Proceedings of ICBSPH 2026 Symposium: Beyond Calories: Food and Nutrition for Sustainable Health
DOI: 10.54254/2753-8818/2026.NL33418

The Mechanism of Action and Clinical Application of Saccharomyces boulardii in Childhood Enteritis

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Abstract. Diarrhea is one of the major health threats to children under five years old worldwide, and repeated intestinal inflammation can also lead to malnutrition, growth retardation and other problems. Saccharomyces boulardii is the infrequent non-pathogenic fungal probiotic used in clinical practice. Compared with traditional probiotics, it has the unique advantages of antibiotic resistance, acid resistance and heat resistance, and can reach the intestine smoothly to exert its effects. This paper sorts out the multidimensional action mechanisms of Saccharomyces boulardii, including antagonizing pathogens in the intestine, regulating body nutrition and immunity, and reducing intestinal mucosal inflammation. Meanwhile, the clinical application effects of this probiotic in children with acute infectious diarrhea, antibiotic-associated diarrhea (ADD) and chronic diarrhea were introduced, and the clinical safety and potential risks of this probiotic were analyzed. Saccharomyces boulardii can effectively shorten the course of diarrhea, reduce the frequency of bowel movements, and is well tolerated. Adverse reactions may occur only in specific populations, and the risk is extremely low. With the development of precision medicine, the application prospects of Saccharomyces boulardii in children's gut health management will be even broader. This article aims to provide a basic reference for research on the restoration of the gut microbiota ecosystem in children.

Keywords: Saccharomyces boulardii, Childhood Enteritis, Mechanism of Action

1. Introduction

According to the World Health Organization (WHO), diarrhea is still the second leading cause of death among children under five years old around the world [1]. Besides directly endangering children's lives, repeated intestinal inflammation caused by diarrhea often leads to serious malnutrition and growth retardation. It has become a major public health problem harming the early growth and development of children worldwide [2]. From a physiological and anatomical perspective, an infant's intestinal structure and function are not yet fully developed. Their intestinal mucosal barrier is relatively weak, and the secretion of stomach acid and digestive enzymes is low. As a result, their ability to fight against pathogens is generally poor. In this situation, children's intestines are easily attacked by pathogenic microorganisms such as rotavirus and pathogenic Escherichia coli. Improper use of antibiotics can also lead to harmful reactions. These external

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factors can destroy the balance of the intestinal microflora, leading to flora imbalance and inflammatory response, and ultimately causing diarrhea in patients.

In the clinical treatment of intestinal microecological disorders in children, Saccharomyces boulardii is the only non-pathogenic fungal probiotics currently used in clinical practice. It has unique advantages different from traditional bacterial probiotics (such as Bifidobacterium and Lactobacillus). Different from bacterial probiotics, Saccharomyces boulardii is a fungus with large cell volume and special cell wall components [3]. Due to its special biological structure, it is naturally resistant to commonly used antibiotics. This property allows it to remain active without being killed when combined with antibiotics in the treatment of bacterial enteritis. Therefore, it can effectively prevent antibiotic-associated diarrhea (AAD) from the beginning [4]. At the same time, this strain has strong acid resistance and heat resistance. It can tolerate the strong corrosive environment of gastric acid and bile, and survive and reproduce in the ileum and colon, against harmful bacteria. These special biological characteristics make Saccharomyces boulardii an ideal choice for clinical improvement of intestinal microecological disorders in children. n order to further understand the clinical value of Saccharomyces boulardii, this article reviews its latest research progress in the treatment of enteritis in children, and analyzes its mechanism of action under different etiologies. This paper aims to provide a new perspective for the study of repairing children 's intestinal microecosystem.

2. The multiple biological mechanisms of saccharomyces boulardii

Saccharomyces boulardii is a special probiotic yeast. It provides rich nutrition and shows excellent biological characteristics at the same time. Its heat resistance and acid resistance enable it to pass through the acidic environment of the stomach smoothly and keep active, so as to enter the intestine and play a multi-dimensional protective role [5]. According to the position and nature of its pharmacological effects, its mechanisms can be divided into intraluminal antagonism, nutritional and immune regulation, and mucosal anti-inflammatory effects.

2.1. Intraluminal antagonism and physical barrier enhancement

Inside the intestinal lumen, Saccharomyces boulardii shows strong ability to resist toxins. It is the only known probiotic that can effectively fight against Clostridium difficile. By secreting a 54 kDa glycoprotein, it directly neutralizes Clostridium difficile toxins A and B, thus playing a key role in preventing and treating ADD. In addition, it can also secrete a 120 kDa glycoprotein to resist cholera toxin, and use protein phosphatase to inactivate lipopolysaccharide (LPS) produced by Escherichia coli [6].

In the aspect of physical defense, the cell wall of this yeast is rich in mannan. It can directly absorb pathogens with fimbriae (such as Escherichia coli and Salmonella) like a "bait", preventing them from adhering to intestinal epithelial cells and excreting them with feces. In addition, Saccharomyces boulardii can significantly increase the expression of tight junction proteins between intestinal epithelial cells, thus strengthening the physical barrier function of the intestine. Simultaneously, it promotes the growth of endogenous probiotics such as Bifidobacterium and Lactobacillus, as well as the synthesis of short-chain fatty acids (SCFAs). Through these effects, it helps maintain the balance of the intestinal microecology and accelerates the recovery of damaged intestinal function.

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2.2. Nutritional metabolism and immune regulation

In terms of nutrition and immune regulation, Saccharomyces boulardii shows a significant "nutritional effect". This yeast can release many kinds of polyamines such as spermidine and spermine in the intestinal lumen. As cell growth factors, these substances can stimulate the expression and activity of disaccharide enzymes (such as lactase and sucrase) in intestinal epithelial cells, and accelerate the maturation and repair of intestinal epithelial cells. It can effectively improve the nutritional absorption during diarrhea in children and shorten the course of viral diarrhea [7].

In addition, Saccharomyces boulardii has a strong immune enhancement function. It can specifically stimulate the intestinal mucosa to produce more sIgA and significantly enhance the local intestinal immune barrier. This immunomodulatory effect is not limited to resistance to viruses, but also improves the body 's overall defense against various pathogenic microorganisms [8].

2.3. Mucosal anti-inflammation and signaling pathway regulation

In terms of mucosal anti-inflammatory effects, studies have confirmed that the yeast can act on a variety of cell signaling pathways and effectively reduce the synthesis and release of pro-inflammatory cytokines. This anti-inflammatory effect can significantly reduce the swelling and congestion of intestinal tissue and create a stable microenvironment for the repair of damaged mucosa [9].

Therefore, the pharmacological mechanism of Saccharomyces boulardii accurately corresponds to the pathological stages of diarrhea, as shown in Figure 1. From neutralizing intestinal toxins, providing physical defense, repairing metabolic nutrition to deep immune and anti-inflammatory regulation, this yeast achieves full coverage of the entire process of diarrhea in children.

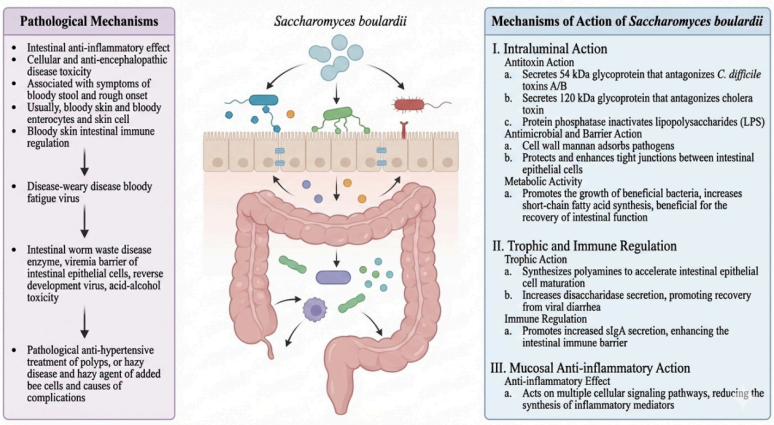


Figure 1. Mechanism of action of Saccharomyces boulardii in the intestinal tract [9]

3. Clinical application of saccharomyces boulardii in various childhood enteritis

Saccharomyces boulardii has demonstrated multidimensional therapeutic value in pediatric clinical practice, and there is a close pathophysiological relationship between its pharmacological mechanism and clinical efficacy.

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3.1. Acute infectious diarrhea in children (viral and bacterial)

Saccharomyces boulardii is widely used as an adjunct therapy in the clinical treatment of acute infectious diarrhea. Multiple randomized controlled trials (RCTs) and meta-analyses have shown that this yeast can significantly shorten the course of diarrhea in children. It can also effectively reduce the frequency of daily bowel movements and shorten hospital stays.

Sajjad et al. found that Saccharomyces boulardii was significantly effective in treating acute watery diarrhea in children aged 2 months to 5 years. It effectively shortened the course of diarrhea, reduced the frequency of bowel movements, and the overall efficacy was satisfactory [10]. Another randomized controlled trial involving 200 children showed similar results. Daily administration of 250 mg of Saccharomyces boulardii significantly shortened the duration of acute diarrhea in children (from 5.5 days to 4.7 days) and reduced hospital stays [11]. In addition, the drug can significantly reduce the frequency of bowel movements in children on the second day of treatment and may reduce the likelihood of diarrhea developing into persistent (protracted) diarrhea.

For a common clinical disease—rotavirus enteritis—Saccharomyces boulardii can enhance the immune barrier by increasing the level of intestinal endocrine immunoglobulin sIgA. At the same time, it can also increase the activity of disaccharidase, relieve osmotic diarrhea caused by viruses, and thus accelerate the recovery of intestinal function. The above clinical evidence emphasizes that early medication within 48 hours of onset is of great significance in improving the prognosis of children.

3.2. Prevention of AAD in children

Excessive use of antibiotics can suppress the growth of beneficial gut microbiota, thereby weakening or damaging the intestinal barrier function and making it more susceptible to pathogenic bacteria. This makes Clostridium difficile more likely to invade intestinal cells, causing AAD. Prevention of AAD is one of the most advantageous clinical applications of Saccharomyces boulardii.

As a kind of fungus, possesses unique inherent antibiotic resistance. This allows it to be administered concurrently with antibiotics in clinical settings without intervals, significantly improving medication adherence in children [12]. Sorensen et al. selected 68 children with antibiotic-associated abdominal pain (AAD) from two medical institutions in India and randomly assigned them in a 1:1 ratio to a probiotic group and a placebo group. Both groups of children took probiotics after taking antibiotics for 3 hours for 7 consecutive days. The results showed that the abdominal pain in the probiotics group was significantly reduced, which effectively improved the overall gastrointestinal health of the children, and shortened the duration of abdominal pain in AAD by 0.6 to 1.95 days [13]. Its mechanism of action is that the yeast can secrete substances such as protein phosphatase, thereby resisting toxins and protecting the growth of endogenous beneficial bacteria (such as Bifidobacterium and Lactobacillus) in the intestine. In this way, it can maintain intestinal microecological balance and reduce the incidence of AAD and pseudomembranous colitis.

3.3. Persistent and chronic diarrhea in children

For persistent chronic diarrhea with a long course of disease, the nutritional repair function of Saccharomyces boulardii has become the key to clinical treatment. These children are often accompanied by intestinal mucosal atrophy and malabsorption. Saccharomyces boulardii directly acts on the damaged intestinal mucosa by synthesizing polyamines to accelerate the maturation and

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regeneration of intestinal epithelial cells. This nutritional effect can not only improve the absorption of nutrients such as carbohydrates in the intestine, but also strengthen the physical barrier by enhancing the tight junction of the intestine and effectively prevent disease recurrence.

Sidiki et al.used Saccharomyces boulardii to treat 178 children with chronic diarrhea from 2 months to 12 years old. Compared with the control group, the average number of defecations per day decreased to 1.4 times on the 6th day of treatment, while the average number of defecations per day in the control group remained at 3.7 times. The duration of diarrhea in the treatment group was 3.2 days, and that in the control group was 5.2 days. The results showed that the average defecation frequency of the Saccharomyces boulardii group was significantly reduced and returned to normal level, and the drug tolerance was good. No adverse reactions were reported during the treatment [14]. In addition, its regulation of cell signaling pathways can continuously reduce mucosal inflammation and provide stable rehabilitation support for children with long-term intestinal dysfunction.

4. Safety and tolerability evaluation

Saccharomyces boulardii has shown good safety in clinical application in pediatrics. As a fungal probiotic, it can be completely excreted with feces. This biological characteristic lays the foundation for its safe application.

4.1. Overall tolerability

A multicenter randomized controlled trial involving 317 children aged 6 months to 5 years provides strong evidence for the safety evaluation of Saccharomyces boulardii [15]. This study compared the efficacy of Saccharomyces boulardii and four Bacillus subtilis mixtures in the treatment of acute gastroenteritis in children. The results confirmed that Saccharomyces boulardii significantly shortened the duration of diarrhea (64.6 hours vs 78.0 hours), improved clinical efficacy, and had good clinical tolerance. No obvious adverse reactions were observed during treatment and follow-up. This high-quality evidence-based medical study further confirms the safety advantages of Saccharomyces boulardii in children and provides strong support for its use as a first-line adjuvant therapy.

4.2. Risk and early warning of severe adverse reactions

As a live bacterial preparation, the most concerning serious risk of Saccharomyces boulardii is fungemia. Although this disease is extremely rare in ordinary children, it still needs to be closely monitored in some pathological conditions. Large-scale retrospective clinical studies have provided accurate reference data for the incidence of fungal infection.

An analysis of 16404 inpatient data showed that the actual incidence of brucella-associated mycosis was very low, at about 0.11 % (or 1.70 cases per 10,000 patient days) [16]. The study further highlighted that admission to the intensive care unit (ICU) is a key risk factor for bacteremia, with a risk of 6.55 times higher than that in the general ward. Despite this risk, its overall incidence is not higher than other common hospital-acquired bloodstream infections. This suggests that clinical practice should focus on closely monitoring critically ill children and children with indwelling catheters in ICU, rather than blindly excluding medication. In addition, in terms of immune-related risks, it is necessary to be alert that Saccharomyces boulardii may induce non-IgE-mediated severe allergic reactions-food protein-induced enteritis syndrome (FPIES).

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Clinical case reports showed that 7 healthy infants (4-10 months old) with no history of allergy developed recurrent severe vomiting, extreme sleepiness, pale complexion, cyanosis and other sepsis-like symptoms within 1-3 hours after taking the yeast [17]. Although these symptoms may subside within 24 hours of discontinuation, this strongly reminds clinicians that the possibility of developing acute systemic allergic reactions should be carefully evaluated and closely monitored, even when Saccharomyces boulardii is used in healthy infants and young children without a history of allergies.

5. Conclusion

Although the efficacy of Saccharomyces boulardii has been widely recognized, further studies are needed to explore its intervention effects on specific rare pathogens (such as parasites or rare enteroviruses). In addition, dietary differences in children from different regions may change the intestinal substrate environment, thereby affecting the efficiency of Saccharomyces boulardii to produce polyamines or short-chain fatty acids. If future studies can combine genomics to screen out children who are most sensitive to the yeast, it will help to improve the accuracy of probiotic treatment in children. In summary, Saccharomyces boulardii plays a central role in shortening the course of acute diarrhea in children, preventing antibiotic-associated diarrhea, and accelerating the recovery of chronic diarrhea through a variety of mechanisms, including intestinal antagonism, enhanced intestinal barrier, nutritional repair, and immune regulation. Its favorable safety record and unique pharmacological properties make it an indispensable drug in the field of pediatric intestinal microecological restoration. With the deepening understanding of precision medicine and dietary interactions, the application prospects of Saccharomyces boulardii in children's intestinal health management will be even broader.

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