# **Review Article**

# PROBIOTICS: FOOD SUPPLEMENT FOR HUMAN CONSUMPTION

## **ABSTRACT**

The human gut *microflora* contains 1000 of dynamic microbial ecosystem to maintain balance between immune boosting and harmful bacteria. The good bacteria reside in healthy human gut and responsible for increasing energy production, inhibiting pathogenic growth. In unhealthy gut microbiota initiates the development of disorders in human body include metabolic disorder, chronic diarrhea, obesity. The article deals with the study of emerging trends in probiotics and developing industrial probiotics products for human body. At present there are many probiotics foodstuff isolated by industries from natural foods includes vegetables, grain, cereals to use in the form of nutrient supplements. Human Gut can be enriched with natural, low cost Probiotic supplements to improve lifestyle.

Keywords: Gut microflora, metabolic disorder, immune boosting, probiotics

## Introduction

#### **PROBIOTICS**

Relationship between different class of organisms have been observed since time immemorial. One of the most complex and focused relation has been that of humans and bacteria. Although, most of us are aware of the harmful bacteria which causes disease and illness, it is less sighted upon those bacteria, which not only lives inside our body but also benefits us [1].

Earlier, people used to believe that plants are the only source from which all the immunity booster can be obtained. This notion went on for long until during stone age, man started domestication of livestock and consumption and production of dairy products started from this dairy products, fermentation came into existence [2-4]. The ancient history says that once shepherd was walking in the hot summer of Turkish desert carrying goatmilk in the bottle made of the skin of that goat. After sometime, he observed that the milk has turned into something thick, tasty and creamy texture. This new creamy thing was called Yogurt. This was the time when people starting yogurt and it helped them maintaining good health. This made them believe that yogurt have some therapeutic properties. Little did they know it was the bacteria in it which helped maintaining good environment in their digestive system. The therapeutic properties of these products were of traditional belief until the concept of probiotics flourished [5-7]. The word probiotics was brought into existence by the German researcher Werner Kollath in 1953 to assign "dynamic substances that are essential for life [8].

The cutting edge history of probiotics begins toward the start of 1900s with the spearheading investigations of things to come Nobel laureate Elie Metchnikoff, a Russian researcher working at the Pasteur Institute in Paris. Louis Pasteur distinguished the microorganisms answerable for the procedure of aging, while Metchnikoff gave first to locate a shot the conceivable impact of these organisms on human wellbeing [9-10]. He related the upgraded life span of Bulgarian country individuals to the standard utilization of matured dairy items, for example, yogurt. He connected this to the Bulgarian bacillus that was found by a Bulgarian doctor Stamen Grigorov, and he later proposed that lactobacilli may neutralize the harmful impacts of gastrointestinal digestion that added to ailment and maturing [11]. The logical speculation of Metchnikoff supported the creation and advancement of the dairy business in France, the first in Europe, on account of the utilization of a matured milk acquired from Bacillus bulgaricus. In 2013 a specialist agreement archive had been distributed on the extension and suitable utilization of the term probiotic: live microorganisms which when consumed inadequate amount gives a medical benefit to the consumer of these probiotics [12-14]. Present day innovation has likewise chosen those strains creating an aged milk with great natural and healthful characteristics, more than different strains do. Yogurt and different nourishments produced using fermented milk can be viewed as the principal functional food [15].

Probiotics comprises of those bacteria which not only naturally lives inside human gut but also benefits them by providing protection against bad microorganisms and boost the immune system. On the other hand, probiotics have been distinguished and described as living microbial feed booster of health that helpfully influence the host body by enhancing its intestinal microbial balance. Probiotics were initially used to improve the health people through the balance of the microbes present in the intestine [16-18]. At present, a less number of acknowledged strains of Lactobacilli and Bifidobacteria are accessible for human use to reduce the chances of gastrointestinal contaminations or cure these diseases. Some of the helpful impacts of probiotic utilization incorporate improvement of intestinal wellbeing by the help of microbiota, and incitement and advancement of immune system, combining and upgrading the bioavailability of supplements, decreasing effects of lactose intolerance, and diminishing the danger of certain different ailments [19]. The increased use of probiotics in today's life says a lot about its use and necessity to the mankind. That's why they are produced in larger quantities by different scientific

methods. For any probiotic substance to work properly, it should be at the highest of its function for human benefit. That particular strain of probiotic should be able to colonize and acceptable to immune system. There should not be any reaction from immune system against these microbiotas [20]. Then only it qualifies as probiotics. There are various ways for the production and checking of the probiotics. [21-22].

Supplementation with probiotics, prebiotics, and synbiotics has given some outstanding results against various gut pathogens because of their unique and distinguished capability to fight with pathogenic microbes for unique binding site, to keep away pathogens or to maintain, adjust and change the host's immunity by starting the operation of unique features in and outside the host's gut[23-25].

#### **MECHANISM OF ACTION**

As probiotics are defined as microorganisms which provide human gut with variety of good bacteria and strengthen the immune system. The intestinal tract is a wide diversemicro colony where varied 500 types of microbe'sflourish [26-27]. A single layered epithelium is the only layer that isolates these benefitting microorganisms and pathogens from the immune cells, and accordingly epithelial hindrance work is an important part in the process of protection, components required to avert infection and irritation. The epithelial boundary comprises of a thick mucus cell layers having secretory IgA antibodies and antimicrobial chains just as unique junctional structure that control movement of substances and microbes across the layer between cellas and tissues. Probiotics are live microorganisms that gives benefit to the host and that have been given to improve sicknesses including anti-toxin related looseness of the bowels, irritable bowel syndrome, inflammatory bowel diseases. Probiotics certainly functions by the enhancement of boundary capacity, immune system working process, and firm adhesiveness to the mucus and epithelium[28-29]. The mechanism of actiongives details about impacts of the various accessible probiotics with an important uplifting on intestinal barrier work and the immune response corresponding to probiotics.

The intestinal epithelium is continuously incontact with luminal substance and the different, gut micro culture. The distal bowel, cecum, and colon have growing bacterial colonization comparative with proximal areas. Approximately, 60% of the feces tissue mass in people is because of microscopic organisms which is there in our body through any means. The small digestive system helps lower quantities of commensal microscopic organisms because of the more hydrogen ion concentration and lower pH from stomach corrosive acid HCl, which catalysts from pancreas that holdcolonization [30]. Approximately 500 types of anaerobic microorganisms are examined to involve the gut microbial culture, and prokaryotes overtakes eukaryotic cells by an exceeding factor of 10in the human body. Since, most of gut microbes can't be purified by standard methods, so a few gatherings are presently taking at distinguishing the different species by polymerase chain reaction of 16S ribosomal nucleic acid(RNA) and looking at the noticeable interchange between generations during wellbeing and diseases [31-34].

To shield all the cells from deliberate immune reactions, the epithelium has created different parts to control bacterial development, restrict direct contact with the microorganisms, and avertbacterial scattering in the basic tissue. Interruption of this obstruction can cause safe resistance to the intestinal microbes and an unseemly provoke reaction, as it has to happen in the gut ailment irritable bowel disease (IBD), ulcerative colitis and Crohn's sickness [35]. The intestinal boundary barriers comprise of the mucous layer, antibody IgA, antimicrobial peptides that protects the host from infection, and the epithelial junctional bond complex. Utilization of bacterial species that doesn't because harm can lead to problematic work by reducing the paracellular entrance, providing natural immunity and resistance

against pathogens and improving the physical barrier of the mucous layer, which may help in prevention against the diseases, prevent constant aggravation and reaction against immune system, and keep up mucosal layer firm [36-38].

#### SYSTEMS OF PROBIOTIC FUNCTION

A typical misguided judgment is that the probiotics should constantly form colonies in the gut to show their effects efficiently and working. But, some of the probiotics like Bifidobacterium become the important part of the human gut [Table:1] but other bacteria like Lactobacillus casei may not. Noncolonizing bacterial probiotics should then in an approximate way should show their effects in a temporary way as they pass on or, probably, by affecting the present microbial connections and effects [39-40].

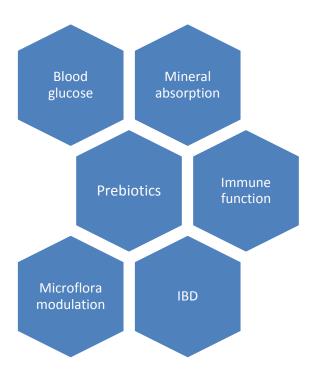
**Table 1: Health benefits of Probiotics** 

Health benefits of Probiotics					
Metabolic benefits	Intestinal Hemostasis	Immunological benefits	Reference		
Reducing cholesterol	Gut barrier	Antibody production	Ref.41		
Against toxins	Improved gut microflora	Boosting immune system	Ref.42		
Controlling body weight	Against colonization of pathogens	Alleviating allergens	Ref.43		
Against Diabetes	Protective against Diarrhea	Preventing IBDs	Ref44		
Lactose intolerance		Anti-proliferative	Ref.45		

## **PREBIOTICS**

Prebiotics which is non-digestible carbohydrate includes flaxseed, garlic, berries, oatmeal, onion, legumes, tomatoes and bananas enrich beneficial microbes. Prebiotics are play role in modulation and enhancing the activity of gut microflora for the benefit of human health. The studies support prebiotics increase activities of *lactobacilli* and *bifidobacteria*, which ferment the carbohydrates and shows immunomodulatory properties in host body. Prebiotics protect infection of gastrointestinal tract by the mechanism of inhibiting the pathogens. The research studies show that prebiotics can improve zinc, iron and calcium absorption which is beneficial for mineralization of bone and enhance calcium uptake in large intestine. There are many evidence which supports prebiotics affects insulin level in the body and reduces the level of glucoseafter the meal. Prebiotics supports bacterial fermentation and modify the insulinemia [46].

Fig 1: Health benefits of Prebiotics



## **SYNBIOTICS**

The research study shows there is additional benefits when probiotics strain specific and prebiotics substance specific can combined together and known as synbiotics which affects, stimulate and enhance the activity and survival of gut microbes. The synbiotics association favors the probiotics products with the help of prebiotics. The enhancement of endogenous microbes in gut maximize when prebioticsstimulate the growth of probiotics. For synbiotics preparations mainly prebiotics compounds contain xylosegosaccharides [(XOS) are polymers of the sugar xylose], fructooligosaccharides and insulin whereas prebiotics includes *Bifidobacteriumstrian*, *B.coagulans*, *Lactobacilli* etc. There are various health benefits of synbiotics consumptions includes liver function improvements in cirrhotic patients, enhanced immunomodulating property, increased number of gut bacteria etc [47].

#### PRODUCT CREDIBILITY OF PROBIOTICS

At the point when probiotic strains are chosen, properties significant for adequacy and innovative capacity must be evaluated. Since the scope of focuses for in vivo work is wide, spreading over resistant capacities, oral, respiratory, stomach, intestinal, it would be an overwhelming errand to build up a brief of qualities requiredby a probiotic in allcapacities [48]. Essential starting portrayal of strain character and scientific categorization ought to be directed, trailed by assessment with approved tests for both animal model introspection and in limit examination of the host. Innovative strength should likewise be resolved, for example, the capacity of the selected strain to develop to increasing numbers, thought, the balance it

creates, and its fusion into the packing material having great tangible properties for being appropriate and to be fast in its effects, be it in genetic aspect or physiological aspect or both completely through the time it is usable for and at the host's active site. It could be a test to evaluate the balance of the strain sincethe componentslike its reaction, length of the chain and the side effects may lead to the investigation of colony culture happening in vivo [49].

Strain obtained from a probiotic bacterium can be different that means same probiotic can two unique strains as it has been tested in lab and on the animal for trial information in, although the result of the same test can vary in human and most likely uncommon. As a result, the outcomes from the examination that is being clinically tested are relevant just to the strain or strains being assessed in that investigation [45]. Given this, in any case, various strains may have similar impacts, and many other strains have given comparable better impacts. This has been observed that certain unique characters of the species and its expression may be discovered. In current scenario genomics can help in various ways. In this era of technological advancement, strain selection and development is proven to give immense results [46-48]. Different variables include, probiotic development during item make, protection innovation, and the closeness and accuracy in manufacture of the final product may require a skillfull technique. Many research is going on to see the effects of these factors on natural viability [50-52].

#### PROBIOTICS AS FOOD SUPPLEMENTS

There are various ways for consumption of great microorganisms that is probiotics into our gut: aged nourishments that is fermentation and dietary enhancements that is quality of food intake. Aged nourishmentsis the best way to take probiotics in our diet [53-54]. These are easily available over market place, and are suggested by doctors during digestion related issues. Aging fermentation is probably the most established method for food conservation. Humankind has been maturing fermented foods and beverages like brew and wine for quite a long time. Foods that are fermented experience a procedure of lactofermentation wherein the main microbe feed on the starch and sugar present in the food resulting in production of an acid called lactic acid [55-56]. This procedure give rise to a complex structureto protects the food but also elevate thevaluable compound and nutrients like vitamin B complex, and omega-3 unsaturated fats, all combined in one. Another approach to see maturation is conversation of food into something different as in modified food. Some conversations are cabbage which changes to sauerkraut, cucumbersuse to make somepickles, soybeans modified on miso, and milk is used to create different products like butter, curd, cheese and thick cream.nut this doesn't mean all fermentation leads to probiotic formation [57].

Although the importance of fermented product containing probiotics is great, their taste and smell can be very solid and not likely to many people, which might be the reason for some people to not consume it. And since the flavors are not liked by many, these are modified and fixed with some other flavors to make it more likely hence increasing its consumption. For example, yogurt comes in many flavors other than its basic flavor, probiotics drink has a lot of flavors which add to its taste [58-59]. The most well-known fermented foodthat normally have probiotic content in it are yogurt, pickles, kefir, sauerkraut miso, tempeh, kimchi, sourdough bread, few cheese and a few drink like chaasor buttermilk [60].

Yogurt which is the most popular form of probiotic edible is considered as the excelling of probiotic nourishments as it contains a flavor that is comfortable to mix and adjust with Western palates. Also it can be prepared at home with easy techniques and consumed all over the world. Hence the probiotic content in yogurt can vary from 90 billion to 500 billion of viable cells of microbes also known as culture forming units (CFU). Yogurt contains a lot of lactobacillus which works positively for the digestive system [61-66].

Thus fermented food helps. us have the essential probiotics required to our immune system and maintain good health. Other than having it for breakfast or a late morning nibble, one can substitute yogurt at whatever point one use mayonnaise in egg plate of mixed greens or potato serving of mixed greens, or in practically any preparing formula. [67].

#### MANUFACTURE OF PROBIOTICS

The assembling procedures of LAB and bifidobacteria for dietary enhancements and dairy applications share the accompanying advances practically. Solidified seed stock, which has been deliberately arranged to comprise of a solitary unadulterated strain and confirmed to be liberated from contaminants by quality control (QC) testing, is utilized in a set number of successive seed maturations to accomplish the ideal inoculum volume and is eventually moved to the fundamental aging vessel for development. On the other hand, solidified direct tank immunization material comprises of a bigger measure of concentrated cells that can be utilized to straightforwardly vaccinate the fundamental aging vessel [68]. The point of the two methodologies is to restrict the quantity of ages from seed stock to item, along these lines diminishing any potential hazard for hereditary float. The warmth treated medium utilized in the seed scale up and fundamental aging is a mix of water, nitrogen sources, sugars, salts, and micronutrients vital for development. The maturations are painstakingly controlled and after the aging in the fundamental tank is finished, the cells are focused by isolating the cells from spent medium through centrifugation. Contingent on the last item application, stabilizer arrangements (i.ecryoprotectants to shield cells from injury during freezing or potentially lyoprotectants to shield cells from injury during freeze-drying) might be added to the phones before freezing. Cryoprotectants hinder the pace of ice development by means of expanding the arrangement consistency and keeping the shapeless structure of ice in nearness of the cell. Lyoprotectants settle the lipid bilayer structure of the cell layer without water. Ordinarily utilized cryo-and lyoprotectants are starches and peptides. In the dairy business, skim milk powder is frequently utilized. When the probiotic concentrate is mixed with the cryoprotectant arrangement, different freezing procedures can be applied. One straightforward freezing strategy comprises of emptying cryoprotected gather into jars and inundating the fixed jars into a fluid nitrogen shower.

The solidified jars would then be able to be transported to organizations consolidating probiotics in food or drinks. Then again, a progressively profitable strategy comprises of pelletizing the cryoprotected concentrate by trickling the concentrate through aligned openings into a shower of fluid nitrogen. The pellets, which are regularly circles of 4-5 mm in measurement, are then collected at the base lastly gathered into packs that are put away and transported at a temperature extending from −45 to −55 °C. Then again, solidified cell pellets can be utilized for freeze-drying (lyophilization) to a dried finished result. The solidified pellets are moved onto plate which are put on racks. The racks have the ability of being temperature controlled and are dynamically warmed once vacuum is built up in the freeze-drying chamber. An elective alternative comprises of filling plate with the cryoprotected concentrate [69]. The plate are then positioned on temperature-controlled racks which are at first chilled off to frosty temperatures under climatic tension. When the mass in every plate is solidified, the racks are bit by bit warmed once vacuum is applied. The applied vacuum regularly fluctuates somewhere in the range of 100 and 1000 mTorr and the racks' temperature somewhere in the range of −40 and +40 °C. Freeze-drying length changes as an element of the strain, its plan, and the freeze-drying cycle however normally takes a couple of days to be finished. The upside of freeze-drying is that the procedure keeps up the probiotic cells at a low temperature to constrain harm to the cells' structure and metabolites [70].

## PROBIOTICS IN INDIA

Probiotics in India whether knowingly or unknowingly has been consumed since a long time. But if we talk about production level for the current situation, India holds 1% of the total market all over the world. Most of the probiotics items accessible are predominantlymade from milk that is dahi and a couple of probiotic drinks like flavored milk, lassi, and buttermilk. Although there has been some changes in market scenario and acceptance of other products over these products have been observed which are probiotic advanced juices, vitamin elevated cereal, nourishment bars etc. [71]. In India brand has played a significant role in the production and consumption of these probiotics. The utilization of these manufactured probiotics by per person is 300 grams which is mostly slanted towards urban cities. At present, different companies comprise of 75 to 80% of dahi production because of their bigger establishment and quality trust. Whereas, rest of the 20 to 25% is manufactured by local companies. As the international market is also growing, companies are making their mark. The competition between business companies like Reliance, ITC and CavinKare will increase giving rise to production of good quality products. Since yogurt is consumed in very large amount by the whole population, it alone runs the all over companies worth 1000 crore INR which comprises unflavoured and flavoured yogurt and its varieties, packaged drinksand furthermore the solidified yogurt service market. 20 to 25% of the compound annual growth rate (CAGR) depends on this yogurt and its product.

Indian market relies on dairy products for their probiotics requirement and some marked and trusted brands that offers probiotic food item which people generally rely upon includesMother Dairy, Amul, Yakult, Nestle, Danone, Tablets India, Unique Biotech, Dr Reddy Laboratorie, Zeus Biotech, etc. These are the companies which makes the backbone of the probiotic industry by their contribution in probiotic food developments and by gaining people's trust which expands the scope of more probiotic development and consumption. In the field of probiotics, Amul has done some great works by presenting the concept and manufacturing, Sugar Free Prolife Probiotic Ice Cream, Prolife Lassi, Amul in 2011 presented Fruit Yogurtthat has different flavors like, Strawberry, Pineapple, and Vanilla. It also started manufacture of sweet curd known as MishtiDoi. In 2007, a joint venture between two companies namely Japan's Yakult Honsha and The French-Danone Group happened giving rise to Yakult Danone India Pvt Ltd, released a probiotic fermented milk drink which have more than 6.5 billionbeneficial microbes namely Lactobacillus casei strain Shirota in a 65ml small bottle and is available in the market in the pack of 5 bottles. Mother dairy extended the range withthe new product of an aged milk refreshment called Nutrifitin having two different flavor common within population which were strawberry and mango. [72]. All of these brand excelled in enormous content of good bacteria braced with 5 active nutrients, viz., iron, iodine, calcium, zinc and vitamin A (Table:2).

Table 2: Commercial formulation in India[73,74]

Probiotics organisms	Type of formulation	Uses
used		
B. fidium B.longum L.acidophilus S thermophillus	Actigut (Capsules)	Diarrhea treatment, Vaginal yeast & other bacterial infections
L. acidophillus	Becelac (Capsules)	Improve RBCs, Strong bones, digestive health
L. sporogenes B.mesentericus	Vi Bact (Sachet)	Diarrhea

S. faecalis		
C. butyricum		
L.reuteri	Ecoflora (Capsules)	Improving digestion
L.rhamnosus		
L.sporogenes	Vizyl (Capsules)	Treating Diaarrhea
B. mesentericus		
C.butyricum		
S.faecalis		

## **CONSUMER'S PREFERENCE**

Since large population depends upon dairy products and its consumption, so people have their own way of consuming these probiotics. There are homemade forms like paneeer, curd, yogurt, cheese, chaas, kimchi, pickle etc. In India, dahi is very important part of the daily diet and could be made at home very easily due to the availability of minimum temperature and conditions required. However, in the west, yogurt formation at home is not that valued and hence it is mostly purchased from the grocery stores to fulfill the requirements of probiotics. This demand for yogurt from the market lead to search of more effective and enhanced quality of probiotic consumption be it yogurt or drinks.Rural area public have strong believed on homemade preparations and not giving enough importance to the nutritional content in the manufactured products. The product quality depends upon number of factors such as consumer response, funding, and production quality [75,76,77]. Different variables incorporate the cases and features of the item, for example, medical advantages and the information of the utilitarian fixings present in the item. Slowly people are getting health conscious and have knowledge about most the aspects of food intake. Probiotics have successfully maintained its healthy impact on consumers in the place of certain products claiming benefit and not be able to stand on the terms. This is reason why probiotic industry and research is growing in India. Probiotics are living microbes which when administered in satisfactory sums present medical advantages to the host as said by WHO. For food industry, the matter of concern is customer satisfaction, their suggestions and response, sentiments and conduct so as to maintain a good image in the market by gaining consumer trust and their faith in consumption of their item by the consumers [78].

## CONCLUSION

The study concludes that in today's era, probiotics are essential for human body to maintain proper gut function. Probiotics shows health benefits in treating various diseases and disorders so as to protect the homeostasis a human body maintains and comes as a boon to maintain all the gut related problems and is a great immune enhancer and healthy environment outside. Since it is widely used all over the world, it has been included in dietary essentials. In today's world, where diseases and pandemics are increasing probiotics comes as an aid to many of them through various protective effects and methods. Based on the scientific evidence available to support health benefits of probiotics, varieties of probiotic food available in the market. For the health benefits of society Industry need to established more effective methods for selecting probiotic strain, enhanced quality, safety, efficacy, shelf life of product and labelling claims includes more clear mentioned dosage on product. Globally researchers should come forward to work together to address challenges for the production of probiotics products. A will help the countries to make universally acceptable evidence based guidelines for good and quality manufacture practice for the production of probiotics.

## **COMPETING INTERESTS**

Authors have declared that no competing interests exist

## **REFERENCE**

- 1. Sanders ME, Akkermans LM, Haller D, Hammerman C, Heimbach J, Hörmannsperger G, et al.Safety assessment of probiotics for human use. Gut Microbes. 2010;1(3):164–85.
- 2. Sanders ME, Merenstein DJ, Ouwehand AC, Reid G, Salminen S, Cabana MD, et al. Probiotic usein at-risk populations. J Am Pharm AssocJAPhA. 2016;56(6):680–6.
- Lau CS, Chamberlain RS. Probiotics are effective at preventing Clostridium difficileassociateddiarrhea: a systematic review and meta-analysis. Int J Gen Med. 2016; 22(9):27– 37.
- 4. Hamad A, Fragkos KC, Forbes A. A systematic review and meta-analysis of probiotics for the management of radiation induced bowel disease. ClinNutrEdinbScotl. 2013;32(3):353–60.
- 5. Dang Y, Reinhardt JD, Zhou X, Zhang G. The effect of probiotics supplementation on Helicobacter pylori eradication rates and side effects during eradication therapy: a meta-analysis.PloS One. 2014;9(11):e111030.
- 6. Bindels LB, Delzenne NM, Cani PD, Walter J. Towards a more comprehensive concept for prebiotics.Nat Rev GastroenterolHepatol 2015;12:303–10.
- 7. Floch MH, Walker WA, Sanders ME, Nieuwdorp M, Kim AS, Brenner DA, et al. Recommendations for probiotic use 2015 update: proceedings and consensus opinion. J ClinGastroenterol 2015;49Suppl 1:S69–73.
- 8. Gibson GR, Roberfroid MB. Dietary modulation of the colonic microbiota: introducing the concept of prebiotics. J Nutr1995;125:1401–12.
- Goldenberg JZ, Ma SS, Saxton JD, Martzen MR, Vandvik PO, Thorlund K, et al. Probiotics for the prevention of Clostridium difficile—associated diarrhea in adults and children. Cochrane DatabaseSyst Rev 2013;CD006095. doi: 10.1002/14651858.CD006095.pub3. PubMed PMID: 23728658.
- 10. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scopeand appropriate use of the term probiotic. Nat Rev GastroenterolHepatol2014;11:506–14.
- 11. Du Y-Q, Su T, Fan J-G, Lu Y-X, Zheng P, Li X-H, et al. Adjuvant probiotics improve the eradication effect of triple therapy for Helicobacter pylori infection. World J Gastroenterol. 2012 Nov 21;18(43):6302–7.
- 12. Bekar O, Yilmaz Y, Gulten M. Kefir improves the efficacy and tolerability of triple therapy in eradicating Helicobacter pylori. J Med Food. 2011;14(4):344–7.
- 13. Tong JL, Ran ZH, Shen J, Zhang CX, Xiao SD. Meta-analysis: the effect of supplementation with probiotics on eradication rates and adverse events during Helicobacter pylori eradication therapy. Aliment PharmacolTher. 2007;25(2):155–68.
- 14. Francavilla R, Polimeno L, Demichina A, Maurogiovanni G, Principi B, Scaccianoce G, et al. Lactobacillus reuteri strain combination in Helicobacter pylori infection: a randomized, doubleblind, placebo-controlled study. J ClinGastroenterol. 2014;48(5):407–13.

- 15. Emara MH, Mohamed SY, Abdel-Aziz HR. Lactobacillus reuteri in management of Helicobacter pylori infection in dyspeptic patients: a double-blind placebo-controlled randomized clinical trial. TherAdvGastroenterol. 2014;7(1):4–13.
- 16. Hungin AP, Mulligan C, Pot B, Whorwell P, Agréus L, Fracasso P, et al. Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice an evidence-basedinternational guide. Aliment PharmacolTher2013; 38:864–86.
- 17. N. Kobyliak, C. Conte, G. Cammarota, A.P. Haley, I. Styriak, L. Gaspar, *et al.*Probiotics in prevention and treatment of obesity: a critical viewNutr Metab,2016; 1-13
- 18. G.R. Gibson, M.B. RoberfroidDietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr,1995;125:1401-1412
- H.J. HamasalimSynbiotic as feed additives relating to animal health and performanceAdv Microbiol,2016;6:288-302
- 20. G.P.A. Bongaerts, R.S.V.M. SeverijnenA reassessment of the PROPATRIA study and its implications for probiotic therapyNature Biotechnol,2016;34;55-63
- 21. R.M. Patel, P.W. DenningTherapeutic use of prebiotics, probiotics, and postbiotics to prevent necrotizing enterocolitis: what is the current evidence?Clin Perinatol,2013;40:11-25
- 22. S.U. IslamClinical uses of probioticsMedicine (Baltimore),2016;95:1-5
- 23. M.F. Ooi, N. Mazlan, H.L. Foo, T.C. Loh, R. Mohamad, R.A. Rahim, *et al.*Effects of carbon and nitrogen sources on bacteriocin-inhibitory activity of postbiotic metabolites produced by Lactobacillus plantarum I-UL4Malays J Microbiol,2015;11:176-184
- 24. Ambalam, P.; Raman, M.; Purama, R.K.; Doble, M. Probiotics, prebiotics and colorectal cancer prevention.BestPract. Res. Clin. Gastroenterol.2016;30:119–131.
- 25. Bautista-Gallego, J.; Ferrocino, I.; Botta, C.; Ercolini, D.; Cocolin, L.; Rantsiou, K. Probiotic potential of aLactobacillusrhamnosuscheese isolate and its effect on the fecal microbiota of healthy volunteers. Food Res. Int. 2019;119: 305–314.
- 26. Tarrah, A.; de Castilhos, J.; Rossi, R.C.; da Duarte, V.S.; Ziegler, D.R.; Corich, V.; Giacomini, A.InvitroProbiotic Potential and Anti-cancer Activity of Newly Isolated Folate-ProducingStreptococcusthermophilusStrains.Front. Microbiol.2018;9:2214.
- 27. Bermúdez-Humarán, L.G.; Salinas, E.; Ortiz, G.G.; Ramirez-Jirano, L.J.; Morales, J.A.; Bitzer-Quintero, O.K.From Probiotics to Psychobiotics: Live Beneficial Bacteria Which Act on the Brain-Gut Axis.Nutrients2019;11:890
- 28. Cicenia, A. Scirocco, M. Carabotti, L. Pallotta, M. Marignani, C. SeveriPostbiotic activities of lactobacilli-derived factorsJClinGastroenterol, 2014, 48, S18-S22
- 29. G.R. Gibson, R. Hutkins, M.L. Sanders, S.L. Prescott, R.A. Reimer, S.J. Salminen, et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebioticsNat Rev GastroenterolHepatol, 2017;14:491-502
- 30. M. Kano, N. Masuoka, C. Kaga, S. Sugimoto, R. Iizuka, K. Manabe, et al. Consecutive intake of fermented milk containing Bifidobacteribreve strain Yakult and galacto-oligosaccharides benefits skin condition in healthy adult womenBiosci Microbiota Food Health, 2013;32: 33-39
- 31. K. Nomoto, Prevention of infections by probiotics, J. Bio-sci. Bioeng. 2005;100:583–592
- 32. .C. Maldonado Galdeano, A. de Moreno de LeBlanc, E.Carmuega, R. Weill, G. Perdigón, Mechanisms involved intheimmunostimulation by probiotic fermented milk, J.Dairy Res. 2009;76:446–454
- 33. .M. Medina, E. Izquierdo, S. Ennahar, Y. Sanz, Differentialimmunomodulatory properties of Bifidobacterium logumstrains: Relevance to probiotic selection and clinical applications, Clin. Exp. Immunol. 2007;531–538.

- 34. D. Kelly, J.I. Campbell, T.P. King, G. Grant, E.A. Jansson, A.G. Couttset al., Commensal anaerobic gut bacteria atte-nuate inflammation by regulating nuclear-cytoplasmicshuttling of PPAR-gandRelA, Nat. Immunol. 2004;5:104–112.
- 35. .K.Arunachalam, H.S. Gill, R.K. Chandra, Enhancement of natural immune function by dietary consumption of Bifido-bacterium lactis (HN019), Eur. J. Clin. Nutr. 2000;54:263–267.
- 36. B.L. Chiang, Y.H. Sheih, L.H. Wang, C.K. Liao, H.S. Gill, Enhancing immunity by dietary consumption of a pro-biotic lactic acid bacterium (Bifidobacterium lactisHN019):Optimization and definition of cellular immune re-sponses, Eur. J. Clin. Nutr. 2000;54849–855.
- 37. H.S. Gill, K.J. Rutherfurd, J. Prasad, P.K. Gopal, Enhance-ment of natural and acquired immunity byLactobacillusrhamnosus(HN001), Lactobacillus acidophilus(HN017) andBifidobacteriumlactis(HN019), Br. J. Nutr. 2000; 83:167–176.
- 38. .Q. Shu, H.S. Gill, A dietary probiotic (Bifidobacterium lactisHN019) reduces the severity of Escherichia coliO157:H7infection in mice, Med. Microbiol. Immunol. 2001; 189:147–152
- 39. Peiren J, Buyse J, De Vos P, Lang E, Clermont D, et al. Improvingsurvival and storage stability of bacteria recalcitrant to freeze-drying: accordinated study by European culture collections. ApplMicrobiolBiotechnol2015;99: 3559-3571.
- 40. Champagne CP, Gardner NJ, Roy D. Challenges in the addition of probiotic cultures to foods. Crit Rev Food SciNutr2005;45: 61-84.
- 41. Eric Banan-MwineDaliri, Fred Kwame Ofosu, Chen Xiuqin, Ramachandran Chelliah, and Deog-Hwan Oh\* Probiotic Effector Compounds: Current Knowledge and Future Perspectives Front Microbiol. 2021; 12: 655705.
- 42. TolulopeJoshuaAshaoluImmune boosting functional foods and their mechanisms: A critical evaluation of probiotics and prebiotics. 2020;130: 110625
- 43. Mohamed Zommiti, Marc G. J. Feuilloley and Nathalie Connil. Update of Probiotics in Human World: A Nonstop Source of Benefactions till the End of Time Microorganisms 2020; 8:1907
- 44. Neel Jayesh Shah, \*Onkar C. Swami. ROLE OF PROBIOTICS IN DIABETES: A REVIEW OF THEIR RATIONALE AND EFFICACYEMJ Diabet. 2017;5[1]:104-110.
- 45. BathalVijaya Kumar &SistlaVenkata Naga Vijayendra&ObulamVijayaSarathi. ReddyTrends in dairy and non-dairy probiotic products -a review.Journal of Food Science and Technology Mysore- 2015;52(10) DOI 10.1007/s13197-015-1795-2
- 46. Gibson GR, Walton GE. Impact of high fat diets, prebiotics and probiotics on gut microbiota and immune function, with relevance to elderly populations. Nutrition and Aging. 2015;3(2-4):171-92.
- **47.** Zhang MM, Cheng JQ, Lu YR, Yi ZH, Yang P, Wu XT. Use of pre-, pro-and synbiotics in patients with acute pancreatitis: a meta-analysis. World J Gastroenterol: WJG. 2010;16(31):3970.
- 48. Olson D, Aryana K. An excessively high Lactobacillus acidophilusinoculation level in yogurt lowers product quality during storage. FoodSciNutr2008;41: 911-918.
- 49. Jacobs S, Verbeke W, Sas B. Mode of delivery of probioticsConsumers' preference and its determinants. Agro food Industry Hi Tech.2014;25: 6.
- 50. Champagne CP, Ross RP, Saarela M, Hansen KF, CharalampopoulosD.Recommendations for the viability assessment of probiotics asconcentrated cultures and in food matrices. Int J Food Microbiol2011; 149:185-193.
- 51. Kozubsky L, et al. Lactobacillus johnsoniiLa1 antagonizes Giardiaintestinalis in vivo. Infect Immun,2005;73:1265-9

- 52. Ivey KL, Lewis JR, Hodgson JM. Association between yogurt,milk,cheese consumption and common carotid artery intima-media thicknessand cardiovascular disease risk factors in elderly women. Am J Clin Nutr.2011;94(1):2349
- 53. Jaeger SR.Non-sensory factors in sensory science research. FoodQualPrefer 2006;17(1-2): 132- 144
- 54. Johnson MS, Jumbo Lucioni P, Watts AJ, Allison DB, Nagy TR Effect of dairy supplementation on body composition andinsulinresistance in mice. Nutr.2007;23(1112):83643
- 55. Kiessling G, Schneider J, Jahreis G (2002) Long term consumptionoffermented dairy products over 6 months increases HDLcholesterol.Eur J ClinNutr.2002;56(9):843-9
- 56. Kumar M, Kumar R, Poovai PD, KalaichelvanPT.Probiotics and multitude of health benefits. J Res Bio2012;2: 102-13
- 57. Caro DS, Tao H, Grillo A, Elia C, Gasbarrini G, Sepulveda AR &Gasbarrini A. Effects of Lactobacillus GG on genes expression pattern in small bowel mucosa. Dig Liver Dis.2005; 37: 320–332.
- 58. Chen JJ, Wang R, Li XF &Wang RL.Bifidobacteriumlongum supplementation improved high-fat-fed-induced metabolic syndrome and promoted intestinal Reg-I gene expression. ExpBiol Med 2011;236: 823–831.
- 59. Collins JK, Thornton G &Sulliva GO (1998) Selection of probiotic strains for human application. Int Dairy J .1998;8: 487–490.
- 60. Conly JM, Stein K, Worobetz L & Rutledge-Harding S.The contribution of vitamin K2 (metaquinones) produced by the intestinal microflora to human nutritional requirements for vitamin K. Am J Gastroenterol.1994;89: 915–923.
- 61. Dambekodi PC & Gilliland SE. Incorporation of cholesterol into the cellular membrane of Bifidobacteriumlongum. J Dairy Sci.1998; 81: 1818–1824.
- 62. Delzenne N & Reid G. No causal link between obesity and probiotics. Nat Rev Microbiol.2009; 7: 901.
- 63. Delzenne NM, NeyrinckAM, Ba¨ckhed F &CaniPD.Targeting gut microbiota in obesity: effects of prebiotics and probiotics. Nat Rev Endocrinol.2011;7: 639–646.
- 64. Desjardins ML & Roy D.Growth of Bifidobacteria and their enzyme profiles. J Dairy Sci.1990;73: 299–307.
- 65. Donkor ON, Henriksson A, Vasiljevic T & Shah NP.Rheological properties and sensory characteristics of set-type soy yogurt. J Agric Food Chem.2007;55: 9868–9876.
- 66. Nagpal R, Yadav H, Puniya AK, Singh K, Jain S & Marotta F. Potential of probiotics and prebiotics for synbiotic functional dairy foods. Int J Probiotics Prebiotics.2007; 2: 75–84.
- 67. Nagpal R, Kumar A & Arora S. In-vitro probiotic potential of lactobacilli from indigenous milk products. Int J Probiotics Prebiotics.2010;5: 103–110.
- 68. Nagpal R, Behare PV, Kumar M et al.Milk, milk products and disease free health: an updated overview. Crit Rev Food Sci Nutr.2011; 99999: 1549–7852.
- 69. Naito E, Yoshida Y, Makino K, Kounoshi Y, Kunihiro S, Takahashi R, Matsuzaki T, Miyazaki K & Ishikawa F Beneficial effect of oral administration of Lactobacillus casei strain Shirota on insulin resistance in diet-induced obesity mice. J ApplMicrobiol 2011;110: 650–657
- 70. Chaafsma G. State of art concerning probiotic strains in milk prod-ucts. IDF Nutr News Lett 1996;5:23–4.21.
- 71. Molin G. Probiotics in foods not containing milk or milk con-stituents, with special reference to Lactobacillos planturum299v.Am J ClinNutr 2001;73(suppl):380S–5S.22.
- 72. Sekine K, Toida T, Saito M, Kuboyama M, Kawashima T. A new morphologically characterized cell wall preparation (whole peptido-glycan) from Bifidobacteriuminfantis with a

- higher efficacy on theregression of an established tumor in mice. Cancer Res 1985; 45:1300–7.23.
- 73. Farmer RE, Shahani KM, Reddy GV. Inhibitory effect of yoghurt components upon the proliferation of ascites tumor cells. J DairySci1987; 58:787–8.24.
- 74. Guidelines and criteria for evaluation of efficacy, safety and health claim of probiotic in food products in India. ILSI, India. [Cited Sep 2012]. Available from http://www.ilsi-india.org/PDF/Probiotic-in-Food-Products.pdf
- 75. Balaji R. Raja1 and Kantha D. Arunachalam.Market potential for probiotic nutritional supplements in IndiaAfrican Journal of Business Management.2011;5(14):5418-5423,
- 76. Kurt Fenster, Barbara Freeburg, Chris Hollard, Connie Wong, Rune Rønhave Laursen, and Arthur C. Ouwehand, The Production and Delivery of Probiotics: A Review of a Practical Approach. Microorganisms. 2019 Mar; 7(3): 83.
- 77. Steward-Tull DES. The immunological activities of bacterial pepti-doglycans. Ann Rev Microbiol 1980; 34:311–40.25.
- 78. Okutomi T, Inagawa H, Nishizawa T, Oshima H, Soma GI, MizunoDI. Priming effect of orallyadministered muramyldipeptideoninduction of endogenous tumor necrosis factor. J BiolResponseMod 1990;9:564–9.26.
- De VreseM, Stegelmann A, Richter B, Fenselau S, Laue C,Schrezenmeir J. Probiotics—compensation for lactase insufficiency. Am J ClinNutr 2001;73(suppl):421S–9S.27.