bacteria to translocate.11 Homeostasis is maintained by the gut microbiome, but the exact method by which it does so is not properly known.6 However, a number of effective mechanisms have been uncovered which directly influence both the host and the response of pathogenic microorganisms by modulating the local and systemic immune responses, regulating intestinal microbial homeostasis, interfering with pathogen colonization, inducing the enzymatic activity that favors absorption and nutrition and stabilizes the GI barrier.8,10,12,13 The following are the key mechanisms by which yeast probiotics (Sb) function:

- **Competitive exclusion:** Gut microbiota binds to the yeast surface irreversibly, preventing their adhesion to the mucous membranes. Proteolytic and steric hindrance activity of yeast can inhibit adherence of bacteria to mucous.14 Yeast cell size is 10 times bigger than bacteria, so one yeast can displace 10 bacteria using steric hindrance.

- **Anti-toxin effect:** Yeast probiotic inhibits the toxin receptor binding site, thereby preventing the toxins from binding to the mucosa. It either stimulates the production of antibodies against the toxins or releases enzymes and proteins, which lead to the proteolysis of toxins.10

- **Immune modulation:** Yeast probiotics stimulate the secretion of secretory immunoglobulin (Ig) A levels in the intestine, which thereby reduces the quantum of the pathogen. It interrupts the NF-κB-mediated signal transduction pathway, which then prevents the synthesis of proinflammatory cytokines.15 Furthermore, the interaction with epithelial cells, monocytes, dendritic cells, lymphocytes, and/or macrophages produces metabolites that stimulate the immune cell via its anti-inflammatory and immunomodulatory response.5,16 For instance, in the case of Clostridium difficile (C. difficile) infection, Sb inhibits MAP kinase and IL-8 levels and modulates the inflammatory process. Additionally, Sb elevated serum IgA and IgG levels in the presence of C. difficile toxins A and B.8,9

- **Restoration of metabolic activities:** Yeast probiotics increase the normal short-chain fatty acids (SCFA) production, which exhibits its antimicrobial activity and re-establishes the normal colonic function.6,15 It also reduces the intracolonic gas produced by the bacteria and metabolizes the nutrient substrate by gas formation as well as improves the colonic propulsion by increasing the intracolonic SCFAs production.11

**Benefits of Yeast Probiotics over Bacterial Probiotics**

Of the several probiotics available, yeast probiotics account for a smaller proportion but are better tolerated when compared with bacterial probiotics. The only yeast probiotic that is commercially available is the Saccharomyces strain, that is, S. cerevisiae and Sb, which have shown varied benefits over bacterial probiotics. The benefits of yeast probiotics over bacterial probiotics are mentioned in Table 2; they are explained as follows:

- They are a suitable option for the treatment of antibiotic-associated diarrhea due to their innate resistance to antibacterial antibiotics. They also reduce the side effects associated with standard triple therapy due to antibiotic use in HPSA infections.12,18

  - Saccharomyces boulardii (Sb) is exceptional since it can thrive at temperatures as high as 37°C and can endure stomach pH values.19

  - A new study on yeast probiotics derived from idli batter, an Indian fermented meal, found additional benefits like tolerance to acid and bile salts, cell surface hydrophobicity, as well as auto-aggregation ability. It was concluded that Sb could exhibit antimicrobial activity against the gut pathogens.17

  - Saccharomyces boulardii (Sb) also has the ability to assimilate cholesterol, as well as the capability to produce products such as phytase, vitamin B12, β-galactosidase, and exopolysaccharides. Hence, its use alone or in combination with the dairy starter increases the nutritional values as well as the shelf life of fermented dairy products.17

  - Saccharomyces boulardii (Sb) is the only probiotic that is effective against C. difficile diarrhea, and due to its stability at the normal temperature, it is an ideal supplement for constipation and diarrhea while traveling.15

- Patients treated with antibiotics usually develop antimicrobial resistance due to its inherent bacterial resistance property and transfer of genes to the bacteria. Resistant genes can be transferred to bacterial probiotics, which may have a negative impact. As no such genetic transfer has been observed between bacteria and yeast, yeast probiotic is considered a better alternative to bacterial probiotics.3,8

- Yeast having a larger cell size makes it suitable for interstitial protection due to better coverage.20 As yeast is resistant to an acidic environment it reaches the colon in its active state when compared with bacterial probiotics.21 It also promotes the production of IgA, which protects humans/animals from infections.20

**Role of Yeast Probiotics in the Following Conditions**

Irritable Bowel Syndrome (IBS)—IBS is a common functional GI illness that is characterized by persistent and recurring
abdominal pain or discomfort as well as changed bowel patterns. An estimated 7–22% of the world’s population suffers from this prevalent, chronic, recurring, and remitting GI condition, with a prevalence of 14% in women and 9% in males. There are a number of qualitative and quantitative alterations in the fecal microbiota in IBS, and there is more evidence that substantiates gut dysbiosis as a trigger for IBS. In spite of the range of therapeutic modalities (antidiarrheal, antispasmodics, chloride channel opener, guanylyl cyclase C agonist, and newer gut serotonin modulators), patients continue to suffer from recurrence of symptoms, high relapse rate, and low tolerance threshold to side effects. In view of the association of IBS with dysbiosis, the use of probiotics has also been incorporated into the therapeutic armamentarium for IBS. A major accomplishment is the development of a therapeutic option that, albeit slightly, relieves the disease’s symptoms. The intestinal barrier function, gut-brain axis, immunological activation, and GI motility and sensation are only a few of the pathways that the gut microbiota influences the pathophysiological mechanisms. IBS symptoms, including bloating and abdominal pain, can be alleviated through yeast probiotics like Sb. Additionally, as shown in Table 3, Sb causes a variety of distinct effects, both in a dysbiotic condition and in the avoidance of dysbiosis.

**Efficacy of Yeast Probiotics in IBS**

The effectiveness of yeast probiotics in reducing IBS symptoms is summarized in Table 4. The pooled relative risk for improvement in overall IBS symptoms in 14 probiotic treatment arms was 0.77 [95% confidence interval (CI)—0.62–0.94], according to a meta-analysis of 20 randomized clinical trials with 1,404 participants and 23 probiotic treatment arms. Moreover, probiotics were linked to decreased abdominal discomfort when compared to a placebo (Relative Risk (RR) = 0.78; 95% CI—0.69–0.88). The average pain grade and stomach discomfort were observed to be reduced by 38% with the use of *S. cerevisiae* CNCM I-3856. In order to treat IBS, yeast probiotics can alter the intraluminal milieu and reduce inflammation. The effectiveness of the probiotic *S. cerevisiae* in the treatment of IBS was examined in a study by Helo et al. In this trial, *S. cerevisiae* was administered to 177 individuals in doses of 1000 mg each after meals. After 4 weeks of therapy, it was noted that IBS symptoms such as bloating, discomfort, and irregular stools had improved. According to research by Mearin et al., about 15% of people who fulfill the Rome I criteria for IBS have the diarrhea-predominant variant (IBS-D). Sb affects the way microorganisms migrate through the digestive tract. Sb was utilized to treat IBS-D patients in a different double-blind trial by Mupas et al., and the quantity of stools produced decreased (p < 0.05), while the consistency of the stools enhanced (p < 0.05). In a related trial, mesalazine alone, Sb alone, and mesalazine plus Sb together were used to treat patients. According to reports, adding Sb to mesalazine can improve therapeutic outcomes for IBS, and the probiotic agent has positive benefits on both IBS-related intestinal symptoms and overall quality of life (QoL). Sb has systemic benefits on IBS-D patients that improve their overall health by the suppression of proinflammatory cytokines, which in turn alters the nervous system activity or enhances tryptophan levels.

**Table 3: Mechanism of action of Sb in IBS**

<table>
<thead>
<tr>
<th>Probiotics—creating a beneficial microbiome</th>
<th>Infection and immune activation in IBS</th>
<th>Antimicrobial activity</th>
<th>Trophic action on the intestinal mucosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the case of IBS</td>
<td>In IBS patients, exposure to intestinal infection results in long-lasting, low-grade systemic and mucosal inflammation, which is defined by altered circulating cell populations, immune cell infiltration of the mucosa, and increased cytokine secretion.</td>
<td>Immune activation, gut-brain axis, GI motility and sensation, and intestinal barrier function are pathophysiological processes underlying IBS that are modulated by gut microbiota.</td>
<td>Harms digestive epithelial cells, which are involved in the anti-inflammatory, immune-modulating, and barrier functions of the gut</td>
</tr>
<tr>
<td>Preventive action</td>
<td>Probiotics’ interactions with epithelial cells, monocytes, dendritic cells, lymphocytes, and/or macrophages result in the production of metabolites that activate the immune cell’s reaction, which is anti-inflammatory and immunomodulatory.</td>
<td>Reduction of bacterial and parasitic development. Reduced pathogen translocation in the intestines. The bacterium virulence factors are neutralized. The suppression of host cell adhesion prevents microbes from colonizing the host.</td>
<td>Decreases the number of infected cells while promoting intestinal cell growth and differentiation in reaction to trophic factors.</td>
</tr>
</tbody>
</table>

**Antibiotic-associated Diarrhea (AAD)**

Antibiotic-associated diarrhea (AAD) is associated with the widespread use of antibiotics; hence, its incidence has increased over the years and is reported to be 21.5%. Prevalence of AAD is reported to be in the range of 3.2 to 29% as underlying illness, drugs, surgery, and age alters bowel motility and increase the risk of AAD. Incidence of AAD is more common with clindamycin, cephalosporin, and amoxicillin-clavulanate. Few studies around the world but none from India reported the prevalence of AAD. The most frequent comorbidities of colitis and antibiotic-associated diarrhea (AAD) are colitis and *C. difficile* infection (CDI). From moderate diarrhea to colitis or fulminant pseudomembranous colitis, AAD symptoms might differ. It has been observed that those with other concomitant infections are more susceptible to *C. difficile* antibiotic-associated diarrhea. In a study, it was found that patients with diabetes and hypertension had an estimated 2- and 5-fold higher chance of developing AAD than did people without chronic conditions. For repeated recurrences, fecal replacement therapy and adjunctive treatment with probiotics are recommended. In both a community environment and an institutional environment, Sb, a nonpathogenic yeast, typically grows at body temperature and has been evaluated for its effectiveness in preventing antimicrobial-associated diarrhea. According to reports, Sb can reduce the duration of diarrhea without causing a recurrence through its mechanism of action mentioned in Table 5. Critically ill tube-fed patients can get Sb as a prophylactic therapy, especially those at risk of AAD.
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Table 4: Effectiveness of yeast probiotics in treating IBS

<table>
<thead>
<tr>
<th>Study type</th>
<th>Treatment group</th>
<th>Study population</th>
<th>Dose</th>
<th>Duration</th>
<th>Outcome</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis (double-blind)</td>
<td>two groups: probiotic S. cerevisiae + boulardii and placebo</td>
<td>Patients suffering from IBS-D</td>
<td>9 × 10⁹ cfu/day</td>
<td>4 weeks</td>
<td>Improved symptoms were seen. The number of stools dropped (p 0.05), and their regularity improved (p 0.05).</td>
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<tr>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>35 patients got the placebo, while 37 patients received Sb.</td>
<td>Patients with IBS-D</td>
<td>Sb 750 mg/day</td>
<td>6 weeks</td>
<td>Interleukin-8 (IL-8) and tumour necrosis factor levels in blood and tissues were significantly reduced in the Sb group (p 0.001), while anti-inflammatory IL-10 levels increased along with the tissue IL-10/IL-12 ratio.</td>
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<tr>
<td>Randomized, double-blind, placebo-controlled multicenter trial</td>
<td>Patients treated with either Sb (n = 34), or placebo (n = 33)</td>
<td>Patients with IBS-D and IBS-M</td>
<td>Sb at 2 × 10 live cells as a daily dose</td>
<td>4 weeks</td>
<td>IBS-related symptoms like bowel movement frequency and stool consistency also improved. Overall IBS-QOL improvement was greater in the Sb group than in the placebo group (15.4 vs 7.0%; p 0.05). Sb had a positive impact on QOL and symptoms in patients with diarrhea-predominant IBS or mixed-type IBS.</td>
<td>2</td>
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</tbody>
</table>

IBS, irritable bowel syndrome; IBS-D, irritable bowel syndrome with diarrhea; IBS-M, mixed irritable bowel syndrome; QOL, quality of life; tid, thrice daily; bid, twice daily; qd, once daily; cfu, colony-forming unit; MG, mesalazine group; MSbG, mesalazine and Saccharomyces boulardii group; SbG, Saccharomyces boulardii group.

Table 5: Mechanism of action of Sb in AAD

<table>
<thead>
<tr>
<th>Probiotic—creation of a favorable microbiotic environment</th>
<th>Modulation of gut microbiota composition</th>
<th>Increase modulation of bile acid</th>
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<tr>
<td>AAD mechanism</td>
<td>Antibiotic use alters the composition, function, and biodiversity of the gut’s normal microbiota, which makes it easier for pathogens like C. difficile to colonize.</td>
<td>The main form of bile acid, which is crucial for fat metabolism, is produced by the liver, and the intestinal microbiota converts it into the secondary active form. Antibiotics alter the microbiota, which results in incorrect secondary bile acid conversion.</td>
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<tr>
<td>Preventive action using probiotics</td>
<td>Combining antibiotics and probiotics (Sb) lessened the change in the composition of the bacteria.</td>
<td>Because Sb alters the gut microbiota, its effects are reversed, allowing the gut bacteria to return to normal and produce secondary bile acid.</td>
</tr>
</tbody>
</table>

Efficacy of Yeast Probiotics in AAD

*Saccharomyces boulardii* (Sb) can be prescribed to patients receiving antibiotics as it is naturally resistant to antibiotics. There is a positive trend in the treatment of AAD using Sb for children as well as adults, as results from trials have reported it to be effective in preventing diarrhea caused by various antibiotics such as amoxicillin/clavulanate and by cephalosporins. Surawicz et al. conducted a study to gauge Sb’s efficacy in 180 hospitalized patients consuming different classes of antibiotics. The probiotic was given both during and for two weeks after the antibiotic course. Those receiving Sb experienced significantly fewer episodes of diarrhea (10% compared to 22% in the placebo group; p = 0.038). Adding Sb to β-lactam medicines had a significant preventative effect on diarrhoea in hospitalized patients taking antibiotics, according to an additional study by the same author (7% of Sb vs 15% of placebo, p = 0.02). Very few patients on treatment with Sb developed AAD. 151 adult patients were enrolled by Can et al. who were taking various antibiotics, and they were randomly assigned to either the Sb or placebo group for the length of the antibiotic treatment. When compared to the control group, it was found that significantly fewer patients receiving Sb had AAD (9 vs 1.4%, respectively; p < 0.05). Decrease in the episodes of diarrhea was one of the most common symptom improvements observed across the studies. Furthermore, Kotowska et al. demonstrated the effect of Sb in children with respiratory tract infection and/or otitis media. It was reported that patients consuming Sb had a decreased prevalence of diarrhea compared to placebo [nine of 119 (8%) vs 29 of 127 (23%)]. The therapeutic probiotic Sb utilized in the treatment and prevention of AAD when given adjuvant to antibiotics has been proven to be beneficial. The efficacy of yeast probiotics in improving AAD symptoms is summarized in Table 6.

*Helicobacter pylori* (HpSA) Infection

Almost 4.4 billion people are infected with HpSA worldwide. This microaerophilic gram-negative bacterium colonizes the GI mucosa, and its presence influences the strength of gastric microbial interactions. HpSA is known to cause inflammation and change the microflora, which can lead to a variety of gastric illnesses. In developing nations, HpSA infections are frequently acquired by children and last a lifetime without antibiotic therapy. It is commonly seen that in developing countries, the
prevalence is high compared to developed nations. HpSA infection leads to gastric inflammation and is associated with disorders like a mucosa-associated lymphoid tumor (maltoma), peptic ulcer, gastric cancer, idiopathic thrombocytopenia, and iron deficiency. HpSA infection by itself and its antimicrobial therapy alters the gut microbial ecological balance. Therefore, gut microbial manipulation to restore a eubiotic state becomes imperative. This is where the role of probiotics comes into play. In individuals with HpSA infection, probiotic supplementation has been seen to increase eradication rates, decrease treatment-related side effects, and alleviate specific symptoms. Though Sb–mediated effects in HpSA infection are not completely understood, it has been speculated that it might work by limiting HpSA adherence to epithelial cells and modulating the gastric immune response, summarized in Table 7.

### Efficacy of Yeast Probiotics in HpSA infection

According to research by Dinleyici et al., Sb boosts the HpSA eradication rate, minimizes adverse effects, and improves compliance. However, Hurduc et al., employing the Sb strain, reported no effect on the rate of HpSA eradication but positive health effects in the cases of infection. Sb enhanced anti-HpSA antibiotherapy-associated diarrhoea (p < 0.05), epigastric discomfort (p < 0.01), and treatment acceptability, according to Cindoruk et al. Also, the Sb supplement reduced posttreatment dyspepsia symptoms regardless of the presence or absence of HpSA, but it had no discernible impact on the rate of HpSA eradication (p > 0.05). According to Cardenas et al., patients treated with Sb, in addition to triple therapy for HpSA infection, experienced considerably less abdominal discomfort and other GI side effects (p = 0.028). At the termination of antibiotic treatment and one month later, there was a larger abundance of Enterobacteria and a lower abundance of Bacteroides and Clostridia, as well as a greater diversity of bacteria observed (p = 0.0156). Lastly, a study by Duman et al. evaluated the efficacy of Sb vs triple therapy for the elimination of HpSA. According to the study, considerably fewer patients who received Sb (6.9%) than the control group (15.6%, p = 0.007) developed AAD. Sb is generally effective at eliminating HpSA from the human GI tract and minimizing

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### Table 6: Efficacy of yeast probiotics for the treatment of AAD

<table>
<thead>
<tr>
<th>Reference/author-name</th>
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<th>Treatment group</th>
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<td><strong>Adult</strong></td>
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<tr>
<td>Surawicz et al.</td>
<td>A prospective, double-blind controlled study</td>
<td>Sb and placebo with antibiotics</td>
<td>Hospitalized patients on antibiotics</td>
<td>250 mg capsule bid</td>
<td>Till 2 weeks after the last antibiotic dose</td>
<td>Of the 180 patients, diarrhoea occurred in 14 (21.8%) of 64 (placebo) patients vs 11 (9.5%) of 116 (Sb) patients (p = 0.038). Sb had a 56.7% success rate at avoiding AAD. Compared to 9/199 (4.5) of the patients who received Sb, 33/189 (17.5) of the patients getting a placebo experienced AAD (p = 0.05).</td>
<td>3</td>
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<tr>
<td>Adam et al.</td>
<td>Meta-analysis</td>
<td>Sb vs placebo</td>
<td>388 hospitalized adults</td>
<td>4 × 10⁹ (200 mg)</td>
<td>7 days</td>
<td>In the study group, the rate of onset of antibiotic-associated diarrhoea was 1.4% (1/73) compared to 9% (7/78) in the placebo group (p = 0.05).</td>
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<tr>
<td>Can et al.</td>
<td>Prospective study</td>
<td>Sb vs placebo</td>
<td>151 hospitalized adult patients</td>
<td>1 × 10¹⁰ (500 mg)</td>
<td>Till 48 hours after the last antibiotic dose</td>
<td>In the Sb group, antibiotic-associated diarrhoea occurred in 21% (7/33) and 13.9% (5/36) of cases, respectively (p = 0.05).</td>
<td>3</td>
</tr>
<tr>
<td>Cremonini et al.</td>
<td>A parallel, triple-blind, placebo-controlled study</td>
<td>Sb vs placebo</td>
<td>43 HpSA + adults on triple therapy</td>
<td>5 × 10⁹ (nr)</td>
<td>14 days</td>
<td>Throughout the entire study time, overall diarrhoea rates were 6.9% in the treatment group and 15.6% in the control group (p = 0.007).</td>
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<tr>
<td>Duman et al.</td>
<td>Multicenter, prospective clinical trial</td>
<td>Sb vs placebo</td>
<td>389 adults in Turkey with HpSA + peptic ulcers all received triple therapy</td>
<td>2 × 10¹⁰ (1000 mg)</td>
<td>14 days</td>
<td>Antibiotic-associated diarrhoea in the Sb group was in 3/41 (7.3) patients and 5/45 (11.1) patients in the control group</td>
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<tr>
<td>Bravo et al.</td>
<td>A prospective, randomized, double-controlled, blinded study</td>
<td>Sb vs placebo</td>
<td>89 adult outpatients on amoxicillin</td>
<td>1 × 10¹⁰ (500 mg)</td>
<td>12 days</td>
<td>Anti</td>
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The Role of Yeast Probiotics in Gastrointestinal Conditions: An Overview

The mortality rate of up to 20%, is a highly common and dangerous acquired disease of the GIT in very low-birth-weight (VLBW) infants. NEC may result from intestinal ischemia, protein substrate overgrowth in the intestinal lumen, or pathogenic bacterial colonization of the intestine. Probiotics may prevent NEC by ensuring colonization of the gut with essential microorganisms while preventing an excess of pathogens, improving the function of the gut mucosal barrier, and regulating the immune system. Feeding difficulties generally lead to prolonged scarcity of enteral feeds and dependence on total parenteral nutrition which are a severe concern in a preterm

Necrotizing enterocolitis (NEC), which is characterized by gut wall necrosis and has a mortality rate of up to 20%, is a highly common and dangerous acquired disease of the GIT in very low-birth-weight (VLBW) infants. NEC may result from intestinal ischemia, protein substrate overgrowth in the intestinal lumen, or pathogenic bacterial colonization of the intestine. Probiotics may prevent NEC by ensuring colonization of the gut with essential microorganisms while preventing an excess of pathogens, improving the function of the gut mucosal barrier, and regulating the immune system. Feeding difficulties generally lead to prolonged scarcity of enteral feeds and dependence on total parenteral nutrition which are a severe concern in a preterm

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</tr>
</thead>
<tbody>
<tr>
<td>Cindoruk et al.⁵⁴</td>
<td>A prospective randomized placebo-controlled double-blind study</td>
<td>Sb vs placebo</td>
<td>124 adults with HpSA + dyspepsia</td>
<td>$2 \times 10^{10}$ (1000 mg)</td>
<td>14 days</td>
<td>In the Sb group, antibiotic-associated diarrhea affected 9.5% of patients, compared to 19.6% of patients in the control group ($p = 0.05$). There were [nine (14.5%) vs 27 (43.5%)] epigastric discomfort cases in the control group ($p = 0.01$) After treatment, the treatment group’s GDQ scores were markedly higher (mean ± SD, range — 1.38 ± 1.25 (0–5) vs 2.22 ± 1.44 (0–6); $p = 0.01$)</td>
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<td>Pediatrics</td>
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<tr>
<td>Kotowska et al.⁵⁶</td>
<td>A randomized, double-blind, placebo-controlled trial</td>
<td>Sb in addition to standard antimicrobial therapy (experimental group; $n = 132$) or a placebo (control group; $n = 137$)</td>
<td>269 children (aged 6 months to 14 years) with otitis media and/or respiratory tract infections</td>
<td>Standard antibiotic treatment plus 250 mg of Sb or a placebo</td>
<td>Twice daily for the duration of antibiotic treatment</td>
<td>Additionally, Sb decreased the risk of antibiotic-associated diarrhea when compared to placebo (4 of 119 (3.4%) vs 22 of 127 (17.3%); RR: 0.2; 95% CI: 0.07–0.5). No adverse events were observed</td>
<td>2</td>
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<tr>
<td>Riaz et al.⁵²</td>
<td>Double-blind, randomized placebo-controlled clinical trial</td>
<td>For 5 days, Sb 250 mg twice daily was compared to a placebo.</td>
<td>108 children 3–59 months</td>
<td>250 mg bid</td>
<td>5 days or till recovery</td>
<td>When compared to the placebo group, the mean postintervention duration of diarrhoea was considerably (95% CI = 28.13–5.43) shorter in the Sb group (52.08 ± 57 h) ($p = 0.004$). The Sb group’s first semi-formed feces appeared after less time (39.4 ± 23.09 h; 95% CI: 25.4–3.87) than did for the control group (54.13 ± 28.21 h; $p = 0.009$).</td>
<td>2</td>
</tr>
</tbody>
</table>

bid, twice daily; Sb, *Saccharomyces boulardii*; AAD, antibiotic associated diarrhea; SD, standard deviation

### Role of Sb in Other Disorders

Acute gastroenteritis—also known as “acute infectious diarrhea,” this condition is marked by repeated watery stools as a consequence of compromised electrolyte and fluid absorption in the GI tract, which is typically brought on by pathogenic microorganisms, GI tract infections, nutritional deficiencies, allergies, intoxications, or impaired absorption.¹² The inclusion of *S. boulardii* to standard rehydration therapy in contrast with a placebo was linked with a decrease in the frequency of diarrhea by almost 24 hours. There was a significant decline in the duration of hospitalization, no. of days with vomiting, frequency of stools, and risk of diarrhea which was evident from the second day onwards. The frequently used dose of *S. boulardii* was at least 500 mg given daily which provided additional benefit than <300 mg dose.¹ According to recent studies, the increase in the immune response of *S. boulardii* may be attributed to changes in the serum levels of IgA, cluster of differentiation 8, and C-reactive protein.⁵²⁵⁸

Necrotizing enterocolitis (NEC), which is characterized by gut wall necrosis and has a
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**Table 7: Mechanism of action of Sb in HpSA infection**

<table>
<thead>
<tr>
<th>Reference/author-name</th>
<th>Study type</th>
<th>Treatment group</th>
<th>Study population</th>
<th>Dose</th>
<th>Duration</th>
<th>Outcome</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cindoruk et al.54</td>
<td>A prospective, randomized, placebo-controlled study</td>
<td>Clarithromycin, amoxicillin, and lansoprazole triple treatment with Sb or placebo</td>
<td>124 patients with HpSA infection</td>
<td>1 gm qd (250 mg sachets, 500 mg bid)</td>
<td>2 weeks</td>
<td>The therapy group’s rate of HpSA eradication was higher (71%; 44/62) than the control group’s (59.7%; 37/62) ($p &gt; 0.05$).</td>
<td>2</td>
</tr>
<tr>
<td>Cardenas et al.55</td>
<td>Single-blind randomized trial</td>
<td>Treatment as usual (amoxicillin, tindazole, and omeprazole) or treatment as usual + Sb CNCM I-745</td>
<td>18–55 years of patients with typical dyspepsia symptoms</td>
<td>Approximately 22.5 × $10^9$ cfu; $n=2$</td>
<td>2 weeks</td>
<td>When used in addition to the standard triple therapy for <em>Helicobacter pylori</em> infection, Sb CNCM I-745 reduced the incidence of GI side effects that might be caused by alterations in gut microbiota. There were also lower rates of associated GI symptoms ($p = 0.028$) and increased numbers of bacteria with even bacterial diversity ($p = 0.0156$).</td>
<td>2</td>
</tr>
<tr>
<td>Cremonini F et al.67</td>
<td>A parallel, triple-blind, placebo-controlled study</td>
<td>Sb (Codex, Smith-Kline Beecham, Italy) in comparison to a placebo, LGG, and a combination (L acid and Bifid lactis)</td>
<td>43 HpSA+ adults on triple therapy</td>
<td>$5 \times 10^9$ (nr)</td>
<td>14 days</td>
<td>Eliminated in 16/20 (80%) in the placebo group and in 17/21 (81%) for LGG and blend. For Sb, signs appeared in 4/21 (19%) while they did not in the control group (12/20, 60%). ($p &lt; 0.05$)</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 8: Efficacy of yeast probiotics for the treatment of HpSA infection**

<table>
<thead>
<tr>
<th>Study type</th>
<th>Treatment group</th>
<th>Study population</th>
<th>Dose</th>
<th>Duration</th>
<th>Outcome</th>
<th>Evidence level</th>
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</thead>
<tbody>
<tr>
<td>Adult</td>
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<td>2 weeks</td>
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<td>Eliminated in 16/20 (80%) in the placebo group and in 17/21 (81%) for LGG and blend. For Sb, signs appeared in 4/21 (19%) while they did not in the control group (12/20, 60%). ($p &lt; 0.05$)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Three groups were randomly assigned to receive either SbI or LB or antimicrobial therapy (lansoprazole, clarithromycin, and amoxicillin).</td>
<td>182 children (71.7%) who were colonized by Hp, and 141 of them completed their treatment (22.5% dropout)</td>
<td>Children from group L received a capsule containing $10^{10}$ heat-killed and lyophilized LB. For Sb: 250 mg of lyophilized Sb</td>
<td>Antibiotics for 8 days or Sb or LB daily for 8 weeks</td>
<td>In the Ab, SbI, and LB groups, HpSA were eliminated in 66, 12, and 6.5% of the children, respectively. In contrast, no spontaneous clearing was seen in the untreated children. A slight but noticeable change in the? Children who received living SbI had DOB (−6.31; 95% CI: −11.84—0.79), but those who received LB (0.70; 95% CI——5.84–7.24) did not.</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Omeprazole/esomeprazole, amoxicillin, and clarithromycin—the standard triple eradication treatment, with or without Sb</td>
<td>90 symptomatic children (range 3–18 years) with HpSA infection</td>
<td>250 mg bid</td>
<td>Triple eradication therapy for 7–10 days; Sb for 4 weeks</td>
<td>Of the 145 children studied, 90 (62%) had HpSA infection; age and socioeconomic position had positive and negative correlations, respectively ($p = 0.002$, $p &lt; 0.005$). The overall incidence of HpSA eradication was 87.7% (control group—80.9%; Sb group: 93.3%; $p = 0.750$). In the Sb group, the frequency of side effects was lower—8.3% in the probiotic group compared to 30.9% in the control group ($p = 0.047$).</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

bid, twice daily; qd, once daily; cfu, colony-forming unit; DOB, delta (13) CO (2) over baseline value before and after treatment, HpSA: *H. pylori* stool antigen, LB, *Lactobacillus acidophilus*, SbI, *Saccharomyces boulardii* plus inulin

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**Table 7: Mechanism of action of Sb in HpSA infection**

<table>
<thead>
<tr>
<th>Probiotic—creation of a favorable microbiotic environment</th>
<th>Adhesion inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Helicobacter pylori</em> infection mechanism</td>
<td>Due to the fact that HpSA encode the outer membrane proteins sialic acid-binding adherence and blood group antigen-binding adhesion, which can effectively bind to the recognition site and result in long-term colonization, HpSA has the ability to adhere to the epithelial cell. As a result, they can readily invade immune and epithelial cells in unfavorable circumstances.</td>
</tr>
<tr>
<td>Prevention action using probiotics</td>
<td>By displaying neuraminidase activity that is specific for sialic acid, Sb eliminates the HpSA binding site and reduces the bacteria’s adhesion to the host cell.</td>
</tr>
</tbody>
</table>
The role of yeast probiotics in GI diseases, primarily IBS,AAD, and HpSA infection, is addressed in the current review. IBS is characterized by frequent, chronic stomach aches or uneasiness and irregular bowel movements. Sb also improves the general health of individuals with IBS by having systemic effects, such as the modulation of proinflammatory cytokines (which in turn modulates nervous system activity) or a rise in tryptophan concentration. It can shorten the duration of diarrhea without recurrence. It can be prescribed to severely ill tube-fed patients having risk factors for AAD as a prophylactic. Also, it has been noted that Sb supplementation increased eradication rates and decreased side effects from treatment and specific symptoms in individuals with HpSA infection. In adults and children receiving antibiotic treatment, the American Gastroenterological Association supports Sb with a conditional recommendation and low-quality data for preventing CDI. According to the World Gastroenterology Organization’s (WGO) Global Guidelines for Probiotics and Prebiotics, the S. cerevisiae strain Sb CNCM I-745 can be used in adults to treat acute and anti-inflammatory-associated diarrhea as well as to prevent diarrhea caused by C. difficile. The WGO also advises Sb CNCM I-745 to be used as coadjuvant therapy for HpSA eradication and for the treatment of IBS. Additionally, it recommends its use in pediatrics to treat acute gastroenteritis, HpSA infection, NEC, and to prevent antibiotic-associated diarrhea.

Conclusion

This review emphasizes how numerous clinical trials and experimental investigations have backed the use of Sb as a potent biotherapeutic agent capable of preventing and/or treating a number of GI illnesses. Current research suggests that Sb’s advantages are temporary and independent of host gut colonization, setting it apart from other popular bacterial probiotics in terms of its mode of action. It supports the natural microbiome’s equilibrium and is important for controlling the secretory activities of intestinal epithelial cells, which aids the patient’s nutritional needs. Despite the possibility of fungemia following Sb therapy, none of the clinical trials has revealed any negative outcomes. Patients with immunodeficiency disorders and those at risk for adverse effects, however, should be handled carefully. Several of the unanswered problems regarding the fundamentals of probiotics, the makeup of the human gut flora, survivability and fecal recovery rates, physiological and immunological impacts, and more must be addressed in future research. Additionally, the most effective dosages, treatment durations, comparisons of various probiotic strains and types, single vs combined probiotics, probiotics combined with prebiotics, the effectiveness of various probiotics in various disease states, and safety of probiotics in patients with compromised gut epithelial integrity need to be assessed.

References

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