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Entry

Saccharomyces cerevisiae: Multifaceted Applications in One Health and the Achievement of Sustainable Development Goals

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Definition: *Saccharomyces cerevisiae* (SC), a yeast with an extensive history in food and beverage fermentations, is increasingly acknowledged for its multifaceted application in promoting and benefiting all aspects of a 'One Health' approach, including the prevention and control of zoonoses. For instance, SC contributes to environmentally sustainable agricultural practices through the reduced use of toxic agents, thus minimizing air and soil pollution while enhancing crop quality. Additionally, this versatile yeast can improve the health of domestic and farm animals, leading to more efficient and sustainable food production, while fostering synergistic impacts across environmental, animal, and human health spheres. Moreover, SC directly applies benefits to human health by promoting improved nutrition, improving gut health through probiotics, as an alternative to antibiotics, and treating gastric disorders. By aligning with several Sustainable Development Goals (SDGs), SC is vital in advancing global health and well-being, environmental sustainability, and responsible consumption and production. This entry illustrates the numerous benefits of SC and highlights its significant impact on a global 'One Health' scale, promoting the achievement of SDGs through its unique characteristics and deeper understanding of its contribution to the One Health concept.

Keywords: *Saccharomyces cerevisiae*; brewer yeast; baker yeast; One Health; Sustainable Development Goal; agricultural practices; probiotics; antibiotic alternatives; gastric disorder treatments

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1. Introduction

The concept of One Health emerged in the early 2000s in response to the spread of pathogenic avian influenza H5N1, which threatened human and animal health, the food industry, and the global economy [1]. One Health recognizes the interdependence of human, animal, and environmental health. As the human population expands, our interactions with both domestic and livestock animals, as well as with the environment, are becoming increasingly frequent. This growing closeness is accompanied by intensified human activities, such as large-scale farming and agriculture, which can damage the environment and increase the risk of zoonoses and favor emergence of new diseases.

The One Health approach is a collaborative, multisectoral, and transdisciplinary effort to address health challenges at the intersection of environmental, animal, and human health. One Health emphasizes the interconnected nature of well-being across domains and focuses on disease prevention and surveillance. This approach encourages cooperation among professionals from various disciplines, such as public health, environmental science, and related fields. By promoting innovative solutions that consider the complex relationships between these domains, One Health contributes to a healthier and more sustainable future. This concept aligns with the principles of the Sustainable Development Goals (SDGs) established in 2015 by the United Nations. Both frameworks address global challenges holistically and interconnectedly, covering various social, economic, and environmental issues [2]. Several SDGs are closely linked to the One Health approach, such as good health and well-being (SDG 3), clean water and sanitation (SDG 6), sustainable cities and communities (SDG 11), climate action (SDG 13), and life on land (SDG 15).

Saccharomyces cerevisiae (SC), commonly known as baker's or brewer's yeast, is a versatile microorganism used for centuries in food and beverage production. Beyond its traditional uses, it has diverse applications in biotechnology, biofuel production, and bioremediation. With a flexible genome spanning 12 megabases and containing around 6000 genes, SC is well-suited for various research and technological applications. Its short doubling time of approximately 90 min. and ability to grow in both aerobic and anaerobic conditions further enhance its usefulness [3]. One particularly well-studied strain is *S. cerevisiae var. boulardii* (SCb), which exhibits a trisomy chromosome IX, contributing to its enhanced growth rate and ability to thrive in acidic environments [4,5]. Today, SCb is mainly used as a dietary supplement for healthy individuals and is the most prominent probiotic yeast. Various extracts, such as inactivated dried form, yeast cell wall, yeast extracts, and yeast fermentation byproducts, are used in many fields. These extracts find applications in the food supplement and cosmetic industries (due to their high amino acid or protein content) and in the food and drug industries (for antioxidants such as glutathione peptide, minerals, and vitamins). Probiotics are defined by the Food and Agriculture Organization (FAO) and World Health Organization (WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [6]. Probiotic and supplement consumption has risen in recent decades, and sales are estimated to reach USD 69.3 billion by 2023 [7]. Today, yeast-based probiotics have expanded beyond food supplements and are also used in the food industry to improve soil and crop quality [8].

This entry explores the diverse roles of SC in promoting the One Health approach and advancing the SDGs. As a key player in numerous aspects of human and animal health and food and environmental quality, SC impacts One Health globally. The following sections highlight the various ways SC improves human, animal, and environmental health and supports the achievement of the SDGs.

2. Plants and Environment

2.1. Agriculture: Yeast-Based Fertilizers and Biocontrol Agents

Industrial fertilizers are commonly used in agriculture to increase crop yields, but they are associated with serious environmental and health concerns [9]. In contrast, biofertilizers such as SC-based compounds can efficiently improve soil and crop quality while reducing the need for fertilizer use [10]. For example, SC-inoculated corn plants exhibit significantly increased growth (shoot and root dry weight) and phosphate intake [11]. In other crops, such as lettuce and maize seeds, adding SC boosts chlorophyll content [12]. The innovative reuse of SC brewing waste (exhausted yeast and malt from the fermentation process) in compost can improve soil quality and act as an inorganic nitrogen source for plant growth [13]. The SC-assisted fermentation of coffee waste effectively converts it into ammonia for fertilizer use [14]. Preliminary findings indicate that direct application of dried SC in soil, seeds, or foliage can improve plant growth and serve as a biocontrol agent against fungal pathogens in soil [15,16].

Most chemical agents used to protect crops from plant pathogens negatively impact the environment and human health. Antagonistic yeast species, particularly SC, are becoming increasingly popular as an effective alternative to harmful fungicides [15,17]. The biocontrol activity of yeast is attributed to several mechanisms, including (i) competition for essential nutrients such as iron and methionine [18]; (ii) space competition inhibiting biofilm formation of phytopathogens [19]; (iii) secretion of enzymes such as chitinases, glucanases, lipases, or proteases; (iv) release of volatile organic compounds (VOCs) such as hydrocarbons and phenolic compounds [20]; (v) mycoparasitism (or fungivory) in crops [12,21]; and (vi) induction of plant immune responses, e.g., Cerevisane active ingredient yeast cell walls of SC strain LAS117) and its formulation Romeo® [22–24]. Ongoing mechanistic studies continue to explore the full extent of plant defense stimulation.

Mycotoxins produced by fungal plant pathogens (FPP) such as *Aspergillus carbonarius*, *Aspergillus ochraceus*, *Aspergillus parasiticus*, and *Fusarium graminearum* are estimated to contaminate 60 to 80% of crops worldwide. Different sectors, including the agro-industry, embrace environmentally sustainable practices to reduce synthetic fungicide use but face increased fungi and mycotoxin contamination in fields and during crop storage [25–28]. The harmful effects of food-borne mycotoxins on human health are considered a global health issue [29]. SC strains can effectively inhibit mycotoxigenic fungi growth and reduce mycotoxin levels [25,28] by adsorbing them in the cell wall and lowering polyketide and secondary metabolite production [25,26,30–32].

2.2. Environmental Benefits: Lowering Greenhouse Gas Emissions and Enhancing Bioremediation

In the beer fermentation process, the surplus yeast obtained during brewing, also known as "Brewer's spent yeast" (BSY), has nutritional and health benefits that are not yet fully explored. Finding sustainable ways to utilize this agro-industrial byproduct could be both environmentally and economically relevant [13,33]. Such sustainable practices have also been established for crops such as coffee, corn, and sugarcane, which provide a commonly used and economical substrate—sucrose, for yeast-derived bioethanol in the biorefinery industry [34]. These practices involve using yeast-based fermentation to produce bioethanol and biofuels [14]. The biofuel/biochemical industry is growing as a more sustainable alternative to fossil fuels. Today, the bioethanol industry alone has generated over 100 billion liters worldwide [35]. The biorefinery concept relies on using renewable raw materials obtained through microbial fermentation by organisms such as SC, which plays a significant role in bioethanol production. To enhance the fermentative capacity, genetic and metabolic engineering efforts are being made to optimize these bioprocesses [36–39]. For example, rewiring central carbon metabolism ensures a 30% yield increase of free fatty acids, which can be used as biofuel [35].

Moreover, microorganisms can be harnessed as bio-decontaminating agents for polluted food and environments, a process known as bioremediation. Some probiotic strains can exhibit bio-removal abilities, enabling them to decontaminate foodstuffs of heavy metals and harmful mycotoxins [40–44]. This bioremediation approach has the potential to provide a sustainable and eco-friendly solution for mitigating the risks posed by food and environmental pollution. SC can act as a biosorbent for many heavy metals such as lead (Pb) [41], cadmium (Cd) [45], mercury (Hg) [46], nickel (Ni), chromium (Cr), and arsenic (As) [47] by sequestering these elements in available cellular binding sites [45]. Recent studies have reported that SC can trap between 65% and 79% of Pb and Cd from contaminated soil and significantly reduce zearalenone mycotoxin levels in silage by over 90% within 2 days through SC degradation and adsorption [48,49]. Furthermore, decontamination can be further enhanced by yeast bioengineering. For example, engineered strains of SC with integrated human recombinant MT2 and GFP-hMT2 genes demonstrated an increased capacity for copper ion bioremediation [50]. Another approach to reducing environmental pollution is decreasing the methane generated by cattle farming, which substantially contributes to global greenhouse gas emissions; however, this prospect requires further investigation [51,52].

3. Animals

3.1. Animal Health

Incorporating yeast-based food supplements into the animal diet can enhance their health in line with the One Health approach [53]. A recent meta-analysis found that incorporating SC into the diet of dairy cows resulted in higher milk yield (1.18 kg/d compared to 1.61 kg/d; $p < 0.05$), as well as increased milk fat yield (0.06 kg/d; $p < 0.05$)

and milk protein yield (0.03 kg/d; $p < 0.05$) [54]. The authors also reported positive effects of SC on improved growth performance, enhanced rumen development, and increased immunocompetence in calves [54]. Additionally, SCb has been shown to decrease the incidence of diarrhea in calves bred in commercial farming environments, allowing them to maintain their growth performance while also positively affecting their gut microbiome composition similar to that of healthy animals [55]. Furthermore, adding SC enzymatically hydrolyzed yeast (EHY) and autolyzed yeast (AY) to broiler chicken and quail feed improved growth performance. Similarly, the dietary inclusion of AY in laying hens resulted in enhanced egg production and weight. Overall, these performance improvements are attributed to the yeast components, i.e., mannan-oligosaccharides and β-glucans, providing pre- and probiotic benefits to the animal's gut [56]. Additionally, the health and performance of farmed fish may also be improved by including SC in their diets, resulting in improved growth, disease resistance, and a healthier microbiota [57–59].

According to the neutral ecology theory, SC may not occupy a specific ecological niche [60]. However, in nature, SC can be found in oak bark, soil, and insects. It takes refuge in the gut of insects, such as wasps and drosophila, for breeding. Still, these hosts also benefit from SC as it enhances their immune system, provides essential nutrients for proper development, and attracts other insects as food sources [8,61].

The global market for animal probiotics was valued at USD 3.76 billion in 2022 and is expected to reach USD 7.47 billion by 2032 ("Fact.MR—Animal Probiotics Market—Global Insights 2022 to 2032" 2022). Additionally, the use of yeast-based supplements in pets has been shown to improve their health. For example, including SC-based products in the diets of healthy pet rabbits has been shown to improve their gut microbiota [62]; and the digestibility of crude fiber and ashes by adult cats was enhanced [63].

3.2. Food Quality

In the context of the One Health approach, the well-being and quality of the food produced by animals are closely tied to the quality of food they consume, underscoring the significance of their interdependence. Research has shown that mycotoxin contamination in feed crops can negatively impact animal health, reduce farm productivity, and cause economic losses [64]. A recent meta-analysis focusing on the effects of SC on the poultry industry, specifically broiler farming, found that yeast cell wall extract (YCWE) can mitigate the adverse effects of mycotoxin consumption by binding to mycotoxins in the feed [65].

Feeding farm animals antibiotics to prevent the spread of pathogens, such as *Salmonella enterica serovar typhimurium*, to humans has been a common practice for a long time. However, the adverse effects of using antibiotic growth promoters (AGPs) have raised concerns, such as the development of antibiotic-resistant bacteria and the build-up of antibiotic residue in food products. As an alternative, pre- and probiotic food additives influence the gut microbiota, reduce the growth of pathogenic bacteria, and enhance the mucosal immune system. For example, the combination of SCb-based probiotics with β-galactomannan (βGM) prebiotics can strengthen the immune response against *Salmonella enterica* in porcine intestinal epithelial cells (IECs) by promoting the secretion of anti-inflammatory cytokines and favoring dendritic cell maturation [66]. SC can also decrease inflammatory responses induced by F4+ enterotoxigenic *Escherichia coli* in porcine IECs [67]. In poultry, SC-based probiotics increase cellular immune response ($p = 0.019$). No presence of *Salmonella* sp. was found in tested animals, and the growth of *E. coli* was significantly reduced [68]. Additionally, the harmful effects of pesticides, such as hindered growth, are reduced when the animal diet is supplemented with SC, e.g., the Nile tilapia fish *Oreochromis niloticus* [69].

4. Humans

4.1. Nutrition

In the context of the holistic One Health approach, SC has a long history of use in food and beverage fermentation, including bread, beer, and wine. Today, SC-based fermentation is utilized to create new food products that cater to dietary and nutritional needs, promoting human health.

Protein is an essential part of the human diet, serving as the backbone of muscle and bone tissue, necessary for crucial cellular and physiological processes, and is involved in maintaining, growing, and repairing body tissue [70]. While animal-based products such as meat and eggs have traditionally been the primary protein sources, current dietary guidelines advocate for incorporating other protein sources such as plants (e.g., beans, peas, lentils) and nutritional yeast (Nooch). Nooch is an environmentally friendly, easily digestible, and affordable alternative to animal-based protein, rich in B vitamins, minerals, and antioxidants [71]. Yeast-protein production can utilize various waste substrates, resulting in protein biomass ranging from 33% for treated distillery sludge to 54% for spruce-derived sugars and protein hydrolysates from chicken byproducts [71].

Yeast can enhance the flavor of food by improving taste, emphasizing flavors, and acting as an efficient flavor distribution method [72,73]. Microencapsulation, employed in the food industry since the 1950s, involves surrounding a core material (e.g., a bioactive compound) with a microcapsule. This technique can protect compounds, improve shelf life and food stability, and provide controlled bioavailability of core materials. Ingredients that are unstable or sensitive to food processing are protected by the capsule, which can mask undesirable flavors, colors, or textures [74]. SC is particularly suitable for micro-encapsulation for the food industry as it is biodegradable, affordable, and does not impact the food's flavor or color [75,76]. Other essential features of microcapsules are photochemical, oxidative, and thermal stability, release mechanism, and functionality of the core compound following release. Microencapsulation techniques are either chemical (interfacial polymerization, emulsification, phase separation, coacervation, and liposome formation) or physical/mechanical (solvent evaporation, fluidized-bed coating, extrusion, emulsification, and spray drying) [74,76]. The most popular encapsulation method is spray drying, which is simple, fast, and cost-effective but not adapted to temperature-sensitive compounds. At low temperatures, extrusion can be used but is difficult to implement on a large scale and has low productivity. Finally, coacervation, a modified emulsification method, is adapted to hydrophobic compounds and has up to 99% encapsulation yield. Nonetheless, experimental parameters need to be carefully controlled [77]. It should also be noted that yeast-based microencapsulation can be extended to the delivery of other molecules [74,75,78].

SC also plays a role in human nutrition by acting as a potent cell factory following the bioengineering of endogenous pathways. This applies to complex natural products such as L-ornithine, an intermediate of L-arginine [79], and plant metabolic intermediates such as flavonoids [80]. SC's aromatic amino acid pathways can be metabolically engineered to produce key flavonoid intermediates such as naringenin solely from glucose and in higher amounts (40-fold) [80]. Consequently, SC is a powerful food source, encapsulating agent, and de novo cell factory that contributes to sustainable nutrition improvement.

4.2. SC to Improve Health

Aligned with the One Health approach, probiotics, regarded as dietary supplements capable of enhancing human health, can reduce gastrointestinal (GI) infections, control the growth of gut bacteria and fungi, regulate the immune system, and exhibit anti-carcinogenic, anti-mutagenic, and anti-toxin properties [81]. Although the exact mechanisms behind these benefits are not fully understood, probiotics may work by competing for nutrients, colonizing space, and occupying binding sites on IECs. Furthermore, probiotics have been administered as an alternative to antibiotics. A randomized controlled trial reported that preoperative treatment with SCb-based probiotics in patients undergoing colon resection can significantly regulate the intestinal immune response, such as T cell activation and IL-1β production. This results in a lower rate of postoperative infections (13.3% in SCb-treated patients compared to 38.8% in the control group; $p > 0.05$) [82]. Each probiotic strain has unique characteristics and benefits, allowing the combination of different probiotics to achieve a potent response [4]. Clinical trials have revealed that SCb probiotics are highly effective in treating GI disorders that cause diarrhea. Antibiotic-associated diarrhea (AAD) is caused by prolonged use of antibiotics, and the preferred treatment for both adults and pediatric patients is probiotics. Moreover, SCb probiotics significantly reduce the rapid stool frequency in patients with acute diarrhea [4,83]. Additionally, SC probiotics (strain CNCM I-3856) have demonstrated multiple properties that inhibit diarrhea caused by the Enterotoxigenic *Escherichia coli* (ETEC) [84].

Chronic GI disorders, such as irritable bowel syndrome (IBS), can lead to discomforts such as abdominal pain, bloating, and changes in bowel habits. This syndrome can affect up to 20% of the population in given geographical locations and can significantly reduce their quality of life. According to the Rome III IBS diagnostic criteria, IBS is characterized by abdominal pain or discomfort, which is connected to at least two of the following symptoms: relief with defecation and changes in stool frequency or consistency. The SC CNCM I-3856 strain has been effective in reducing abdominal pain (Relative Risk = 1.3, 95% Confidence Interval 1.04, 1.6) and in the overall management of IBS [83,85,86]. Crohn's disease (CD) and ulcerative colitis (UC) are collectively known as inflammatory bowel disease (IBD) [87]. UC is limited to the colon and rectum, while CD may affect any segment of the GI tract. IBD is often treated by broad-spectrum antibiotics. However, with rising reports of antibiotic resistance, SC-based probiotics are being used as an alternative [4]. Probiotics can maintain a healthy gut microbiome, reduce pro-inflammatory cytokines secretion, and treat the pathogenesis of UC. A study in a CD animal model—CEACAM6-expressing mice—showed that SC reduced colitis induced by Adherent-invasive *Escherichia coli* (AIEC) [88]. This may be effective for a sub-group of CD patients more susceptible to AIEC colonization due to abnormal CEACAM6 expression of the ileal mucosa. Studies in CD often linked to the over-colonization of damaging bacteria show that SCb treatment lowers intestinal permeability ($1.6 \times 10^{+9}$/d for 4 months) [89], reduces relapses, and has no adverse events (1 g/day for 3 to 6 months) [90]. However, some studies report no significant benefit [91]; thus, further research is needed.

The balance of microorganisms in the vaginal microbiome is delicate, much like the gut microbiome. Bacterial vaginosis (BV), a common vaginal dysbiosis, can cause serious obstetrical and gynecological complications and impact women's quality of life. Currently, antibiotics are often ineffective in treating BV; however, SC-based probiotics show promising results in treating BV by inhibiting the development of *Gardnerella vaginalis* biofilm [92–94]. Furthermore, the yeast *Candida albicans* commonly lives on the skin, gut, mouth, and vagina and can cause a range of disorders if it overgrows. The current treatment strategy uses antifungal drugs with several side effects and contributes to the emergence of resistant strains. The use of selected SC strains, such as SC CNCM I-3856 (live or inactivated cells), is effective against oropharyngeal and vaginal candidiasis. Indeed, a lower bacterial load in the oral cavity, esophagus, stomach, and duodenum was reported, and the antimicrobial capacity of neutrophils was consistently improved [95,96]. Other research indicates that the adherence capacity of the infecting agent to healthy epithelial cells was reduced, and virulence was suppressed following SC treatment [97].

5. Conclusions and Perspectives

The significance of *Saccharomyces cerevisiae* in the context of One Health and its alignment with the Sustainable Development Goals (SDGs) stems from its involvement in the intersection of environmental, animal, and human health.

In the context of One Health, it is essential to highlight the major contributions of SC. The distinct properties of SC hold considerable importance in the prevention and management of zoonoses while fostering synergistic impacts across environmental, animal, and human health spheres. Examining the intricate engagement of SC within the One Health approach highlights its capacity as an essential resource for promoting sustainable development.

The current agricultural practices cause severe environmental and health problems, making it crucial to find sustainable solutions following SDG 2, which focuses on ending hunger, achieving food security, and promoting sustainable agriculture. The use of yeast as natural fertilizers can be one solution, as SC-based biofertilizers not only enhance crop growth and nutrient uptake (e.g., phosphorus and nitrogen), but also act as a biocontrol agent against soil-borne pathogens (e.g., mycotoxins, fungal pathogens, and bacteria), thereby replacing the need for harmful chemicals. Additionally, SC fermentation of agro-industry byproducts can generate bioethanol and biofuels, which decrease greenhouse gas emissions and provide a sustainable alternative to fossil fuels, and supports SDG 7, which aims to ensure access to affordable, reliable, sustainable, and modern energy. Efforts are underway to optimize the fermentative capacity of SC, given that this method is more cost-effective, environmentally friendly, and sustainable than current practices.

In the animal health domain, supplementing animal feed with SC-based supplements aligns with SDG 3, which emphasizes ensuring healthy lives and promoting well-being for all, including livestock. This includes enhancing nutrient absorption, food digestion, gut, and immune system health, boosting performance (e.g., growth, egg or milk production, and milk fat and protein yield), decreasing negative impacts from contaminated feed, and a lower dependence on antibiotics.

Furthermore, SC's applications in human health are also directly linked to SDG 3. SC contributes to human health through its role in probiotics, flavor enhancement, and as a protein source in the form of nutritional yeast. Using SC in probiotics positively impacts gut health, supports the immune system, and serves as an alternative to traditional antibiotics for gastrointestinal disorders, such as irritable bowel syndrome, Crohn's disease, and bacterial vaginosis. Nooch, an emerging alternative yeast-based biomass, provides a cost-effective, easily accessible, and sustainable protein source derived from food processing waste and byproducts, aligning with SDG 12, which promotes responsible consumption and production.

Therefore, SC can play a role at each stage of a One Health approach to promote sustainable health, aligning with the SDGs. The field of yeast-based biotechnology is rapidly growing due to its promising prospects for the agrifood, nutrition, and health industries.

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Abbreviations

AAD: antibiotic-associated diarrhea; AGP, antibiotic growth promoters; AIEC, adherent-invasive Escherichia coli; As, arsenic; AY, autolyzed yeast; BSY, brewer's spent yeast; BV, bacterial vaginosis; CD, Crohn's disease; Cd, cadmium; Cr, chromium; EHY, enzymatically hydrolyzed yeast; ETEC, enterotoxigenic Escherichia coli; FAO, Food and Agriculture Organization; FPP, fungal plant pathogens; GI, gastro-intestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IECs, intestinal epithelial cells; Hg, mercury; Ni, nickel; Pb, lead; SC, Saccharomyces cerevisiae; SCb, Saccharomyces cerevisiae var. boulardii; SDG, sustainable development goal; UC, ulcerative colitis; VOCs, volatile organic compounds; WHO, World Health Organization; YCWE, yeast cell wall extracts; βGM, β-GalactoMannan.

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