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RECENT ADVANCES ON EFFICACY OF PROBIOTIC YEASTS IN HUMAN WELFARE: AN OVERVIEW

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ABSTRACT

Due to the enormous benefits for human health, probiotics have gained popularity in the current era of science and have received a lot of public interest recently. Many bacterial strains have been used as probiotics for commercial applications. For a long time, the only yeast, *Saccharomyces cerevisiae var. boulardii*, was referred to be a probiotic. Interest in the probiotic potential of different yeast strains has grown in recent years. The purpose of the present review is to explore the updated information on the efficacy of various yeast strains as probiotics for human welfare.

Keywords: beneficial effects, efficacy, fermented food, probiotic, yeast

INTRODUCTION

Probiotics are live, non-pathogenic microbes that are crucial for maintaining human health. Yeast has been considered as an important probiotic in human microbiome. Since the 1950s, probiotic yeast (*Saccharomyces boulardii*) has been available for purchase, and clinical research using it started in 1977 convincingly showed its nonpathogenic nature for safe usage (**McFarland, 2010**). Mangosteen and lychee fruits were used to isolate *Saccharomyces cerevisiae* subtype in 1923, which was then dubbed *Saccharomyces cerevisiae* var. *boulardii* (**Altmann, 2017**). This strain could provide better protection against microbial infections as well as toxic compounds which could prevent intestinal epithelial cell damage (**Capece *et al.*, 2018**). Many studies indicate the potential properties of *S. boulardii* to treat various GI tract disorders, especially caused by pathogens like *Helicobacter pylori*, *Salmonella*, and *Clostridium difficile* infections (**Hudson *et al.*, 2016**). A well-known probiotic yeast *called S. boulardii* has been utilised to treat numerous GI tract illnesses in people (**Sen and Mansell, 2020**). There is a scope to improve probiotic attributes of *S. boulardii* using *Saccharomyces cerevisiae* genetic engineering tools (**Pais *et al.*, 2020**). *S. boulardii*'s phylogenetic clusters are closely related to strains of *S. cerevisiae* (**Khatri *et al.*, 2017**). The prevalence of *Saccharomyces* strains in the human GI tract is obvious given that live *S. cerevisiae* and other related organisms have been intentionally consumed by humans for thousands of years in the form of bread, beer, and other fermented foods and beverages. However, only a few strains of *S. cerevisiae* have shown health benefits in humans (**Fernandez-Pacheco *et al.*, 2018**). *Saccharomyces* species are well characterized as probiotics and used to treat various disorders (**Nash *et al.*, 2017; Sambrani *et al.*, 2021**). *S. cerevisiae* BEL 9 and *S. cerevisiae* BEL 1 were isolated from lychee fruits which indicated good viability at various stress conditions (**Khan *et al.*, 2020**). Similarly, *S. cerevisiae* C41 strain was isolated from Tibicos and identified as potential probiotics (**Romero-Luna *et al.*, 2019**). *Saccharomyces cerevisiae* isolated from caterpillar frasses showed significant probiotic properties (**Khisti *et al.*, 2019**).
Diutina rugosa 14 and *Diutina rugosa* 8 were found to have potential as biotechnological probiotics after being isolated from pistachio fruits (**Fernández-Pacheco *et al.*, 2021**). The advantages of probiotic yeasts include immunomodulation through general gut microbiota maintenance through precise interactions (**Lai *et al.*, 2019**). *Debaryomyces*, *Candida*, *Pichia*, *Candida*, *Hanseniaspora*, *Kluyveromyces*, and *Metschnikowia* are known as possible probiotic yeasts. The size of yeasts, which is 10 times bigger than that of bacteria and makes up less than 0.1 percent of the microbiota in the gut, may allow for better coverage of probiotic yeast colonization throughout the GI tract (**Hsiung *et al.*, 2020**). To make fermented foods, yeast strains have been utilized as a starter culture. During this fermentation process, probiotic may produce secondary metabolites viz. fatty acids, esters, acetates and alcohols that gives better aroma to the foods and beverages. This enhances the overall quality of the foods that have undergone fermentation. Nowadays, starter cultures should be made from practically all of the yeast species in the genus *Saccharomyces* (**Arevalo-Villena et al., 2017**). According to **Agarbati *et al.* (2020)**, yeast strains isolated from dairy products and natural habitats were recognized as probiotics from the genera *Kluyveromyces*, *Brettanomyces*, *Saccharomyces*, *Rhodotorula*, and *Pichia*. The list of potential probiotic yeasts is constantly being expanded, but *S. boulardii* is still the only probiotic yeast with a regulatory framework and widespread commercial acceptability. **Table 1** shows the list of probiotic yeasts reported by various workers.

Table 1 List of Probiotic yeast strains

S. No.	Probiotic yeast	References
1.	*S. cerevisiae and S. cerevisiae var. boulardii*	Diosma *et al.*, 2014; Gil - Rodriguez *et al.* 2015
2.	*Cryptococcus spp.*	Aloglu *et al.*, 2016
3.	*Candida famata*	Al -Seraih *et al.*, 2015
4.	*C. tropicalis*	Ogunremi *et al.*, 2015
5.	*Debaryomyces hansenii*	Ochangco *et al.*, 2016
6.	*Issatchenkia orientalis*	Ogunremi *et al.*, 2015
7.	*Kluyveromyces lactis*	Binetti *et al.*, 2013
8.	*Kluyveromyces marxianus*	Binetti *et al.*, 2013; Diosma *et al.*, 2014; Smith *et al.*, 2015
9.	*Metschnikowia gruessii*	Smith *et al.*, 2015
10.	*Pichia jadinii*	Buerth *et al.*, 2016
11.	*Pichia kluyveri*	Ogunremi *et al.*, 2015
12.	*P. kudriavzevii*	Ogunremi *et al.*, 2015
13.	*P. pastoris*	Correa Franca *et al.*, 2015
14.	*P. guilliermondii*	Bonatsou *et al.*, 2015
15.	*Wickeramomyces anomalus*	Bonatsou *et al.*, 2015

Recently, the use of yeast as a probiotic has received more attention. More research is needed to discover the new yeast species with potential probiotic properties towards the benefit of the human.

YEASTS IN FERMENTED FOOD PRODUCTS SHOWING PROBIOTIC POTENTIAL

The probiotic yeast strains *Wickerhamomyces anomalus*, *Nakazawaea molendini-olei*, *N. wickerhamii*, *Yamadazyma terventina*, *Candida adriatica*, and *Candida diddensiae* have been isolated from a variety of natural sources, including human breast milk, camel raw milk, virgin olive oil, and rotten fruits (apple, grapes, strawberry) and vegetables (cauliflower, brinjal, tomato, cucumber) (**Ahmad *et al.*, 2019; Zullo and Ciafardini, 2019**). Many fermented foods such as yogurt, kimchi, sauerkraut, kombucha, natto, kefir, pickles, tempeh, green olives, miso, cottage cheese and other type of cheeses contain probiotic yeasts. Some of the foods like beer, chocolate, sourdough bread, soy sauce and wine also contain live probiotics. *Kluyveromyces lactis*, *S. unisporus*, and *S. boulardii* are probiotic yeasts found in kefir grains (**Abraham *et al.*, 2019**). Some foods that have a big impact on the health of the host use these helpful bacteria as additives (**Lokhande *et al.*, 2019**). **Figure 1** shows the list of fermented food sources containing yeasts having probiotic potential.

NOVEL CHARACTERISTICS OF PROBIOTIC YEAST

Novel characteristics of probiotic strains include adhesion ability, auto-aggregation, coaggregation, cell surface hydrophobicity, GIT tolerance, cholesterol assimilation, exopolysaccharide production (EPS**),** production of killer toxins, enzymes**,** antimicrobial substances, and metabolites**.**

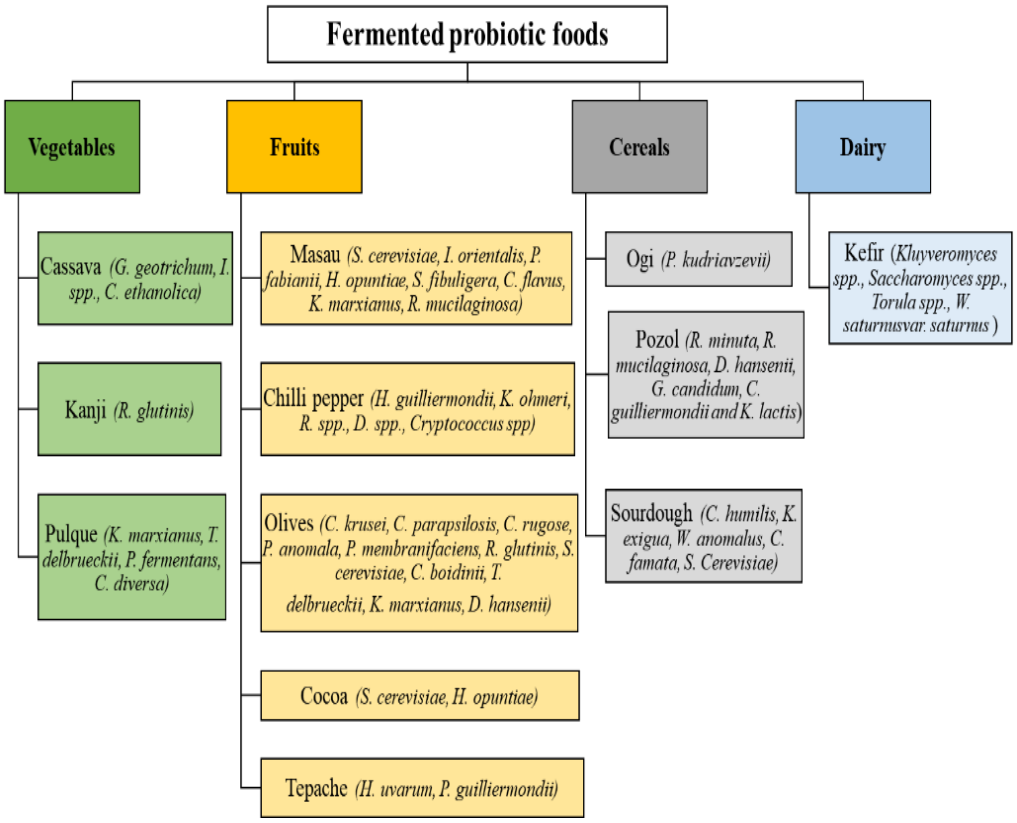

Figure 1 Probiotic yeasts in various fermented foods

Auto-aggregation and Co-aggregation ability

Aggregation between similar microbes called auto- aggregation and in case of co-aggregation, different strains will adhere together. Probiotic strains with the ability to aggregate improved the development of biofilm to defend the host against pathogen invasion through self-recognizing surface components, such as proteins and exopolysaccharides, collectively known as auto agglutinins (**Trunk *et al.*, 2018**). It was discovered that cell surface hydrophobicity was connected to the capacity to co-aggregate with pathogens (**Son *et al.*, 2017**).

Five probiotic yeasts, *B. custersianus* VIT-MN05, *S. fibuligera* VIT-MN04, *L. starkeyi* VIT-MN03, *K. lactis* VIT-MN02, and *Y. lipolytica* VIT-MN01, were examined utilising in vitro techniques for their potential for adhesion, autoaggregation and coaggregation, GIT tolerance, and cholesterol assimilation (**Ragavan and Das, 2017a**). This study showed 92 % auto-aggregation ability for probiotic yeast *L. starkeyi* VIT-MN03. There are reports on probiotic yeasts such as *S. cerevisiae*, *W. anomalus*, *Y. lipolytica*, and *P. barkeri* which showed 80% auto-aggregation ability (**Suvarna *et al.*, 2018**). Yeast strains belonging to *Dekkera*, *Hanseniaspora*, *Kazachstania*, *Kluyveromyces*, *Kwoniella*, *Saccharomycopsis*, *Saccharomyces*, *Torulaspora*, *Wickerhamomyces*, *and Zygosaccharomyces* isolated from kefir milk showed 95% autoaggregation ability (**Hsu and Chou, 2021**).

It was discovered that probiotic yeasts can co-aggregate with the pathogens *Salmonella* sp. and *Klebsiella* sp. *Limosilactobacillus fermentum*, a probiotic bacteria, had the highest capacity for co-aggregation, while *L. starkeyi* VIT-MN03 had capacities of 90% and 92% for co-aggregation of *Klebsiella* sp., and *Salmonella* sp. respectively. However, several yeast strains shown high co-aggregation ability (>80%) for both viruses (**Ragavan and Das, 2017a**). *S. cerevisiae* LPBF3, a probiotic yeast isolated from honey-based kefir beverage, failed to aggregate with pathogenic *E. coli* strain and only had a 22% coaggregation ability with S. aureus pathogen (**de Oliveira Coelho *et al.*, 2019**).

Surface hydrophobicity

The tendency of microbial cells to bind different surfaces (biotic and abiotic) is affected by the hydrophobicity of the cell surface. LAB with strong aggregation abilities has a relatively broad surface hydrophobicity, giving them an added benefit for attachment (**Chen *et al.*, 2018**). According to percent adhesion values, the degree of hydrophobicity was assigned as strongly (>50 %), moderately (20 % –50 %), and weakly (20 %) hydrophobic (**Aziz *et al.*, 2019**). Similar to probiotic bacteria *P. mirabilis* (90 percent), probiotic yeast *L. starkeyi* VIT-MN03 displayed a high hydrophobicity index (**Ragavan and Das, 2017b**). Probiotic yeasts including *Kluyveromyces marxianus* JYC2614, *S. cerevisiae*, and *S. boulardii*, have been reported to have cell surfaces that are respectively, 68%, 73%, and 86% hydrophobic (**Hu *et al.*, 2018; Hsiung *et al.*, 2020**).

GIT tolerance

The survival ability of microbes under simulated GIT has generally been considered a key feature in selecting potential probiotics. The probiotic strain should tolerate stomach acid followed by higher concentrations of bile salt in the GIT. This characteristic feature is crucial for maintaining the viability and survival rate of probiotics in a harsh GIT environment (**Kizerwetter-Świda and Binek, 2016**). Probiotic yeast strains such as *Yarrawia lipolytica*, *S. cerevisiae*, *Debaryomyces occidentalis*, *Debaromyces hansenii*, and *Cryptococcus* sp. were reported for better survival at acidic and GIT conditions (**El-Baz *et al.*, 2018**). Probiotic yeast *Wickerhamomyces anomalus* HN1 showed 61.5 % viability and other yeast strains such as *Pichia manschuria*, *Candida tropicalis*, and *S. cerevisiae*, exhibited significant GIT tolerance after 2 h incubation (**Helmy *et al.*, 2019**). Similar reports were noted for probiotic yeasts *S. unisporus* and *Kluyveromyces lactis* (**Gut *et al.*, 2019**).

Cholesterol assimilation

Numerous mechanisms, such as bile salt hydrolase activity, the synthesis of inhibitory chemicals, and cholesterol assimilation, are involved in the control of cholesterol (**Tomaro-Duchesneau *et al.*, 2014**). The study made by **Ragavan and Das (2017b)** demonstrated the cholesterol assimilation ability of probiotic yeasts. Probiotic yeast *K. lactis* VIT-MN02 showed a 90% cholesterol assimilation rate after 24th h of incubation. The probiotic yeasts viz. *S. boulardii*, *P. kudriavzevii,* and *S. cerevisiae* were also reported for cholesterol assimilation which ranges from 1% to 80% (**Syal and Vohra, 2013**). In another study, yeast strains viz. *Cryptococcus humicola*, *Cryptococcus curvatus*, *Candida kefyr*, and S. *cerevisiae* 832 were noted for increased cholesterol removal (<80%) whereas *Monascus purpureus* CBS was observed for only 2.75 % to 9.27% cholesterol assimilation after 72 hours incubation (**Nguyen *et al.*, 2020**). *Saccharomyces* strains showed cholesterol assimilation ranging from 78.52 to 88.92% and non-*Saccharomyces* strains isolated from milk showed only a 45.7% assimilation rate (**Fernández Pacheco *et al.*, 2021**).

Exopolysaccharide Production (EPS)

Exopolysaccharides (EPS) are extracellular macromolecules excreted by microbes that form a slimy layer around the cell which helps to bound the cell tightly on the surface of the GIT. Production of EPS from probiotics gained more attention due to its applications as drug delivery, bio-flocculants, and bio-absorbents (**Silva *et al.*, 2019**). Probiotic EPS are used to treat various human disorders like inflammatory bowel diseases, cardiovascular diseases, obesity, autoimmune diseases, and especially for colon cancer and gastric ulcers (**Delgado *et al.*, 2020; Saadat *et al.*, 2020**). *S. cerevisiae*, *Candida* sp., and *Pichia* sp., three probiotic yeasts, have been reported for EPS generation and assist in the manufacturing of food and cosmetic items (**Syal and Vohra 2013; Gientka *et al.*, 2016; Yildiran *et al.*, 2019**). The probiotic yeast *L. starkeyi* VIT-MN03 produced six times as much EPS when kept in optimal circumstances utilising the Response surface approach. Probiotic EPS had a flat surface that was good for making films, and it was discovered to be a hetero-polysaccharide (**Ragavan and Das, 2019**). The highest EPS yield was noted for *Candida guilliermondii* and *Candida famata* after optimization of media which ranges from 0.505 and 0.321 129 mg/l respectively (**Gientka *et al.*, 2016**). **Dey *et al.* (2017)** reported the probiotic EPS can be a substantial antimutagenic agent, as shown by its strong binding affinity to the mutagenic compound Glu-P-1. On the generation of EPS by probiotic yeasts, specifically *Wickerhamomyces anomalus* VIT-ASN01 (586.55 mg/l), *S. cerevisiae* VIT-ASN03 (446.88 mg/l), and *Yarrowia lipolytica* VIT-ASN04 (468.72 mg/l).
Probiotic EPS also exhibited significant biosurfactant activity compared to xanthan gum. Additionally, probiotic yeast strains' biosurfactant activity lessens the colonization of harmful bacteria in the stomach (**Ragavan and Das, 2019**). Similar findings about their potential qualities were reported for *P. kluyveri* and *S. cerevisiae* (**Yildiran *et al.*, 2019**). - -Glucan is a yeast by-product with a number of beneficial health effects. The cell walls of many eukaryotic species include a polymer of -(1,3)-D-glucose polysaccharides. *S. cerevisiae*'s cell wall is composed of mannoproteins, -(1,3)-D-glucan, and -(1,6)-D-glucan. The activation of macrophages' non-specific immunological response and stimulation of cell growth are two ways that -glucan is known to have positive effects on health (**Kang *et al.*, 2014**).

Production of Killer toxin

Proteins known as killer toxins bind to particular receptors on the surface of particular microbes. The killer toxin production from yeast species has been well characterized in many studies to prevent spoilage of food products from pathogens (**Mannazzu *et al.*, 2019**). Killer activity by probiotic yeast *Kluyveromyces lactis* VIT-MN02 against food-borne pathogens was reported at optimized conditions (pH 3 at 25°C with 0.5% NaCl) (**Ragavan and Das, 2020a**). According to reports, the yeast strains *Kluyveromyces* sp., *W. saturnus*, *P. anomala*, and *Saccharomyces cerevisiae* produced killer toxin that had similar killing effects on infections (**Golubev, 2013**). The killer toxin was discovered to be 22 kDa (K2), 18 kDa (K3), and 14 kDa (K4) in size. These findings revealed that probiotic yeasts could produce killer toxins to stop bacterial contamination during fermentation (**Meneghin *et al.*, 2010**). The shelf life/quality of the food products is ensured by the antimicrobial protein made by the yeast *Metschnikowia pulcherrima*, which also dramatically decreased the spoiling of ready-to-cook ground beef patties (**Bedir and Kuleaşan, 2021**). It was discovered that the pathogenic yeast *Filobasidiella neoformans* was resistant to the killer toxin produced by *Cryptococcus pinus* VKM Y-2958 (**Kulakovskaya *et al.*, 2019**). The killer toxin activity of probiotic yeast strains from the species *Dekkera* spp, *P. anomala*, *Candida tropicalis*, *Candida pintolopesii*, and *S. cerevisiae* against *Cryptococcus neoformans* has been demonstrated (**Dubash *et al.*, 2010**).

Production of enzymes

Screening for the production of enzymes is the most important criteria for selecting probiotic strain. The enzymes such as ß-glucuronidase, ß-glucosidase and N-acetyl-ß-glucosaminidase are considered as harmful enzymes. These enzymes are associated with GIT diseases and have been reported in some studies. Therefore, care should be taken for selecting probiotic strain producing harmful enzymes. On the other hand, some enzymes, such ß-galactosidases and -glucosidase, are said to benefit the host. In the treatment of lactose intolerance, ß-galactosidases have demonstrated strong activity. Another enzyme, α-glucosidase helps to digest polysaccharide compounds to exert its beneficial effects in the GIT (**Aziz *et al.*, 2019**). The probiotic yeasts viz. *Cryptococcus gastricus*, *Leuconeurospora* sp. produce cellulase enzyme which was reported by **Carrasco *et al.* (2016)**. Catalase is an antioxidant enzyme that gives the first line of defence to the host system. The significant catalase activity observed in probiotic yeasts *Y. lipolytica* and *S. cerevisiae* was reported by **Czech *et al.* (2020)**. Acute lymphoblastic leukaemia and Non-Hodgkin lymphoma (NHL) were two tumours that L-asparaginase was thought to be a promising chemotherapeutic drug to treat. By inhibiting the development of acrylamide, this enzyme also plays a significant function in the food sector in preserving the quality of food. **Ragavan and Das (2020b)** reported two probiotic yeast isolates which showed catalase and L-asparaginase activity.

Production of antimicrobial substances

Antimicrobial substances produced by probiotics are the best replacement for chemical preservatives which can improve the quality of food products. The probiotic yeast isolates showed remarkable antimicrobial activity against common pathogens (**Ragavan and Das, 2017a**). Probiotic yeast substantial antibiotic efficacy against common human infections such as *Enterococcus faecalis*, *E. coli*, *S. typhimurium*, *Pseudomonas aeruginosa*, and *Listeria monocytogenes* was demonstrated by *S. cerevisiae* and *S. boulardii* (**Rajkowska *et al.*, 2012**). Another benefit of *S. cerevisiae var. boulardii* may be its antimicrobial properties and capacity to degrade mycotoxins such as ochratoxin A patulin, and aflatoxins, (**Abdel-Kareem *et al.*, 2019; Liu *et al.*, 2020**). Additionally, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli* and *Bacillus cereus*, growth is inhibited by antimicrobial peptides derived from *S. cerevisiae var. boulardii* (**Naimah *et al.*, 2018**). A typical food-borne infection that causes diarrhea is ETEC (Enterotoxigenic *E. coli*). The main pathogenicity of bacteria is the production of adhesins and enterotoxins. *S. cerevisiae* significantly reduced ETEC growth and toxin generation. The yeast also decreased bacterial adhesion to intestinal Caco-2/TC7 cells. In addition, *S. cerevisiae* reduced the generation of interleukin-8 which is produced by ETEC-infected intestinal cells (**Roussel *et al.*, 2018**).

Metabolites produced by probiotic yeasts

Probiotics have a number of effects, including as preventing pathogen colonization or adhesion, generating metabolites, and modifying the immune system by creating immunoglobulin antibodies (**Chugh and Kamal-Eldin, 2020**). The development and establishment of advantageous microorganisms in the stomach may result in the production of thiamine, folate, propionic acid, folate, and vitamin B12 (**Piwowarek *et al.*, 2018**). B vitamins including B1, B2, B5, B6, B7, and B12 as well as ergosterol, which can be converted to vitamin D2, can all be found in probiotic yeasts. For vitamin B complex, *S. cerevisiae Pichia membranaefaciens*, *Pichia fermentans*, and were reported (**Silva *et al.*, 2011**). Zinc, magnesium, phosphate, iron and absorption in vertebrates are encouraged by the group of fat-soluble chemicals known as calciferol (vitamin D). In recent work, UV-B irradiation of *S. cerevisiae* was used to stimulate the conversion of yeast sterol to ergocalciferol for use as a dietary supplement (**Amiri *et al.*, 2019**). Vitamin A is a necessary human vitamin that aids eyesight, reproduction, immune function, and skin health. Engineered probiotic yeast *Saccharomyces cerevisiae* was reported for synthesis of vitamin A (**Sun *et al.*, 2019**).
In order to stop dangerous microbe adhesion and invasion, probiotics can also change mucin development and the colon's barrier function. Successful probiotics, like *S. boulardii*, should be able to adhere to the intestinal mucous, whereas epithelial cells create mucin to prevent pathogenic bacteria from attaching to them (**Edwards-Ingram *et al.*, 2004**). The amount of accessible pathogen binding sites is decreased as a result of *S. boulardii's* attachment to the mucus membrane. The infections' capacity to connect directly to intestinal receptors and continue with host invasion is constrained by this interaction.

HEALTH BENEFITS RENDERED BY PROBIOTIC YEAST

Probiotic yeast *S. boulardii* has various beneficial properties to maintain host health **(Figure 2**). Probiotic yeast strains were reported for their therapeutic properties to maintain gut microbiota from harsh environmental conditions as well as pathogen colonization (**Table 2**). By producing trophic polyamines or other enzymes, such as alkaline phosphatase, a-glucosidase, maltase-glucoamylase, lactase, and sucrose-isomaltase, probiotic yeast *S. boulardii* promotes improves nutritional absorption and enterocyte maturation (**Moslehi-Jenabian *et al.*, 2010**). Other crucial advantages of probiotic yeasts include enhancing dietary intake, boosting the immune system, preventing GI illnesses, lowering blood cholesterol levels, and, most significantly, reducing the chance of colon cancer (**Saber *et al.*, 2017**). Key metabolic pathways that regulate metastasis, angiogenesis, inflammation, apoptosis, differentiation, and cell proliferation have been

demonstrated to interact with probiotics and their metabolites. Probiotics also affect the function of GI enzymes, prevent pre-cancerous lesions and suppress carcinogenic elements both in vitro and in vivo (**Cousin *et al.*, 2012; Kumar *et al.*, 2013**). One of the leading causes of cancer-related morbidity and mortality in people is colon cancer (**Bocci *et al.*, 2015**). On Caco-2 cell line as opposed to IEC-6 cell line, probiotic yeast showed considerable anticancer action. *K. lactis* VIT-MN02, in particular, demonstrated 75% anticancer efficacy on Caco-2 cells. Therefore, *K. lactis* VIT-MN02, a probiotic yeast, can be utilized to lower the risk of colon cancer. Type 2 diabetes is linked to enzymes like -glucosidase and -amylase. The enzyme -glucosidase is inhibited by *K. lactis* VIT-MN02 (**Ragavan and Das, 2020b**). Hyperglycemia and type 2 diabetes mellitus could both be avoided by inhibiting α-amylase activity (**Ayyash *et al.*, 2018**). The α-amylase enzyme was inhibited by *L. starkeyi* VIT-MN03. As a result, this research demonstrated that the probiotic yeasts *L. starkeyi* VIT-MN03 and *K. lactis* VIT-MN02 can be utilized to maintain or regulate blood sugar levels in humans.

Another study found that *S. cerevisiae* stimulated liquefactive necrosis, and ischemia (coagulative), apoptosis, and tumor degeneration in Swiss albino mice with Ehrlich ascites carcinoma (EAC) (**Ghoneum *et al.*, 2008**). The probiotic *K. marxianus* AS41 isolated from dairy products influences metabolic activity and has pro-apoptotic activity in epithelial cancer cells without affecting normal cells (**Saber *et al.*, 2017**). By inhibiting the mTOR, JAK-1 and AKT-1 pathways, exopolysaccharides produced by *Pichia kudriavzevii* and *Kluyveromyces marxianus* cause apoptosis in many colon cancer cell lines (**Saadat *et al.*, 2020**). In the treatment of colorectal cancer, probiotic yeasts such *Metschnikowia*, *Hanseniaspora*, *Pichia*, *Debaryomyces*, *Candida*, *Kluyveromyces* and *S. cerevisiae var. boulardii* may have anti-cancer characteristics (**Sambrani *et al.*, 2021**). However, it must pass human clinical studies in order to be licenced.

Yeast is a best model organism to investigate the antioxidant activities which has potential industrial applications (**Meng *et al.*, 2017**). *P. fermentans S. cerevisiae* sp. and were found to have antioxidant properties, suggesting that probiotic yeasts can effectively reduce cellular damage caused by oxidative stress (**Chen *et al.*, 2010; Hassan 2011; Sourabh *et al.*, 2011**). Probiotic yeast *L. starkeyi* VITMN03 showed 76% DPPH activity (**Ragavan and Das, 2020b**) whereas 12 strains from *S. cerevisiae* showed only 42% DPPH activity (**de Lima *et al.*, 2017**). Recently, highest antioxidant activity was observed by *Prototheca wickerhamii* 1885 (83%), whereas reference strain *S. boulardii* showed only 70% antioxidant activity (**Ciafardini and Zullo, 2020**). There are reports on probiotic mediated antioxidant activity namely, free radical scavenging activities and H_2O_2 induced stress in GIT which may prevent oxidative damage to maintain host health (**Son *et al.*, 2017; Tang *et al.*, 2017**). The probiotic yeast *S. fibuligera* VIT-MN04 showed more resistance to H_2O_2 up to 86% than other yeasts which could ensure the viability of probiotics during H_2O_2 induced stress conditions. Moreover, probiotic yeast *K. lactis* exhibited 70% hydroxyl radical scavenging activity (**Ragavan and Das, 2020b**).

Figure 2 Health benefits of probiotic yeast *Saccharomyces boulardii*

Table 2 Therapeutic properties of probiotic yeasts

Probiotic yeasts	Therapeutic properties	References
Saccharomyces boulardii	Prevents *Salmonella* & *E. coli* infection	Buts *et al.*, 2006
	Inhibition of toxin production by pathogens like *V. cholerae*, *C. difficile* and *C. perfringens*	Czerucka *et al.*, 2007
	Inhibition of pro-inflammatory cytokine production	Soyturk *et al.*, 2012
Candida krusei	The killer toxin produced by yeast inhibited the growth of pathogenic bacteria such as *S. Typhimurium*, *S. aureus* and *Bacillus cereus*	Ochigava *et al.*, 2011
Pichia rhodanensis, *Pichia spartinae*, *Torulaspora delbrueckii*, *Kluyveromyces lactis* and *Pichia pastoris*	Production of antibodies and human membrane proteins	Goncalves *et al.*, 2013
Pichia kudriavzevii RY55	Mycoccins inhibited the growth of pathogens like *Enterococcus faecalis*, *Klebsiella* sp., *S. aureus*, *H. pylori* eradication	Bajaj *et al.*, 2013
Saccharomyces boulardii	(Neuraminidase from *S. boulardii* removes surface α(2,3)- linked Sialic acid, which is the substrate for *H. pylori* adhesion)	Sakarya and Gunay 2014
	Inhibition of chloride secretion during Rotavirus Diarrhea	Buccigrossi *et al.*, 2014
	Reduced Pro-inflammatory cytokines (IL-8 and TNFα) and increased anti-inflammatory cytokines (IL10) in blood	Abbas *et al.*, 2014
	Reduced cholesterol and uric acid levels	Costanza *et al.*, 2015
S. cerevisiae UFMG A-905 and *S. boulardii*	Immunomodulatory properties through reduction of inflammation and IL-6, TNF-α, Interferon gamma (IFN- γ) and IL-10 production	Palma *et al.*, 2015
Kluyveromyces marxianus & *Metschnikowia gruessii*	Protection and maintenance of epithelial barrier integrity	Smith *et al.*, 2015
Saccharomyces boulardii	Reduced cecal tissue damage, TNFα protein expression, NF-κB phosphorylation and actin disruption caused by *C. difficile* -associated infection	Koon *et al.*, 2016
Saccharomyces cerevisiae	Inhibition of tumor cell proliferation	Sambrani *et al.*, 2021
Saccharomycopsis fibuligera VIT-MN04 and *Lipomyces starkeyi* VIT-MN03	Antagonistic activity against *S. typhimurium* demonstrated using intestinal cell lines	Ragavan and Das 2020b
S. cerevisiae and *S. cerevisiae* var. *boulardii*	Production of vanillic acid, cinnamic acid, phenyl ethyl alcohol (rose oil), erythromycin, amphetamine and vitamin B_6 to exert beneficial effects in host	Datta *et al.*, 2017
Kluyveromyces marxianus PCH397	β-galactosidase-production enhances antioxidant activity	Nag *et al.*, 2022
Saccharomyces cerevisiae and *Kluyveromyces marxianus*	Antifungal activity against moulds species like *A. flavus*, *A. niger*, *P. expansum*, *P. carneum*, *P. spinulosum* and *P. rubens*	Goktas *et al.*, 2021

CONCLUSION

The benefits of probiotic yeasts isolated from various conventionally fermented foods as well as the potential use of these organisms in probiotic products have been studied by the scientific community. More than a decade has been passed on the exploration of the efficacy of probiotic yeast having therapeutic properties for human welfare. Extensive studies have been conducted to fill up the gap between what we know about the important activities of probiotic yeast towards the health benefits. More information has been covered in the field of yeast probiotics by exploiting accumulated knowledge underlying the novel characteristics and other

technological advances as discussed in this review. In order to ensure therapeutic advancement, safety, and the quality of highly consumed probiotic foods containing probiotic yeasts for food firms and human welfare, scientists can use this knowledge at the research and industrial level to re-engineer the goods.

Conflict of interest: None to be declared

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