

## Management of Covid-19 By Using Probiotics (An Overview)

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### ABSTRACT

Probiotics are known to restore a stable gut microbiota by regulating innate and adaptive immunity within the gut, demonstrating the possibility that they may be used to combat COVID-19 because of several pieces of evidence suggesting that COVID-19 has an adverse impact on gut microbiota dysbiosis. Coronavirus disease 2019 (COVID-19) was declared a pandemic at the beginning of 2020, causing millions of deaths worldwide. Millions of vaccine doses have been administered worldwide; however, outbreaks continue. Thus, probiotics and their metabolites with known antiviral properties may be used as an adjunctive treatment to combat COVID-19. Several clinical trials have revealed the efficacy of probiotics and their metabolites in treating patients with SARS-CoV-2. However, its molecular mechanism has not been unravelled. The availability of abundant data resources and computational methods has significantly changed research finding molecular insights between probiotics and COVID-19.

Given that COVID-19 is thought to have a negative effect on gut microbiota dysbiosis and that probiotics are known to restore a stable gut microbiota by modulating innate and adaptive immunity within the gut, it is possible that probiotics may be utilised to treat COVID-19. Beginning in 2020, the coronavirus illness of 2019 (COVID-19), which claimed millions of lives worldwide, was labelled a pandemic. Worldwide, millions of vaccination doses have been given; nonetheless, outbreaks persist. In order to attack COVID-19, probiotics and their recognised antiviral metabolites may be employed as an adjuvant therapy. The effectiveness of probiotics and their metabolites in treating patients with SARS-CoV-2 has been demonstrated in numerous clinical investigations. Its chemical mechanism has not yet been uncovered, though. The research uncovering molecular insights between probiotics and COVID-19 has been considerably altered by the availability of rich data resources and computational tools.

Probiotics are living, gastrointestinal (GI) tract-dwelling bacteria that are advantageous to their hosts and prevent a number of ailments. Following a thorough introduction to probiotics, this article will go into the definition, categorization, and mechanism of action of the most commonly utilised organisms.

**Keywords:** *Coronavirus disease, COVID-19, Probiotics.*

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### INTRODUCTION

The term probiotic means "for life" which is derived from Greek. In 1965 Lilly and Stillwell described substances secreted by one micro-organism that stimulate the growth of another [1,2]. In 1974 probiotic definition was modified by Parker "organisms and substances which contribute to intestinal microbial balance" [1,3]. The current definition of probiotics according to the World Health Organization (WHO) is "live micro-organisms which when administered in sufficient amounts confer a health benefit to the host" [4-6]. Probiotic have therapeutic effects including ability to colonize the intestinal tract, gastric acid and bile salt stability, ability to adhere to the intestinal mucosa [1,7]. Probiotics are found primarily in three main categories in the global marketplace- dietary supplements, foods and pharmaceuticals.

The most commonly used microbes as probiotics include species from the genera *Bifidobacterium*, *Saccharomyces* and *Lactobacillus*. Corona virus disease was declared a pandemic at the beginning of 2020 causing millions of deaths worldwide. Probiotics are known to restore a stable gut microbiota by regulating innate and adaptive immunity within the gut because of several pieces of evidence suggesting that COVID-19 has an adverse impact on gut microbiota dysbiosis. Probiotics and their metabolites with known antiviral properties may be used as a treatment to combat COVID-19. The administration of probiotics is considered to relieve COVID-19 symptoms by boosting immune host response and

improving gut microbiota. As we know that COVID-19 has various mutant which is directly inhibit our immune system and those people who has low immunity can affect badly through the COVID-19. Recently (as of 28 November 2021-time of analysis) a delay super variant of SARS COV-2 with around 50 mutations overall called omicron has been classified as the “variant of concern by world health organization (WHO). Probiotics are a beneficial live microorganism which, when administrated in sufficient quantity are known to participate in metabolism, improving the microbial balance in the gut [8–10]. Probiotics of mainly the strains of lactic acid bacteria, in particular *Lactobacillus* and *Bifidobacterium* genera, show various health effects [11]. Their well-established properties have been extensively studied, primarily modulating the gut microbiota via the growth suppression of opportunistic bacteria [12]. Beyond the gut, probiotics have been reported to exert beneficial health effects through several potential mechanisms, including immunomodulation, epithelial barrier function maintenance, and signal transduction modulation [13]. Mechanisms of action that researchers have discovered in different probiotic strains include modulation of immune system, interactions with gut microbiota, production of organic acids, competitive exclusion, improved barrier function, manufacture of small molecules with systemic effects and production of enzymes.

## CLASSIFICATION OF PROBIOTICS

Microorganisms as probiotics [1, 14, 15] name (e.g., *Lactobacillus*). It organisms based on physical, metabolic , and metabolic end products. second name (e.g., *acidophilus*). It is a much more classification based on them from other species. Even more the same species into subgroups based on have from other of the species(e.g., strain LA5) [1, 16].

### **Lactobacillus species**

The term "*Lactobacillus*" refers to a family of obligate and facultative anaerobes in the human gastrointestinal and genitourinary tracts that produce lactic acid [17, 19–22]. The ability of the bacterium to create lactic acid, not its capacity to digest lactose, is what gives it the name *lactobacillus* [18]. In contrast to antibiotics, *lactobacilli* are utilised therapeutically as probiotics. They are consumed with the purpose of recolonizing the body in order to give nutritional benefits, including the induction of growth factors and an increase in the bioavailability of minerals [22]. They are regarded as "friendly" bacteria. Intestinal permeability is reduced and the mucosal barrier is stabilised by *lactobacilli* [23].

### **Bifidobacterium species**

*Bifidobacterium* is a pleomorphic, anaerobic, Gram-positive rod that does not produce spores. Lactic and acetic acids are by products of the use of glucose by bacteria belonging to the species *Bifidobacterium*. According to secondary sources, the probiotic bacteria known as BB536 was first discovered in the healthy intestinal tract of young children. *Bifidobacteria* appear to lessen the side effects of *Helicobacter* therapy when combined with *Lactobacillus* species and the probiotic yeast *Saccharomyces boulardii*, but they do not appear to increase compliance [24]. Probiotics: A Comprehensive Review of Their Classification, Mechanism of Action, and Role in Human Nutrition is another resource. 23 In severely unwell neonates, *Bifidobacterium infantis* and *Lactobacillus acidophilus* appear to lower the prevalence of NEC and NEC-related death [25].

### **Bacillus species**

As a Gram-positive rod that makes lactic acid, *Bacillus coagulans* is sometimes mistaken for lactic acid bacteria like *lactobacillus*. In reality, some commercial goods containing *B. coagulans* are promoted as "spore-forming lactic acid bacteria" or *Lactobacillus sporogenes*. It produces spores, which is a crucial characteristic for separating these species. Similar to other probiotics like *lactobacillus* and *bifidobacterium*, *B. coagulans* is employed therapeutically; however, *B. coagulans* is not a part of the typical human flora. Probiotics must be able to remain and colonise in the intestinal mucosa in order to be effective at restoring normal flora and preventing pathogenic colonisation. What happens to the *Bacillus* spore when it is consumed by humans is unknown. It is unknown if the *Bacillus* spore is capable of germinating in the intestinal tract or if colonization occurs [26].

### **Saccharomyces spp**

*Saccharomyces cerevisiae*, often known as *S. boulardii*, is a nonpathogenic yeast strain that has been used to treat and prevent diarrhoea caused by a variety of etiologies. In Indochina, tropical fruit skins from which *S. boulardii* was isolated. These fruit skins have been utilised for treating and preventing diarrhoea by Indochina's native population for a very long time [27].

## MECHANISM OF ACTION CONCLUSIONS

The fight against COVID-19 has a long way to go. Despite readily available vaccines and several attempts to immunise against SARSCoV-2, the number of COVID-19 cases rises everyday. The economic system and public health are both being severely hampered by this. Due to the presumable antiviral actions of probiotics and their metabolites, using probiotics as a complementary method in addition to vaccinations to inhibit COVID-19 should be taken into

consideration in this situation. Additionally, probiotics' molecular mechanisms may shed fresh light on how they fight the SARS-CoV-2 infection. Understanding the molecular effects of probiotics on SARS-CoV-2 is possible by utilising substantial advancements in bioinformatics and computational investigations. Probiotics-related research against viruses, such as SARS-CoV-2, can benefit from currently available data on probiotics, human microbiota, health profile, and food, as well as from two well-known computational methodologies, microbiome-driven approach and ensemble-driven docking approach. The case study we conducted and presented demonstrates the feasibility of researching the molecular insight of probiotics against COVID-19. It reveals the antiviral ability of *Lactobacillus plantarum* metabolites PlnE and PlnF against SARS-CoV-2 nsp13 utilising molecular docking approach. As a result, combining probiotic data with already available computational tools will greatly advance COVID-19 research.

## REFERENCES

- Hawrelak J, BNat(Hons)(2013). Probiotics. In: Pizzorno JE, Murray MT, editors. Textbook of Natural Medicine. 4th ed. St. Louis, Missouri: Churchill Livingstone Elsevier. p. 979–94.
- Lilly DM, Stillwell RH(1965). Probiotics: growth-promoting factors produced by microorganisms. Science (New York, NY);147(3659):747–8.
- Parker R(1974). Probiotics, the other half of the antibiotic story. Animal Nutrition and Health; 29:4–8.
- Chen LA, Sears CL(2015). Prebiotics, Probiotics, and Synbiotics. In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th ed. Philadelphia, PA: Saunders Elsevier. p. 19–25.e1.
- Sanders ME(2008). Probiotics: definition, sources, selection, and uses. Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America; 46 Suppl 2:S58–61; discussion S144–51.
- Guarner F, Schaafsma GJ(1998). Probiotics. International Journal of Food Microbiology. 39(3):237–8
- Dunne C, O'Mahony L, Murphy L, Thornton G, Morrissey D, O'Halloran S, et al(2001). In vitro selection criteria for probiotic bacteria of human origin: correlation with in vivo findings. The American Journal of Clinical Nutrition; 73(2 Suppl):386s–92s.
- Mack, D(2005). Probiotics-mixed messages. Can. Fam. Physician Med. Fam. Can. 51, 1455–1457, 1462.
- Bezirtzoglou, E.; Stavropoulou, E(2011). Immunology and probiotic impact of the newborn and young children intestinal microflora. Anaerobe. 17, 369–374. [CrossRef] [PubMed]
- Marinova, V.Y.; Rasheva, I.K.; Kizheva, Y.K.; Dermenzhieva, Y.D.; Hristova, P.K(2019). Microbiological quality of probiotic dietary supplements. Biotechnol. Biotechnol. Equip. 33, 834–841. [CrossRef]
- Salminen, S.J.; Gueimonde, M.; Isolauri, E(2005). Probiotics that modify disease risk. J. Nutr. 135, 1294–1298. [CrossRef]
- Mousavi Khaneghah, A.; Abhari, K.; Es, I.; Soares, M.B.; Oliveira, R.B.A.; Hosseini, H.; Rezaei, M.; Balthazar, C.F.; Silva, R.; Cruz, A.G.; et al(2020). Interactions between probiotics and pathogenic microorganisms in hosts and foods: A review. Trends Food Sci. Technol. 95, 205–218. [CrossRef]
- Wan, L.Y.; Chen, Z.J.; Shah, N.P.; El-Nezami, H(2016). Modulation of Intestinal Epithelial Defense Responses by Probiotic Bacteria. Crit. Rev. Food Sci. Nutr. 56, 2628–2641. [CrossRef]
- Goldin BR(2008). Health benefits of probiotics. The British Journal of Nutrition. 80(4):S203–7.
- Macfarlane GT, Cummings JH(1999). Probiotics and prebiotics: can regulating the activities of intestinal bacteria benefit health? BMJ (Clinical Research ed). 318(7189):999–1003.
- McKane L, Kandel J(1986). Microbiology: Essentials and Applications. New York: McGraw-Hill.
- Fujisawa T, Benno Y, Yaeshima T, Mitsuoka T(1992). Taxonomic study of the *Lactobacillus acidophilus* group, with recognition of *Lactobacillus gallinarum* sp. nov. and *Lactobacillus johnsonii* sp. nov. and synonymy of *Lactobacillus acidophilus* group A3 (Johnson et al. 1980) with the type strain of *Lactobacillus amylovorus* (Nakamura 1981). International Journal of Systematic Bacteriology. 42(3):487–91.
- Vanderhoof JA, Young RJ(2004). Current and potential uses of probiotics. Annals of Allergy, Asthma & Immunology: Official Publication of the American College of Allergy, Asthma, & Immunology. 93(5 Suppl 3):S33–7.
- McGroarty JA(1993). Probiotic use of lactobacilli in the human female urogenital tract. FEMS Immunology and Medical Microbiology. 6(4):251–64.
- Bruce AW, Reid G(1988). Intravaginal instillation of lactobacilli for prevention of recurrent urinary tract infections. Canadian Journal of Microbiology. 34(3):339–43.
- Gupta K, Stapleton AE, Hooton TM, Roberts PL, Fennell CL, Stamm WE(1998). Inverse association of H<sub>2</sub>O<sub>2</sub>-producing lactobacilli and vaginal *Escherichia coli* colonization in women with recurrent urinary tract infections. The Journal of Infectious Diseases. 178(2):446–50.
- Madsen KL, Doyle JS, Jewell LD, Tavernini MM, Fedorak RN(1999). *Lactobacillus* species prevents colitis in interleukin 10 gene-deficient mice. Gastroenterology. 116(5): 1107–14.
- Shornikova AV, Casas IA, Isolauri E, Mykkanen H, Vesikari T(1997). *Lactobacillus reuteri* as a therapeutic agent in acute diarrhea in young children. Journal of Pediatric Gastroenterology and Nutrition. 24(4):399–404.

24. Cremonini F, Di Caro S, Covino M, Armuzzi A, Gabrielli M, Santarelli L, et al(2002). Effect of different probiotic preparations on anti-Helicobacter pylori therapy-related side 36 Probiotics and Prebiotics in Human Nutrition and Health effects: a parallel group, triple blind, placebo-controlled study. *The American Journal of Gastroenterology*. 97(11):2744–9.
25. Hoyos AB(1999). Reduced incidence of necrotizing enterocolitis associated with enteral administration of Lactobacillus acidophilus and Bifidobacterium infantis to neonates in an intensive care unit. *International Journal of Infectious Diseases: IJID: official publica- tion of the International Society for Infectious Diseases*. 3(4):197–202.
26. Duc le H, Hong HA, Barbosa TM, Henriques AO, Cutting SM(2004). Characterization of Bacillus probiotics available for human use. *Applied and Environmental Microbiology*. 70(4):2161–71.
27. Buts JP(2005). [Lyophilized Saccharomyces boulardii: example of a probiotic medicine]. *Revista de gastroenterologia del Peru: organo oficial de la Sociedad de Gastroenterologia del Peru*. 25(2):176–88.
28. O'Toole PW, Cooney JC(2008). Probiotic bacteria influence the composition and function of the intestinal microbiota. *Interdisciplinary Perspectives on Infectious Diseases*. 2008; 2008:175285.
29. Fuller R(1991). Probiotics in human medicine. *Gut*. 32(4):439–42.
30. Fuller R, Gibson GR(1997). Modification of the intestinal microflora using probiotics and prebiotics. *Scandinavian Journal of Gastroenterology Supplement*. 222:28–31.
31. Mack DR, Michail S, Wei S, McDougall L, Hollingsworth MA(1999). Probiotics inhibit enteropathogenic E. coli adherence in vitro by inducing intestinal mucin gene expres- sion. *The American Journal of Physiology*. 276(4 Pt 1):G941–50.
32. Rolfe RD(2000). The role of probiotic cultures in the control of gastrointestinal health. *The Journal of Nutrition*. 130(2S Suppl):396s–402s.
33. Juven BJ, Meinersmann RJ, Stern NJ(1991). Antagonistic effects of lactobacilli and pediococci to control intestinal colonization by human enteropathogens in live poultry. *The Journal of Applied Bacteriology*. 70(2):95–103.
34. Mishra C, Lambert J(1996). Production of anti-microbial substances by probiotics. *Asia Pacific Journal of Clinical Nutrition*. 5(1):20–4.
35. Perdigon G, Alvarez S, Rachid M, Agüero G, Gobbato N(1995). Immune system stimulation by probiotics. *Journal of Dairy Science*. 78(7):1597–606.
36. Link-Amster H, Rochat F, Saudan KY, Mignot O, Aeschlimann JM(1994). Modulation of a specific humoral immune response and changes in intestinal flora mediated through fermented milk intake. *FEMS Immunology and Medical Microbiology*. 10(1):55– 63.
37. Schiffrin EJ, Rochat F, Link-Amster H, Aeschlimann JM, Donnet-Hughes A(1995). Immuno- modulation of human blood cells following the ingestion of lactic acid bacteria. *Journal of Dairy Science*. 78(3):491–7.
38. Schultz M, Sartor RB(2000). Probiotics and inflammatory bowel diseases. *The American Journal of Gastroenterology*. 95(1 Suppl):S19–21.
39. Sutas Y, Hurme M, Isolauri E(1996). Down-regulation of anti-CD3 antibody-induced IL-4 production by bovine caseins hydrolysed with Lactobacillus GG-derived enzymes. *Scandinavian Journal of Immunology*. 43(6):687–9.
40. Peltó L, Isolauri E, Lilius EM, Nuutila J, Salminen S(1998). Probiotic bacteria down-regulate the milk-induced inflammatory response in milk-hypersensitive subjects but have an immunostimulatory effect in healthy subjects. *Clinical and Experimental Allergy: Journal of the British Society for Allergy and Clinical Immunology*. 28(12):1474– 9.
41. Miele E, Pascarella F, Giannetti E, Quaglietta L, Baldassano RN, Staiano A(2009). Effect of a probiotic preparation (VSL#3) on induction and maintenance of remission in children with ulcerative colitis. *The American Journal of Gastroenterology*. 104(2):437–43.
42. Vanderhoof JA, Young RJ(1998). Use of probiotics in childhood gastrointestinal disorders. *Journal of Pediatric Gastroenterology and Nutrition*. 27(3):323–32.
43. Wilson KH, Perini F(1988). Role of competition for nutrients in suppression of Clostridium difficile by the colonic microflora. *Infection and Immunity*. 56(10):2610–4.