Effects of *S. Cerevisiae* var. *Boulardii* in gastrointestinal disorders

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**Abstract**

The increasing interest in the consumption of products containing probiotics is the result of numerous researches on their beneficial influence on human health. The promising one includes the improvement of prevention of various gastrointestinal disorders, the enhancement of immune function and the prevention of recurrent respiratory infections. Probiotics are available in a wide range of products with different benefits. Understanding their functional properties is an important aspect of health and well-being claims. Future studies are necessary to demonstrate the safe character of probiotics. This paper reviews the main effects of probiotic strain *S. cerevisiae* var. *boulardii* on gastrointestinal disorders. It has a beneficial physiological effect by the reduction of gastro-intestinal discomfort. The administration of the yeast, alone or in combination with other treatment, shows anti-inflammatory and immuno-modulatory effects.

**Keywords**: *S. cerevisiae* var. *boulardii*, probiotics, gastrointestinal disorders

1. Introduction

*Saccharomyces boulardii* is a probiotic yeast which was isolated by the scientist Henri Boulard in 1923. It was first isolated from lychee fruit and mangosteen fruit in Indochina. At the beginning, in the 1950s, it was used in France to treat diarrhea. It grows at 37°C, at unusually high temperature for yeast strains [1]. *S. boulardii* is different from *S. cerevisiae* through several metabolic, taxonomic and genetic properties [2]. The genes of *S. boulardii*, similar to that of *S. cerevisiae*, are generally used in genetic manipulation such as promoters and resistance markers. A major similarity of the yeasts orthologs has been discovered using sequencing [3]. As we can see in Fig. 1, *S. boulardii* is closely related to *S. cerevisiae* strain [4].

Mitterdorfer *et al.* [5] suggested that *S. boulardii* and *S. cerevisiae* species have in common so many molecular clustering characteristics that they cannot be regarded as different species. The term “*boulardii*” is not an accepted taxonomic classification, according to the current nomenclature like the International Code of Botanical Nomenclature (ICBN). The most proper classification is *S. cerevisiae* var. *boulardii*. [6]. Fietto *et al.* [7] showed that *S. boulardii* and *S. cerevisiae* are almost identical as regards their genetic characteristics. However, they have metabolically and physiologically distinct behaviours. *S. boulardii* have essential characteristics for yeast that can be used as a probiotic, like resistance to high temperature and acidic conditions and growth yield [8].
Probiotics have been defined by the World Health Organization expert group as 'live microorganisms which when administered in adequate amounts confer a health benefit on the host'. They must be capable to tolerate gastrointestinal conditions (acid, bile, enzymes, and low levels of oxygen) and deterring pathogens. In the case of *S. cerevisiae* var. *boulardii*, the main health benefit is correlated with the maintenance of healthy microbiota, by decreasing the numbers or colonization of pathogens. It is also associated with other health benefits like stimulation of immune system, prevention of allergies, prevention of diarrhea, prevention of intestinal infection caused by pathogens, stimulation of digestion and absorption of nutrients [9, 10, 11, 12, 13, 14, 15]. The probiotic yeast is effective if the yeast is used alone, or as a complementary treatment, in a daily dose higher than 10⁹/d, for a time interval from 7 days to 6 months [16].

The anti-inflammatory mechanisms of action of *S. cerevisiae* var. *boulardii* are: the inhibition of proinflammatory cytokines’ development, the inhibition of “bacteria overgrowth” and adhesion to host cells, and the interference with pathogenesis, trapping T cells in mesenteric nodes [17]. *S. boulardii* secretes medium-chain fatty acids and 2-phenylethanol that inhibit the morphological transition and adhesion of *C. albicans* [18]. The decrease of viable and active bacterial cells and the elimination of pathogens, bound to yeast surface within the gastrointestinal tract, limit bacterial growth and infections caused by human pathogens [19].

European Food Safety Authority frequently rejects health claims of probiotics [20]. In order to accept a health claim, every correlation between a food or a constituent and a claimed effect must form a coherent opinion [21]. Currently, in Europe there is no particular legislation or legal definition of probiotic and functional foods, no class to which they belong [22]. Only Novel Food Regulation regulates the use of microorganisms for human consumption (258/97 EEC). On the other hand, the legislative framework regarding the safety of probiotics in human use is nearly non-existent [23]. In order to offer consumers the confidence in probiotic products, an approach needs to be found to provide the convenient communication for probiotics health benefit.

**Figure 1.** Phylogenetic tree of the *Saccharomyces* sensu stricto complex, (A) Construction with the full data set for each species. (B) Rearrangement that occurred when Ty-related open reading-frames were removed from the data sets of all species.

2. Prevention and treatment of diarrheal disease

“Diarrhea” is characterized by an increase in the water content and volume of fecal matter. Epidemiologically, it is defined as a decrease in consistency and an increase in frequency of bowel movements to stools per day. Diarrhea can be: “infectious” - diarrhea caused by an infectious etiology; “acute” - an episode of diarrhea of <14 days; “persistent” is the diarrhea lasting >14 days and “chronic” - diarrhea that lasts >30 days [24]. Kotowska *et al.* [25] conclude that *S. boulardii* can be used as complementary treatment in children who
are submitted to antibiotic therapy to prevent the occurrence of antibiotic-associated diarrhea. The effect of *S. boulardii* on the intestinal anaerobe microflora can explain the protective impact of this probiotic on the diarrheal diseases appearing in patients under exclusive enteral nutrition. The use of *S. cerevisiae* var. *boulardii* significantly increases three short-chain fatty acids, i.e. acetic, propionic and butyric acid [26].

Clinical studies support the reduction of diarrhea duration if *S. boulardii* is administered to children within 72 hours after the debut of acute diarrhea [27]. *S. boulardii* can be used as an additional treatment in children, for the oral rehydration in the management of acute diarrhea [28]. In the case of children with persistent diarrhea, it significantly decreases the number of stools, shortening the duration and symptoms of diarrhea [29, 30, 31, 32, 33]. *S. boulardii*, combined with oral rehydration solution, reveals a beneficial response in acute watery diarrhea, especially on the duration of diarrhea, on the consistency and frequency of stools [34].

In the post-antibiotic period, *S. boulardii* had an important influence on the restoration to the normal levels of the *C. coccoides*, *Bacteroides* and *Enterobacteriaceae* strains. The use of *S. boulardii* can restore the balance of the dominant anaerobic microbiota after treatment with amoxicillin-clavulanic acid. The specific immune reaction to microbial-associated molecular patterns can be influenced by the use of the yeast. This result also suggests that *S. boulardii* contributes in keeping the intestinal homeostasis [35]. The antibiotic-associated diarrhea has been shortened significantly by the treatment with *S. boulardii* [36, 37]. It also shows a remarkable effect on the cure and prevention of diarrhea in dogs with lincomycin-induced diarrhea [38].

### 3. Prevention and treatment of bowel diseases

Inflammatory bowel diseases included two major disorders: ulcerative colitis and Crohn’s disease. The diffuse mucosal inflammation is limited to the colon characterized ulcerative colitis. The use of *S. boulardii* during maintenance treatment with mesalamine for 4 weeks resulted in clinical remission, which was endoscopically confirmed in approximately two-thirds of the patients experiencing a clinical flare-up of ulcerative colitis [39].

Crohn’s disease may affect any part of the gastrointestinal tract by patchy, transmural inflammation [40]. Dalmasso et al. [41] conclude that administration of *S. boulardii* can have a favorable effect in the treatment of inflammatory bowel diseases (IBD). *S. boulardii* may control inflammation and help epithelial reconstruction which is important in IBD [42]. In the case of patients submitted to the maintenance treatment with mesalamine and *S. boulardii*, it was noted that Crohn’s disease clinically recurred to a significantly lesser extent (6.25%) than in the case of subjects submitted only to the administration of mesalamine (37.5%) [43]. However, after steroid or salicylate therapies, administration of *S. boulardii* does not appear to have any beneficial effects on patients with Crohn’s disease in remission [44].

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain or discomfort, defecation or a change in intestinal [45]. Akhondi-Meybodi et al. [46] showed that the use of *Saccharomyces boulardii* can be efficient in improving the symptoms, particularly pain severity, flatulence, belching, diarrhea, and eructation. However, Kabir et al. [47] conclude that the use of *S. boulardii* for 30 days was unsuccessful for the treatment of patients with diarrhea- predominant irritable bowel syndrome. *S. boulardii* cannot ameliorate individual symptoms in patients with diarrhea-predominant or mixed-type irritable bowel syndrome, but it can enhance the quality of life, better than placebo [48].

Mucositis is characterized by an increase of intestinal permeability and intestinal inflammation. Studies with *S. boulardii* conclude that it cannot improve the symptoms of mucositis like mucosal lesions, intestinal permeability and sIgA secretion in mice [49].

### 4. Prevention and treatment of infections

Uncomplicated diarrhea, nonspecific colitis or pseudomembranous colitis characterized the intestinal infection with *Clostridium difficile*. A prospective double-blind study showed that a combination of *S. boulardii* and a standard oral antibiotic can be more effective in preventing
Clostridium difficile infections recurrences than standard therapy alone [50]. Spielholz [51] suggests that the symbiotic tablet, containing Saccharomyces bouardii and Bacillus coagulans, and a prebiotic, i.e. fructooligosaccharide, can prevent antibiotic-associated diarrhea and C. difficile infection in patients submitted to antibiotic treatment within a nursing home.

Infection with Helicobacter pylori is one of the most frequent human infections worldwide and its symptoms include a number of critical gastrointestinal conditions such as chronic gastritis, peptic ulcer disease, and gastric malignancy [52]. Saccharomyces bouardii seems to be a hopeful treatment that reduces H. pylori infections. Regular consumption of the probiotic yeast has been shown capable to eradicate 12% of colonization with Helicobacter pylori in infected children [53]. Kyriakos et al. [54] conclude that the complementary use of S. bouardii and classic therapy (omeprazole 20 mg bid, clarithromycin 500 mg bid and amoxicillin 1 g bid), in order to reduce H. pylori infection, lead to higher rates of eradication of this pathogen. S. bouardii can reduce treatment-related diarrhea and improve its compliance with the treatment.

One of the most significant causes of neonatal and post-weaning diarrhea in piglets is the infection caused by enterotoxigenic Escherichia coli. The treatment with Saccharomyces cerevisiae var. Bouardii, in combination with b-galactomannan, can be used to prevent E.coli K88 infection. The use of an in vitro model for pig intestinal cells showed the ability of the probiotic yeast to reduce pathogenic inflammation [55].

5. Control and effect on parasitosis

Toxocarasis is a chronic tissue parasitosis, most commonly correlated with the etiologic agent nematode Toxocara canis. It is defined by the migration and permanence of larvae of helminthes in humans. The treatment with S. bouardii may differently control this parasitosis, showing a significant decrease in the intensity of toxocarasis [56].

Giardia lamblia is a microscopic single-celled parasite that causes the intestinal infection called giardiasis. The symptoms include diarrhea, pale greasy stools, stomach cramps, gas, nausea, vomiting, bloating, weight loss, and weakness. S. bouardii appears to improve clearance of the infecting pathogen [57].

6. Safety

The main risk of consumption of S. cerevisiae var. bouardii is fungemia [58]. It is defined as the presence of fungi or yeast in blood. Fungemia can appear on patients with high infection risk [59, 60, 61], when the package containing the lyophilized probiotic is opened, without being taken preventive infection control measures in the patient’s room. This risk can be reduced by carefully hand washing and changing gloves before the administration of the probiotic product [62].

7. Conclusions

Future studies are necessary to improve reliability of taxonomic classification of S. bouardii strain. This can improve the efficiency and activity of products containing probiotics strains. The influence, the mechanisms of action and the functional role of S. bouardii in human health must be established. The demonstration of the health claims has to be stable in human intervention studies. It is important to understand the role of probiotics in food matrix related to isolated component. The risk of fungemia should be evaluated before using the S. cerevisiae var. bouardii strain in the prevention and treatment of diarrheal, infections, parasitosis and bowel diseases.

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