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# Use of yeasts for prevention and therapy

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## ABSTRACT

Yeasts are a rich source of amino acids, proteins, several dietary minerals (e.g. chromium, selenium, zinc, iron, magnesium, cooper, manganese), and the B vitamins, particularly recommended for a vegan or vegetarian diet as well as for young people during maturation. One of the most well-known species of yeasts used in health and wellness is *Saccharomyces cerevisiae* (the common name is brewer's yeast). They are often used as a source of B vitamins (B1, B2, B3, B5, B6, B7 and B9). Typically, brewer's yeast is used as a protein, vitamin and mineral supplement, energy booster, immune enhancer, or vehicle where other compounds can be inserted to create a commercialized health product. The biomass of brewer's yeast is also considered as an extensive source of bioavailable minerals, particularly chromium and selenium. Chromium is an essential trace mineral, since being part of glucose tolerance factor it helps the body maintain normal blood sugar levels, thereby decreasing appetite (especially for sweet foods). Another yeast species *Yarrowia lipolytica* contains high levels of many important nutrients, exogenous amino acids, proteins, different minerals, and lipid compounds as mainly unsaturated fatty acids (about 90%). This yeast species is a rich source of nutrients for vegans, vegetarians, athletes and a dietary supplement for people after recovery. *Saccharomyces boulardii*, a yeast species, has been found to be an effective probiotic. The clinical activity of *S. boulardii* is especially relevant to antibiotic-associated diarrhoea and recurrent *Clostridium difficile* intestinal infections. In conclusion, several studies indicate that nutritional yeasts as well as *S. boulardii* are important products for prophylactic and/or therapeutic purposes.

**Keywords:** yeast, *Saccharomyces cerevisiae*, *Yarrowia lipolytica, Saccharomyces boulardii,* dietary supplements, probiotics

## INTRODUCTION

Yeasts, especially *Saccharomyces cerevisiae* (also known as brewer's yeast or baker's yeast) are interesting because they possess several nutritional properties and they are used in the food and pharmaceutical industry. The food industry produces dietary supplements with a high nutritional value made from living *S. cerevisiae* cells and the yeast extracts. *S. cerevisiae* is yeast that hold the GRAS status (Generally Recognized As Safe) and have therefore always been considered as safe. Brewer's yeast possess high quality proteins, which contain a good composition of amino acids. They contain a high level of lysine and an abundance of isoleucine and threonine. Therefore supplements of brewer's yeast are very useful for low-calorie diets that are deficient in proteins.

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Brewer's yeast produce the abundance of the vitamin B complex including B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B9 (folic acid), and H or B7 (biotin), but they do not produce B12 vitamin [29]. These vitamins help break down carbohydrates, fats, and proteins, which provide the body with energy. They also support the nervous system, help maintain the muscles used for digestion, and keep skin, hair, eyes, mouth, and liver healthy [31]. Brewer's yeast are also a rich source of minerals and oligoelements, particularly chromium and selenium [10, 29]. European Food Safety Authority (EFSA) approval for human health claims linking dietary intake of selenium yeast to "protection of DNA, proteins and lipids from oxidative damage, normal function of the immune system, normal thyroid function and normal spermatogenesis" [13]. Chromium brewer's yeast may help high blood sugar. Although some studies suggest that chromium may help reduce body fat, the amount of fat lost is small compared to what can be lost with exercise and a well-balance diet. However, brewer's yeast is also used as a protein supplement and energy booster, so it may help maintain a healthy weight

[29]. Slimming treatments with yeast beverage that is drunk before a meal in order to reduce appetite are also known. *S. cerevisiae* produces also other bioavailable minerals e.g. zinc [1, 10], copper, manganese [1], iron [35] and magnesium [15]. There are essential minerals that participate in the natural physiological and metabolic process of organisms. Additional, the metabolism of several trace elements is altered in diabetes mellitus and that these nutrients might have specific roles in the pathogenesis and progress of this disease [22]. In order to manufacture a yeast formulation abundant with microelements, yeasts may be cultured in a medium supplemented with selected minerals. In example, selenium yeast produced by growing S. cerevisiae in a selenium-rich media is a recognized source of organic food-form selenium. Brewer's yeast takes up inorganic Se from the culture medium and converts it into selenomethionine [38]. Selenomethionine furthermore can replace methionine in proteins, making it the only seleno-amino acid that can be significantly stored in organs and tissues. In humans, in absolute amounts, most of it is stored in the skeletal musculature. Selenium yeast may be prepared by two methods – by adding sodium selenite to the suspension of yeast and drying the obtained mixture, or by a slow addition of sodium selenite during the yeast's growth. In the first case, selenium is bound to the microbial cell wall by means of ionic bonds, however, it still remains a four-valent selenium, considered as selenium in inorganic compound. In the latter case, yeast's cells reduce selenite to selenide and incorporate it into cellular components in place of sulphur. Selenium combinations obtained that way are in 50-80% organic compounds, which are much better absorbed by the human body and longer persist [19].

Brewer's yeast possesses high levels of fibers such as â-glucans [36] and mannans [7]. β-glucans are soluble fibers with physiological functions, such as, interference with absorption of sugars and reduction of serum lipid levels [36]. Polysaccharides such as β-(1→3), β-(1→6) and β-(1→3) glucans are main components of the fungal cell wall, apart from glycoproteins. Polysaccharides and glycoproteins form a layered structure, where glycoproteins are located outside, while the inner layer consists of polysaccharides and chitin. β-glucans help again obesity and help to reduce the risk of cardiovascular diseases [3].

## *SACCHAROMYCES CEREVISIAE* FOR PREVENTION AND THERAPY

There are many products containing brewer's yeasts available on the market of dietary supplements. These formulations are often supplemented with plant raw materials (mint, lemon balm, horsetail, nettle) or A, C and E vitamins. Powder supplements (which may be used to sprinkle food or may be dissolved in a small amount of juice or water), capsules or tablets are known. Formulations containing brewer's yeast may be used for a longer period of time, although it is recommended to make periodic intervals in the consumption of such dietary supplements. Available medical literature emphasises particularly beneficial importance of yeast biomass enriched with chromium and selenium for health [29].

Inorganic chromium compounds are very poorly absorbed by the human body (1-3%). This fact is of concern as glucose metabolism disorders are observed in the deficiency of this element. Trivalent chromium with nicotinic acid and amino acids forms a glucose tolerance factor (GTF) that facilitates passing of glucose, fatty acids and amino acids into cells, and accelerates their metabolism [28]. Animal studies showed that the body of mice with induced diabetes inadequately transformed inorganic chromium compounds into a biologically active GTF factor [41]. The results of these experiments most likely translate into the human population. Sherman et al. and other authors also reported lack of chromium supplementation efficacy when administered as inorganic compounds [39]. In contrast, other studies showed high bioavailability of organic chromium compounds. It is believed that brewer's yeast is a particularly abundant source of the GTF factor [28]. Diabetics run the higher risk of developing chromium deficiency. It is most likely that insulin administration causes the increased elimination of this element from the body, predisposing to its deficiency [30]. Laboratory tests showed significantly lower concentrations of chromium in hair, liver and plasma of individuals suffering from diabetes [9]. In a study conducted by Król et al., supplementation with brewer's yeast enriched with chromium (500 µg of chromium/day for 8 weeks) did not produce the expected hypoglycaemic benefits in patients with type 2 diabetes either, although it increased chromium concentration in plasma and hair [25]. In contrast to the above results, in the experiments conducted by Lai et al, chromium derived from yeast biomass significantly reduced glucose level and LDL cholesterol fraction concentration without food in rats with diabetes induced in laboratory conditions [26].

In turn, multi-mineral yeast biomass Cr, Se and Zn-enriched administered to diabetic mice, after 8 weeks of the supplementation, decreased levels of glucose, triglycerides and total blood cholesterol, with a simultaneous increase in the HDL cholesterol fraction, blood glutathione and the activity of superoxide dismutase and glutathione peroxidase, were observed in the animals. Furthermore, treatment with multi-mineral yeast biomass showed a protective effect on pancreatic islets, giving no side effects [20]. Similar results were presented by Khosravi-Boroujeni et al., who had demonstrated that the consumption of brewer's yeast for a period of 8 weeks reduced the cardiometabolic risk in type 2 diabetic patients with hypercholes-

terolemia [24]. Just as diabetic patients, the elderly belong to a group at risk of developing chromium deficiency. The decrease in chromium level associated with age may lead to glucose metabolism disorders, development of coronary heart disease, atherosclerosis and type 2 diabetes. Supplementation of 9 g per day of chromium brewer's yeast for 8 weeks resulted in improved outcomes of the oral glucose tolerance test, lower cholesterol level and total lipid level values as well as in a decreased insulin secretion. This effect was observed in 11 (out of 12) elderly patients, out of which four were suffering from mild diabetes which did not require insulin administration [34].

In view of the fact that the results of studies on benefits of using yeast biomass in patients with impaired carbohydrate metabolism are markedly different in global literature, it has been suggested that the final effect of brewer's yeast supplementation may depend on the value of initial glucose level. It is highly likely that the cardiometabolic risk factors are also affected by yeast biomass components other than chromium [37].

Preliminary studies showed a link between an elevated selenium level and a reduced risk of tumour development [11], including prostate [4], nonmelonoma skin, colorectal, and lung cancers [19]. In a study conducted by El-Bayoumy et al., in which healthy patients took selenium-enriched yeasts for 9 months (247 μg/day), a rise in glutathione (GSH) level and a decline in bound glutathione / free glutathione ratio were found, suggesting a reduction of oxidative stress. Furthermore, a small but significant decrease in the PSA (prostate-specific antigen) level after 3 and 9 months of the treatment was also observed. Nevertheless, the authors emphasised the importance of continuous selenium supplementation as this favourable effect had not been recorded after 3 months since the therapy's completion [12]. Another linked it to a reduced risk of a second skin cancer [29]. Selenium yeast supplement on selenoprotein activity (SeP) also has been used to study the effects of selenium status and the risk of developing cancers or precancerous lesions [6]. A clinical trial to test the effects of a dietary supplement with selenium yeast in patients with carcinoma of the skin had promising secondary endpoint results, showing it was associated with lower lung, colorectal, and prostate cancer incidence and in reduced lung cancer mortality [4]. Selenium yeast supplementation, together with supplementation with beta carotene and E vitamin, were associated with reductions in total mortality, cancer mortality and incidence, especially of stomach cancer [2]. The dietary Se may have an advantage in improving Se status and reducing cancer risk. SeP with Se supplementation may be crucial to its chemo preventive action [18].

Brewer's yeast, especially *S. cerevisiae* Hansen CBS 5926 strain may be regarded as an alternative treatment of acne more and more widely accepted by patients [43]. The one preliminary study found that taking a specific kind brewer's yeast product (EpiCor) may help prevent colds and flu. This yeast-based product had significantly fewer symptoms and significantly shorter duration of symptoms when compared with subjects taking a placebo [29].

## *YARROWIA LIPOLYTICA* AS A SOURCE OF BIOACTIVE COMPOUNDS

*Yarrowia lipolytica* is one of the most extensively studied "non-conventional" yeasts, being capable of producing important metabolites and having an intense secretory activity. It is considered as nonpathogenic and several processes based on this organism were classified as GRAS by the FDA (Food and Drug Administration, USA) [5, 17, 21]. *Y. lipolytica* is found primarily in foods with high proportions of fat and/or protein, particularly in fermented dairy products and meat (e.g. cheese, butter, cream, margarine, yoghurt, salami, Spanish fermented sausages). The natural occurrence of this yeast in food, is an additional argument in favor of its safety. The occasional occurrence of opportunistic infections of *Y. lipolytica* in immunocompromised and catheterized patients does not differ from other microorganisms with a history of safe use, such as *Saccharomyces cerevisiae* [17].

Very interesting ability of *Y. lipolytica* strains is to grow on olive mill wastewater based medium and produce high-value compounds [5]. It can accumulate lipids intracellularly to ≥ 40 % of its cell dry weight. *Y. lipolytica* biomass contains about 9 % intracellular lipids. The lipids of this yeast represented high level unsaturated fatty acids about 90%, which contained over 50% oleic acid, about 27 % linoleic acid and about 10% linolenic acid [32]. Biomass of *Y. lipolytica* is characterized by a high content (over 50%) of protein and essential amino acids [21]. The yeast protein contains a high amount of lysine, phenylalanine and valine [32]. The amount of essential amino acids was in agreement with FAO standards for fodder yeast, with lysine and phenylalanine which were present in the yeast biomass in higher amounts [21]. Furthermore, yeast protein characterized by high biological value of about 80% [32]. In addition, this yeast, when grown under nutrient-limited conditions, is able to produce organic acids e.g. citric acid from a variety of carbon source, including sugars, alkanes, plant oils, starch hydrolysates, ethanol, and raw glycerol [5]. *Y. lipolytica* can be made to synthesize some practically important compounds e.g. α-ketoglutaric acid, succinic acid, diethyl succinate and unusually large amount of γ-aminobutyric acid under the conditions of thiamine deficiency [21]. This yeast is also rich a source of minerals, particularly chromium and selenium [33]. It contains β-glucans as naturally component its cell wall [14]. *Y. lipolytica* has been in use or is considered for multiple industrial applications as a high-quality

protein source for livestock feeding [17]. Some valuable metabolites of *Y. lipolytica* such as α-ketoglutaric acid, succinic acid, diethyl succinate, biomass enriched with protein and essential amino acids, can be used in food and medical industries. The unique amino acid composition of the yeast makes it possible to use its biomass as a component of parenteral nutrition mixtures and a basis for neuroleptics [21].

## *SACCHAROMYCES BOULARDII* AS A PROBIOTIC

Although most probiotics are bacteria, one strain of yeast, *Saccharomyces boulardii*, has been found to be an effective probiotic in double-blind clinical studies [40]. Probiotics are defined as live micro-organisms which confer a health benefit on the host. *S. boulardii* is a strain of yeast which has been extensively studied for its probiotic effect. It is especially interesting because of its ability to resist the action of gastric acid and bile [16]. Several clinical trials and experimental studies strongly suggest a place for *S. boulardii* as a biotherapeutic agent for the prevention and treatment of several gastrointestinal diseases. *S. boulardii* mediates responses resembling the protective effects of the normal healthy gut flora [23]. The clinical activity of *S. boulardii* is especially relevant to antibiotic-associated diarrhoea and recurrent *Clostridium difficile* intestinal infections. Experimental studies clearly demonstrate that *S. boulardii* has specific probiotic properties, and this data has opened the door for new therapeutic uses of this yeast as an "immunobiotic" [8].

The multiple mechanisms of action of *S. boulardii* depend mainly on antimicrobial activity such as the inhibition of growth of bacteria or parasites, reduction of gut translocation of pathogens, neutralization of bacterial virulence factors, suppression of host cell adherence that interferes with bacterial colonization and antitoxin effects such as the inhibition of toxin receptor binding sites, the stimulation of antibody production against *C. difficile* toxin A and direct proteolysis of the pathogenic toxins (e.g. produce a serine protease that cleaves *C. difficile* toxin A) or secretion of enzymatic proteins against pathogens (e.g. a 63 kDa phosphatase that destroys the endotoxin of pathogenic *Escherichia coli* and a 120 kDa protein that reduces the effects of cholera toxin [23], and on stimulating effects on the intestinal mucosa such as trophic effects on the brush border enzymes and immunostimulatory effects [23, 43]. At present, in pediatric populations, there is evidence that *S. boulardii* is beneficial for the treatment of acute gastroenteritis and the prevention of antibiotic-associated diarrhea. More data are needed to confirm other indications such as travellers' diarrhea, *Helicobacter pylori* eradication, and inflammatory bowel disease [43]. *S. boulardii* was found to be significantly efficacious and safe in 84% of those treatment arms. A meta-analysis found a significant therapeutic efficacy for *S. boulardii* in the prevention of antibiotic-associated diarrhea (AAD). In adults, *S. boulardii* can be strongly recommended for the prevention of AAD and the traveler's diarrhea. Randomized trials also support the use of this yeast probiotic for prevention of enteral nutrition-related diarrhea and reduction of *H. pylori* treatment-related symptoms. *S. boulardii* shows promise for the prevention of *C. difficile* disease recurrences; treatment of irritable bowel syndrome, acute adult diarrhea, Crohn's disease, giardiasis, human immunodeficiency virus-related diarrhea; but more supporting evidence is recommended for these indications.

The use of *S. boulardii* as a therapeutic probiotic is evidence-based for both efficacy and safety for several types of diarrhea [27]. It is also used for other inflammatory disorders, acute gastroenteritis in children, chronic diarrheas in patients with AIDS and diarrheas caused by *Vibrio cholerae* and several *Enterobacteriaceae* [8].

## CONCLUSION

It was shown in this work that yeast such as *Saccharomyces cerevisiae* and *Yarrowia lipolytica* are a rich source of exogenous amino acids, proteins and several bioavailable dietary minerals. Biomass of yeasts may be used as food or dietary supplements, particularly recommended for a vegan or vegetarian diet as well as for young people during maturation. Due to high amount of proteins, they may also be used as an aid for people who build muscle mass or convalescents. In turn, the multiple prophylactic and therapeutic effects of *Saccharomyces boulardii* in inflammatory gastrointestinal diseases underline the efficacy of this probiotic yeast in enteric diseases.

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