Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Special Issue -1]2022 : 123-129

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Therapeutic Potential, Health Benefits and Mechanism of Action of Probiotics: A Concise Review

Nirmala Sehrawat[1], Mukesh Yadav*[1], Sunil Kumar[1], Sneh Lata[2], Ashwani Kumar[3], Amit Kumar[4], Manoj Singh[1], Vikas Kumar[1]

[1]Department of Biotechnology, Maharishi Markandeshwar (Deemed to be University), Mullana-Ambala, Haryana, India
[2]University Institute of Biotechnology, Chandigarh University, Gharuan, Punjab, India
[3]Department of Biotechnology, Chaudhary Bansi Lal University, Bhiwani 127021, Haryana, India
[4]Department of Biotechnology, School of Engineering and Technology, Sharda University, Greater Noida, India
*Corresponding Author Email Id: mukeshyadav7@gmail.com

ABSTRACT

Probiotics are the microorganisms that provide health benefits to hosts when administered in adequate amounts. Probiotic strains are mainly consumed in form of fermented dairy products and also as commercially available supplement. Probiotic strains are well known for their beneficial effects on human health. Various probiotics strains are commercially available these days and have been found effective in management of overall health and some specific diseases. Probiotics also have beneficial affect on immune system, inflammation and several digestive tract specific disorders. Further, probiotics strongly affects the gut microbiome. Gut microbiota is very important to maintain balanced homeostasis. Probiotics have emerged as candidate of interest in prevention and management of several diseases including specific cancers. Probiotics along with prebiotics in forms of synbiotics may be the functional food of importance in future. Probiotics along with prebiotics are the major focus of research in management of gut health, prevention and management of various diseases. Further research is required on the specific diseases management, over all health benefits and related aspects.

Keywords: *Probiotics, gut health, health benefits, therapeutics potential, disease management*

Received 23.02.2022 Revised 12.03.2022 Accepted 29.03.2022

INTRODUCTION

Probiotics are non-pathogenic microbes, that play an important role in the host`s health benefits when administered in sufficient quantities [1]. Probiotics refers to beneficial microbes as bacteria and yeast which play an important role in human gut health and also strengthen the immunity. In other words, probiotics are "live strains of strictly selected microorganisms which, when administered in adequate amounts, give health benefits to the host" [2]. Not only the intact living probiotics but, the dead probiotics and their metabolic secretions have the similar response in different biological activities [3; 4]. Selection of suitable probiotic strains and application of an appropriate dose affects the efficacy of probiotic preparations. Also, the safety assessment of probiotic strains is very important for their optimal usage [5]. As per the suggestions of the WHO, FAO and the European Food Safety Authority (EFSA), the selection process of new probiotic strains must meet both safety and functionality criteria, and those related to their technological usefulness [6].

The major characteristics of probiotics include their resistance to gut conditions, survival in gut, adhesion to mucosal or epithelial cells, antimicrobial resistance and bile salt hydrolase potential [2]. Also, probiotics have been reported to have properties of immune-stimulation, antagonistic activity against pathogens, anti-mutagenic and anti-carcinogenic activities [4; 7]. Probiotics and their probioactive cellular materials form several beneficial effects in the gastrointestinal tract. They have been reported to have beneficial affects on digestion. Specific cellular constituents in probiotic lactic acid bacteria induce potential adjuvant effects such as cell mediated immune responses modulation, reticulo-endothelial system activation, cytokine pathways augmentation, and interleukins and tumor necrosis factors regulation [8].

Probiotics are mostly categorized into bacterial or lactic acid and non-lactic acid bacteria strains, and also in some cases yeast strains. Lactobacillus, Lactococcus, Bifidobacterium and Enterococcus are common bacterial probiotics [4; 9]. Some other bacterial strains have also been reported for their probiotic attributes. Several yeasta have also been investigated for their probiotics potential including *Saccharomyces cerevisiae* var. boulardii, Candida, Kluyveromyces, Pichia, Debaryomyces, Hanseniaspora, and Metschnikowia [10; 11; 12].

Among bacteria, the most extensively studied and characterized probiotics belongs to the lactic acid bacteria (LAB) group. Among yeasts, *Saccharomyces cerevisiae* var. boulardii has been studied more elaborative. Bacteria of the genera Bifidobacterium and Faecalibacterium are also studied in an elaborative way [13; 14]. Several bacteria have been used for a long time in several industrial processes for the production of fermented foods, such as cheese, yogurts, etc. and they frequently present probiotic properties [15]. Many probiotics strains are able to colonize the gastrointestinal tract (GIT) and stimulate the immune system [16; 17]. The resistance to antibiotics in probiotic strains should be analyzed in order to assess their safety, as well as the level and the source of this resistance [18].

MECHANISM OF ACTION OF PROBIOTICS

Probiotics improves the gut environment and supports the balanced gut microbiota. They affect the digestion, metabolic processes and the immunological response.Along with theessential nutrients and beneficial microorganisms, the gastro-intestinal lumen also has pathogenic microorganisms, toxins, and some foreign antigens [19; 20]. Epithelial cells in the intestinal mucosa create a selectively permeable barrier between the lumen environment and the internal body tissues [21]. This barrier is the first line of host defense against harmful microbes in gut innate immunity (GIT) but several factors such as stress or disease conditions can disrupt this barrier [22]. Certain probiotic microorganisms can enhance the function of intestinal barrier. Probiotics mediated restoration of the GIT mucosa barrier function has been reported in both *in vitro* and *in vivo* models [23; 24]. Re-establishment of barrier functions may be related to the alterations in secretion of mucus or chlorides, or the changes in the expression of tight junction proteins by epithelial cells [25].

Consumption of probiotics exerts health benefits for human, mainly for GIT diseases and for several other metabolism associated diseases also including cancer, depression, atopic dermatitis, obesity and type 2 diabetes [26; 27; 28; 29; 30]. Therefore, the possible mode of actions of the probiotics may include homeostasis of intestinal microbiota, protection of the epithelial barrier, maintenance of epithelial integrity, growth inhibition of harmful microbial population through competition (for available nutrients & adhesion sites), competitive elimination of pathogenic microorganisms, production of antimicrobial substances, production of SCFAs with anti-inflammatory properties, effect on various cellular, molecular-immunological pathways, alteration of cell signaling pathway, interaction with the gut-brain axis and also modulation of the host immune system [31; 32; 33; 34; 35; 36; 37]. Majority of these aspects have been studied extensively and under consideration for elucidation of mechanisms related to probiotics.

The probiotic have the ability to modulate the composition of gut microbial. Probiotics enhance the beneficial microbial population and suppress the growth of harmful/ pathogenic bacteria in the gut. Several probiotics have been found to produce antimicrobial peptides, acetic acid, lactic acid as well as propionic acid, and therefore, alters the intestinal pH. This alteration consequently inhibits the growth of several pathogenic gram-negative bacteria [38]. Various probiotic strains have been reported to inhibit the disease causing harmful bacteria. Probiotic strains have been reported to, inhibit the *Helicobacter pylori, Salmonella enterica* [39; 40; 41] and decrease the fecal coliforms and clostridia [42]. Probiotics also significantly affect the gut microbiota composition and therefore, resulted in increase of anti-inflammatory metabolites generating bacteria as *Prevotella* and *Oscillibacter*[43]. Also, some microbial communities in gut supports production of short-chain fatty acids (SCFAs) and contributes to the production of important metabolites like acetate, propionate, and butyrate depending on the fermentation of fiber-rich prebiotics [44]. The SCFA have significant role in stimulating intestinal hormones production, lipogenesis and also affects the various mechanisms/ pathways associated with cell proliferation, apoptosis, and immune system [36; 45]. Although, lactic acid bacteria are not directly concerned in SCFA production, but certain probiotic species such as*Bifidobacteria*and *Lactobacilli* can affect the composition of the gut microbiota and therefore have an effect on the production of SCFA. Production of butyrate by some members ofFirmicutes families (Ruminococcaceae, Lachnospiraceae, and Clostridiaceae) also have beneficial role, promote apoptosis and inhibit cancer cell proliferation *in vitro*[45; 46].

The intestinal epithelial barrier plays a crucial role in maintaining host homeostasis [47]. Scientific reports on probiotics have suggested that regular consumption of probiotics may lead to the improved profile of the intestinal microbiota and it may result in reduced chronic inflammation as well as the

reduced production of carcinogenic compounds [48; 49; 50; 51]. It has been found that the fermented products and metabolites generated due to probiotics and prebiotics have the potential to prevent disruption of the intestinal epithelial barrier [52]. Scientific reports have revealed that probiotic culture, may preserve epithelial barrier function, can reduce the intestinal permeability and inhibit the inflammatory response [53; 54; 55; 56]. Inhibitory activity of *L. plantarum* have been reported earlier against the transepithelial resistance of Caco-2 cells [55]. Probiotic products also help to reduce intestinal permeability and inflammatory response in patients [54]. The microorganism or their produced metabolites generally interact with the immune system and epithelial cells [57]. Probiotic also have the ability to reinforce the expression of tight junction protein i.e. mucin gene (MUC2 and MUC3), which enhance the intestinal gut barrier functions. Hence, the probiotics play protective role in retaining the mucus layer integrity, which is vital for an efficient intestinal barrier function [58]. Various scientific findings have revealed the protective role of probiotics in mutagen-induced DNA damage or DNA adducts formation in the colonic epithelium [59; 60]. Probiotics showed protection against enterocyte apoptosis and 5-fluorouracil (5-FU) induced loss of intestinal barrier function [61]. Probiotics in particular, the lactic acid bacteria, have also been reported to possess ability to modulate host immune system. This immune-modulatory action further causes suppression and regression of carcinogenesis.

THERAPEUTIC POTENTIAL AND HEALTH BENEFITS OF PROBIOTICS

Probiotics directly or indirectly improve human health by affecting the colonizing microbiota(Figure 1). These microorganisms reside in the host body symbiotically and nourish it internally [62]. Probiotics have great therapeutic potential to treat or prevent dental caries, periodontal diseases, urogenital infections, gastrointestinal infections, intestinal membrane injury, inflammation, diabetes, obesity and carcinogenesis [63; 64]. Probiotics stimulates and controls the response of the immune system by triggering the action of specific genes of cells responsible for activating gastrointestinal hormone release [62; 65]. The use of antibiotics, immunosuppressive therapy and irradiation for treatment of a particular disease cause alterations in the microbioata composition of GI tract which later on results in dysbiosis and onset of metabolism associated diseases. Therefore, the introduction of beneficial bacterial species to GI tract may be a very attractive option to re-establish the microbial equilibrium and prevent disease Earlier studies also reported effectiveness of probiotics to treat several disease/disorders or infections in various clinical conditions such as infantile diarrhoea, antibiotic-associated diarrhoea, necrotizing enterocolitis, relapsing Clostridium difficle colitis, Helicobacter pylori infections, inflammatory bowel disease (IBD) and surgical infections [65; 66; 67].

Wide range of anti-pathogenic metabolites is produced by various probiotics. These metabolites not only maintain a suitable gut environment but also exert various health benefits including control of diseases. The nervous system is stimulated by the probiotics which possess some physiological functions helpful for the inhibition of the adipose tissue. Various strains of lactobacillus retard the growth of the adipocyte tissues which cause weight loss and decrease the obesity [68]. A species of yeast i.e. *Saccharomyces* boulardii, is used for protection against injury of intestine and inflammation [62]**.** The vaginal infections in women also occur due to abnormal microflora [63].Earlier studies also reported that probiotics also help in neutralizing diabetes (Type-I & Type-II) by increasing bacteroidetes and reducing firmicutes concentration [68; 69; 70].

Probiotics have been reported to have beneficial effects against cancer [65; 71]. Numerous reports along with mechanism are available that describe the anti-cancerous potential of probiotics. Even probiotics have been found effective during various treatment procedures of cancer. Several mechanisms of action are presented that describe the cancer prevention and treatment using probiotics. The probiotics works through, gut microbiota modulation, improvement of gut barrier functions, protective effect of DNA damage of intestinal epithelium, the degradation of potential carcinogens, and also through improving the immune system as well as inflammatory system [65; 71]. Further, the carcinogenesis and the inflammation can be controlled by anti-inflammatory response shown by probiotics.

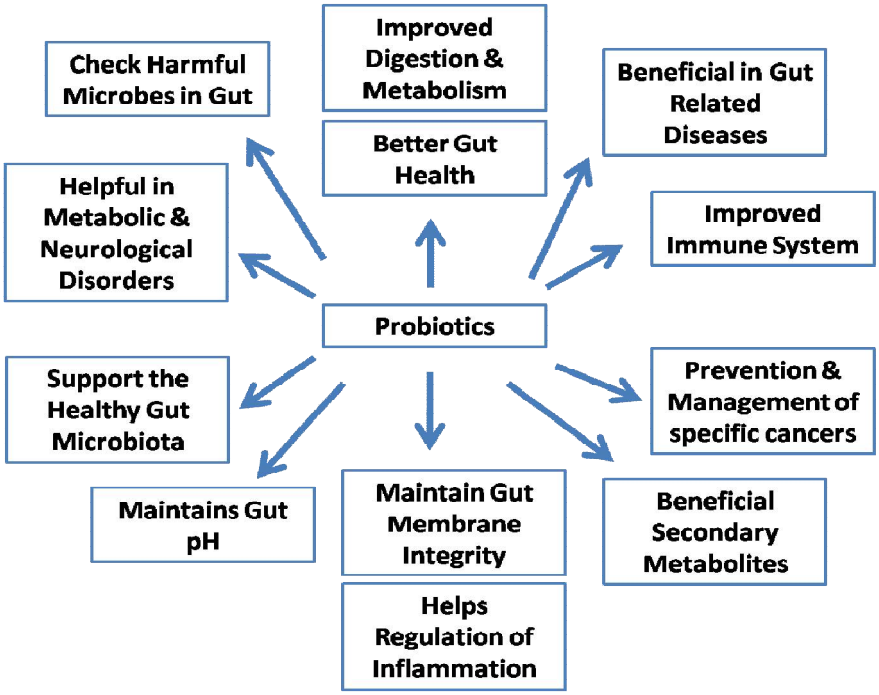

Figure 1: General presentation showing some of the health benefits and therapeutic potential of probiotics.

Probiotics have been studied for their role in prevention, treatment and also in management of colon cancer [72]. The immunomodulatory properties have been found to vary according to probiotics strains. Therefore, all probiotic strains are not equally efficient in modulating the immune system and to prevent the occurrence of colon cancer [51; 65; 71; 72]. Interestingly, not only the whole microbial cell is effective, but also the probiotic derived proteins, cell free supernatant and cell free extracts have been reported for anticancer properties [72]. Probiotic strains improve the safety and reduce the severe gastrointestinal sideeffects associated with anticancer treatments [73]. Along with probiotics, prebiotics are now under consideration for health benefits. Functional foods are of particular interest in today's scenario [74; 75] and require more research in the area. Probiotics have been investigated for their effect on various gut related diseases/ disorders. Probiotics have been found promising and requires more elaborative investigations for management of various diseases/ disorders.

CONCLUSION AND FUTURE PROSPECTS

Probiotics have emerged as important candidate in prevention and management of various diseases. Probiotics are consumed in various forms including fermented dairy products, fermented foods and commercially available supplements. Probiotics are known to have beneficial effect on gut health, microbiome maintenance, prevention as well as management of diseases including specific cancers. Probiotics aid in digestion and also helps the immune system. In most of cases, bacteria are consumed in form of probiotics. Researchers have worked on yeast strains also and some yeast strains are now known for their probiotics attributes. Further, research is required for use of probiotics along with the prebiotics and in form of synbiotics. New probiotics are the need of future and requires extensive research along with mechanistic insights. Probiotics may be the functional food of importance along with the prebiotics in near future.

CONFLICTS OF INTEREST

Authors declare no conflict of interest.

ACKNOWLEDGEMENT

Authors (NS, MY, SK, MS, VK) acknowledge the help and support by Head, Department of Biotechnology, Maharishi Markandeshwar (Deemed to be University), Mullana-Ambala, India.

REFERENCES

1. WHO-FAO. (2006). World Health Organization-Food and Agricultural Organization. Probiotics in food: health and nutritional properties and guidelines for evaluation FAO food and nutritional paper. *FAO/WHO*, Rome.

2. FAO. (2002). Guidelines for the evaluation of probiotics in food. Report of a Joint FAO/WHO Working Group on Drafting Gidelines for the evaluation of probiotics in food. *FAO*; London.
3. Adams CA. (2010). The probiotic paradox: live and dead cells are biological response modifiers. *Nutr Res Rev*.; 23: 37-46.https://doi.org/10.1017/S0954422410000090
4. Bedada TL, Feto TK, Awoke KS, et al. (2020). Probiotics for cancer alternative prevention and treatment, *Biomed Pharmacother.*129:110409.https://doi.org/10.1016/j.biopha.2020.110409
5. Anadón A, Castellano V, Martínez-Larrañaga MR (2014). Regulation and guidelines of probiotics and prebiotics. In: Ötles S, editor. Probiotics and prebiotics in food, nutrition and health. Boca Raton, FL: CRC Press, LLC Taylor & Francis Group. pp. 91–113. ISBN 978-1-4665-8623-9.
6. Markowiak P, Śliżewska K. (2018). The role of probiotics, prebiotics and synbiotics in animal nutrition. *Gut Pathog.*; 10:21. https://doi.org/10.1186/s13099-018-0250-0
7. Mattila-Sandholm T, Myllärinen P, Crittenden R. et al. (2002). Technological challenges for future probiotic foods. *Int Dairy J.*; 12: 173-182. https://doi.org/10.1016/S0958-6946(01)00099-1
8. Kumar M, Kumar A, Nagpal R, et al. (2010). Cancer-preventing attributes of probiotics: an update.*Int J Food SciNutr.*; 61: 473-496, https://doi.org/10.3109/09637480903455971
9. Georgiev KD, Georgieva MP, Iliev IA, et al. (2015). Antiproliferative effect of bulgarian spring water probiotics (laktera nature probiotic®) against human colon carcinoma cell line. *World J Pharm Sci.*; 4: 130-136.
10. Smith IM, Baker A, Arneborg N, Jespersen L. (2015). Non-Saccharomyces yeasts protect against epithelial cell barrier disruption induced by *Salmonella enteric* subsp. Entericaserovar Typhimurium. *LettApplMicrobiol.*; 61: 491-497.https://doi.org/10.1111/lam.12481
11. Ricci A, Allende A, Bolton D, et al. (2016). Update of the list of QPS, recommended biological agents intentionally added to food orfeed as notified to EFSA 5: suitability of taxonomic units notified to EFSA until September 2016. *EFSA J.;* 15: 1-20.
12. Saber A, Alipour B, Faghfoori Z, et al. (2017). Cellular and molecular effects of yeast probiotics on cancer. *Crit Rev Microbiol.*; 43: 96-115.https://doi.org/10.1080/1040841X.2016.1179622
13. Pot B, Foligné B, Daniel C, Grangette C. (2013). Understanding immunomodulatory effects of probiotics. *Nestlé Nutrition Institute Workshop Series*,; 77: 75–90.https://doi.org/10.1159/000351388
14. Chang CW, Liu CY, Lee HC, et al. (2018). *Lactobacillus casei* variety *rhamnosus* probiotic preventively attenuates 5-Fluorouracil/Oxaliplatin-induced intestinal injuryina syngeneic colorectal cancer model. *Front Microbiol.*; 9:983. https://doi.org/10.3389/fmicb.2018. 00983
15. Plavec TV, Berlec A. (2019). Engineering of lactic acid bacteria for delivery of therapeutic proteins and peptides. *ApplMicrobiolBiotechnol.*; 103: 2053-2066. https://doi.org/10.1007/s00253-019-09628-y
16. Wang M, Gao Z, Zhang Y, et al. (2016). Lactic acid bacteria as mucosal delivery vehicles : a realistic therapeutic option. *ApplMicrobiolBiotechnol.* 100:5691–5701.https://doi.org/10.1007/s00253-016-7557-x
17. Mokoena MP. (2017). Lactic acid bacteria and their bacteriocins: classification, biosynthesis and applications against uropathogens: A mini-review. *Molecules.*; 22:1255.https://doi.org/10.3390/molecules22081255
18. Zhang F, Gao J, Wang B, (2018). Wholegenome sequencing reveals the mechanisms for evolution of streptomycin resistance in *Lactobacillus plantarum.J Dairy Sci.*; 101: 2867–2874. https://doi.org/10. 3168/jds.201713323
19. Takahashi T, Nakagawa E, Nara T, et al. (1998) Effects of orally ingested *Bifidobacteriumlongum* on the mucosal IgA response of mice to dietary antigens. *Biosci Biotechnol Biochem.;* 62:10–5
20. Willing BP, Malik G, van Kessel AG. (2012). Nutrition and gut health in swine. In: Chiba LI, editor. Sustainable Swine Nutrition. Chichester: Wiley, pp 197–213
21. Liao SF, Nyachoti M. (2017). Using probiotics to improve swine gut health and nutrient utilization. *AnimNutr.*; 3:331–343.
22. Lee IK, Kye YC, Kim G, (2016). Stress, Nutrition, and Intestinal Immune Responses in Pigs - A Review. *Asian-Australasian J Anim Sci.*; 29: 1075–1082. https://doi.org/10.5713/ajas.16.0118
23. García-Lafuente A, Antolín M, Guarner F. et al. (2001). Modulation of colonic barrier function by the composition of the commensal flora in the rat. *Gut.*; 48: 503-507.
24. Madsen K, Cornish A, Soper P, et al. (2001). Probiotic bacteria enhance murine and human intestinal epithelial barrier function. *Gastroenterol.*; 121: 580-591
25. Yang F, Wang A, Zeng X, et al. (2015). *Lactobacillus reuteri* I5007 modulates tight junction protein expression in IPEC-J2 cells with LPS stimulation and in newborn piglets under normal conditions. *BMC Microbiol.*; 15: 32https://doi.org/10.1186/s12866-015-0372-1.
26. Fedorak RN, Feagan BG, Hotte N, et al. (2015). The probiotic VSL#3 has anti-inflammatory effects and could reduce endoscopic recurrence after surgery for Crohn's disease. *Clin GastroenterolHepatol.;* 13: 928-35.e2. https://doi.org/10.1016/j.cgh.2014.10.031
27. Collins F, Rios-Arce ND, Schepper JD, (2018). The potential of probiotics as a therapy for osteoporosis. *Microbiol Spectr.*; 5:213-233. https://doi.org/10.1128/microbiolspec.BAD-0015-2016
28. Hsieh M-C, Tsai W-H, Jheng Y-P, et al. (2018). The beneficial effects of Lactobacillus reuteri ADR-1 or ADR-3 consumption on type 2 diabetes mellitus: a randomized, double blinded, placebo-controlled trial. *Sci Rep.;* 8:16791. https://doi.org/10.1038/s41598-018-3501435011.
29. Zaharuddin L, Mokhtar NM, Muhammad Nawawi KN, Raja Ali RA. (2019). A randomized double-blind placebo-controlled trial of probiotics in post-surgical colorectal cancer. *BMC Gastroenterol.*; 19:131. https://doi.org/10.1186/s12876-019-10471044

30. Wallace CJK, Foster JA, Soares CN, Milev RV. (2020). The effects of probiotics on symptoms of depression: protocol for a double-blind randomized placebo-controlled trial.*Neuropsychobiol.*; 79: 108–116. https://doi.org/10.1159/000496406
31. Blackwood BP, Yuan CY, Wood DR. et al. (2017). Probiotic Lactobacillus species strengthen intestinal barrier function and tight junction integrity in experimental necrotizing enterocolitis. *JProbiotHealth*, 5:159. https://doi.org/10.4172/2329-8901.1000159
32. Shi Y, Zhai Q, Li D (2017). Restoration of cefixime-induced gut microbiota changes by *Lactobacillus* cocktails and fructooligosaccharides in a mouse model. *Microbiol Res.*; 200:14–24. https://doi.org/10.1016/j.micres.2017.04.001
33. Azad MAK, Sarker M, Wan D. (2018). Immunomodulatory effects of probiotics on cytokine profiles. *BioMed Res Int*, 8063647. https://doi.org/10.1155/2018/8063647
34. Kim N, Yun M, Oh YJ, Choi H-J. (2018). Mind-altering with the gut: Modulation of the gut-brain axis with probiotics. *J Microbiol.*; 56: 172–182. https://doi.org/10.1007/s12275-018-80328034
35. Monteagudo-Mera A, Rastall RA, Gibson GR, et al. (2019). Adhesion mechanisms mediated by probiotics and prebiotics and their potential impact on human health. *ApplMicrobiolBiotechnol.;*103: 6463–6472. https://doi.org/10.1007/s00253-019-099789977
36. Parada Venegas D, De la Fuente MK, Landskron G, González MJ, et al. (2019). Short Chain Fatty Acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. *Front Immunol.*; 10: 277. https://doi.org/10.3389/fimmu.2019.00277
37. Batista VL, da Silva TF, de Jesus LCL. (2020). Probiotics, prebiotics, synbiotics, and paraprobiotics as a therapeutic alternative for intestinal mucositis. *Front Microbiol.*;11:544490. https://doi.org/10.3389/fmicb.2020.544490
38. Šušković J, Kos B, Novak J, (2010). Antimicrobial activity–the most important property of probiotic and starter lactic acid bacteria. *Food Technol Biotechnol.;*48: 296-307
39. Kuo C, Wang SS, Lu C, (2013). Long-term use of probiotic-containing yogurts is a safe way to prevent *Helicobacter pylori*: based on a Mongolian Gerbil's model. *Biochem Res Inter.;* 594561.
40. Chen X, Liu X-m, Tian F, (2012). Antagonistic activities of lactobacilli against Helicobacter pylori growth and infection in human gastric epithelial cells. *J Food Sci.*; 77: M9-M14.
41. Veronique V, Nathalie R, Amin M, (2013). Probiotics enhance the clearance of human papillomavirus-related cervical lesions, *Eur J Cancer Prev*. 22: 46-51
42. Chaikham P, Apichartsrangkoon A, Jirarattanarangsri W, et al. (2012). Influence of encapsulated probiotics combined with pressurized longan juice on colon microflora and their metabolic activities on the exposure to simulated dynamic gastrointestinal tract. *Food Res Inter.;* 49:133-142.
43. Li J, Sung CYJ, Lee N, (2016). Probiotics modulated gut microbiota suppresses hepatocellular carcinoma growth in mice. *Proc Natl Acad Sci.;* 113: E1306-E1315.https://doi.org/10.1073/pnas.1518189113
44. Pérez-Burillo S, Mehta T, Pastoriza S, et al.(2019). Potential probiotic salami with dietary fiber modulates antioxidant capacity, short chain fatty acid production and gut microbiota community structure. *LWT-Food Sci Technol.*; 105: 355-362. https://doi.org/10.1016/j.lwt.2019.02.006
45. Requena T, Martínez-Cuesta MC, Peláez C. (2018). Diet and microbiota linked in health and disease. *Food Funct.*; 9: 688-704. https://doi.org/10.1039/c7fo01820g
46. LeBlanc JG, Chain F, Martín R, et al. (2017). Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *MicrobCell Fact.*; 16:79. https://doi.org/10.1186/s12934-017-0691-z
47. Rios-Arce ND, Collins FL, Schepper JD, et al. (2017). Epithelial barrier function in gut-bone signaling. In McCabe LR, Parameswaran N, editors, Understanding the Gut-Bone Signaling Axis: Mechanisms and Therapeutic Implications. 1 ed. Springer New York LLC. 2017; pp. 151-183. (Advances in Experimental Medicine and Biology). https://doi.org/10.1007/978-3-319-66653-2_8.
48. Hatakka K, Mutanen M, Holma R, et al. (2008). *Lactobacillus rhamnosus* LC705 together with *Propionibacterium freudenreichii* sspshermanii JS administered in capsules is ineffective in lowering serum lipids. *J Am CollNutr.* 27: 441-447. https://doi.org/10.1080/07315724.2008.10719723.
49. Ohara T, Yoshino K, Kitajima M. (2010). Possibility of preventing colorectal carcinogenesis with probiotics.*Hepato-Gastroenterol*.; 57: 1411–1415.
50. Liu Z, Qin H, Yang Z, et al. (2011). Randomised clinical trial: the effects of perioperative probiotics treatment on barrier function and post-operative infectious complications in colorectal cancer surgery–a double-blind study. *Aliment PharmacolTher*.; 33: 50–63.
51. Drago L. (2019). Probiotics and colon cancer. Microorganisms. 7: 66. https://doi.org /10.3390/microorganisms7030066.
52. Commane DM, Shortt CT, Silvi S. (2005). Effects of fermentation products of pro-and prebiotics on trans-epithelial electrical resistance in an in vitro model of the colon. *Nutr Cancer.*; 51:102-109.https://doi.org/10.1207/s15327914nc5101_14.
53. Jones C, Badger SA, Regan M, et al. (2013). Modulation of gut barrier function in patients with obstructive jaundice using probiotic LP299v. *Eur J GastroenterolHepatol*.; 25: 1424–1430. https://doi.org/10.1097/MEG.0b013e328363e26e
54. Ahrne S, Hagslatt M-LJ. (2011). Effect of *lactobacilli* on paracellular permeability in the gut. ***Nutrients***.; 3:104-117.https://doi.org/10.3390/nu3010104

55. Ko JS, Yang HR, Chang JY, Seo JK. (2007). *Lactobacillus plantarum* inhibits epithelial barrier dysfunction and interleukin-8 secretion induced by tumor necrosis factor-α. World journal of gastroenterology: *World J Gastroenterol.;* 13: 1962-1965.
56. Nazir Y, Hussain SA, Hamid AA, Song Y. (2018). Probiotics and their potential preventive and therapeutic role for cancer, high serum cholesterol, and allergic and HIV diseases. *BioMed Res Inter.*; Article ID 3428437. https://doi.org/10.1155/2018/3428437
57. Ivanov II, Honda K. (2012). Intestinal commensal microbes as immune modulators. *Cell Host Microbe,;* 12: 496-508
58. Bermudez-Brito M, Plaza-Díaz J, Muñoz-Quezada S, et al. (2012). Probiotic mechanisms of action. *Annals of Nutr Metabol.*; 61: 160-174.
59. McIntosh GH, Royle PJ, Playne MJ. (1999). A probiotic strain of *L. acidophilus* reduces DMH-induced large intestinal tumors in male Sprague-Dawley rats. *Nutr Cancer.* 35:153-159.
60. Horie H, Zeisig M, Hirayama K, et al. (2003). Probiotic mixture decreases DNA adduct formation in colonic epithelium induced by the food mutagen 2-amino-9H-pyrido [2, 3-b] indole in a human-flora associated mouse model. *Eur JCancer Prev.;* 12: 101-107.
61. Prisciandaro LD, Geier MS, Chua AE, (2012). Probiotic factors partially prevent changes to caspases 3 and 7 activation and transepithelial electrical resistance in a model of 5-fluorouracil-induced epithelial cell damage. *Supportive Care Cancer*,; 20: 3205-3210. https://doi.org/10.1007/s00520-012-1446-3
62. Kerry RG, Patra JK, Gouda S, et al. (2018). Benefaction of probiotics for human health: A review. *J Food Drug Anal.*; 26: 927-939. https://doi.org/10.1016/j.jfda.2018.01.002
63. Waigankar SS, Patel V. (2011). Role of probiotics in urogenital healthcare*. J Mid-Life Health.*; 2: 5-10. https://doi.org/10.4103/0976-7800.83253
64. Kang JH, Yun SI, Park MH, et al. (2013). Anti-obesity effect of Lactobacillus gasseri BNR17 in high-sucrose diet-induced obese mice. *PLoS One.;* 8:e54617. https://doi.org/10.1371/journal.pone.0054617
65. Sharma VR, Sharma N, Sheikh I, et al. (2021). Probiotics and prebiotics having broad spectrum anticancer therapeutic potential: recent trends and future perspectives. *CurrPharmacol Rep.;* 7: 67-79. https://doi.org/10.1007/s40495-021-00252-x
66. Gupta V, Garg R. (2009). Probiotics. *Indian J MedMicrobiol.*; 27: 202-209. https://doi.org/10.4103/0255-0857.53201.
67. Song S, Lee S-J, Park D-J, (2016). The anti-allergic activity of *Lactobacillus plantarum* L67 and its application to yogurt. *J Dairy Sci.* 99:9372–9382. https://doi.org/10.3168/jds.2016-11809.
68. Kobyliak N, Conte C, Cammarota G, et al. (2016). Probiotics in prevention and treatment of obesity: a critical view. *Nutr Metabol.*;13:14. https://doi.org/10.1186/s12986-016-0067-0.
69. Le Barz M, Anhê FF, Varin TV, et al. (2015). Probiotics as complementary treatment for metabolic disorders. *Diabetes Metab J.*; 39: 291–303. https://doi.org/10.4093/dmj.2015.39.4.291
70. Hu C, Wong FS, Wen L. (2015). Type 1 diabetes and gut microbiota: Friend or foe? *Pharmacol Res.* 98:9-15
71. Sharma VR, Singh M, Kumar V, (2021). Microbiome dysbiosis in cancer: Exploring therapeutic strategies to counter the disease. *Semin Cancer Biol.;* 70: 61-70. doi: 10.1016/j.semcancer.2020.07.006.
72. Sehrawat N, Yadav M, Singh M, et al. (2021) Probiotics in microbiome ecological balance providing a therapeutic window against cancer. *Semin Cancer Biol.*; 2021a; 70: 24-36. https://doi.org/10.1016/j.semcancer.2020.06.009.
73. Vivarelli S, Falzone L, Basile MS, et al. (2019). Benefits of using probiotics as adjuvants in anticancer therapy. *World AcadSci J.*; 1: 125-135.
74. Sehrawat N, Yadav M, Kumar S, et al. (2020). Review on health promoting biological activities of mungbean: a potent functional food of medicinal importance. *Plant Arch.;* 20 (Supplement 2): 2969-2975.
75. Sehrawat N, Yadav M, Sharma AK, (2021). Mungbean (*Vignaradiata* L. Wilczek) as functional food, agronomic importance and breeding approach for development of climate resilience: current status and future perspectives. *Asian J Biol Life Sci.;* 10: 87-92. https://doi.org/10.5530/ajbls.2021.10.14

CITATION OF THIS ARTICLE

N Sehrawat, M Yadav, S Kumar, S Lata, A Kumar, A Kumar, M Singh, V Kumar. Therapeutic Potential, Health Benefits and Mechanism of Action of Probiotics: A Concise Review. Bull. Env.Pharmacol. Life Sci., Spl Issue [1] 2022 : 123-129