DBN Review N° 25
A resource about dairy-based nutrition
A product of the Consumer Education Project of Milk SA
www.rediscoverdairy.co.za

The current review focuses on the health effects of dairy-based prebiotics and probiotics on the gut microbiome.

A publication for health professionals

Health effects of dairy foods on the gut microbiome

Current scientific opinion agrees that milk and milk product intake improves dietary quality and can be linked to a reduced risk of obesity and chronic metabolic conditions.[1-3] Although several mechanisms may underlie the health benefits of dairy foods, the recent emphasis on the structure and function of the human gut microbiome has focused attention on the potential role of probiotics and prebiotics in dairy foods in promoting human health.[4]

The word 'probiotic' comes from Greek, meaning 'for life'. The current definition, adopted by the Food and Agriculture Organization of the United Nations and the World Health Organization in 2002, states that probiotics are 'live strains of strictly selected microorganisms which, when administered in adequate amounts, confer a health benefit on the host'.[5] On the other hand, prebiotics are defined as non-digestible dietary compounds that act as a food source for probiotics, stimulating their growth and beneficially changing their composition or activity.[6,7] Lactose and oligosaccharides present in dairy foods serve as prebiotics, whereas probiotics are found in fermented foods that contain probiotic strains of lactic acid bacteria, such as cultured (fermented) milk products and yoghurt that include beneficial probiotic strains. The capacity to modify the microbiome is enhanced when probiotics and prebiotics are combined, and Gibson and Roberfroid consequently defined the term 'synbiotic' to describe a blend of probiotics and prebiotics acting in synergy (as cited by Markowiak and Śliżewska[5]).

The gut microbiome

The gut microbiome refers to the intestinal community of microbes that contribute to maintaining and influencing health.[8,9] This community includes trillions of microbes from more than a thousand bacterial species.[10]

Various and strain-specific mechanisms of action for the beneficial effects of probiotics have been identified, including colonisation of the gut with beneficial microbes; production of beneficial short-chain fatty acids (SCFAs); production of antimicrobial substances; competition with pathogens for adhesion to the epithelium; modulation of immune, endocrine and neurologic functions; and inhibition of bacterial toxin production.[11]

A large body of evidence confirms that lower bacterial diversity in the gut is associated with chronic and inflammatory diseases,[4,8,12] with different disease states being characterised by unique microbiota profiles.[10] Many factors influence the diversity of the gut microbiome and starts at birth already, when the microbiome is determined by the mode of delivery, the mother's health and whether children are breastfed or formula-fed.[13]

Bacterial diversity is an indicator of gut health and although functionally related microbes can compensate for the function of other missing species, certain conditions, such as obesity and metabolic complications, are closely associated with low microbial diversity and dysbiosis.[14-16] A healthy microbiome is characterised primarily by species from the Firmicutes and Bacteroidetes phyla, although some from the phylum Actinobacteria also make a marginal, but important, contribution.[17] The phylum Firmicutes is represented predominantly by the genera *Clostridium, Enterococcus, Lactobacillus* and *Faecalibacterium*, whereas the genera *Bacteroides* and *Prevotella* are the major species from the phylum Bacteroidetes present in the gut microbiome.[18]

The phylum Actinobacteria is represented mainly by *Bifidobacteria*, contributing to lactose utilisation[19] and protecting against adverse health conditions.[20] The species Bifidobacteria and Firmicutes are generally abundant in the microbiome of people from non-westernised communities, whereas Bacteroides are more abundant in the microbiome of people from westernised communities.[21]

Composition of the gut microbiome is fairly stable in a healthy person, but microbial dynamics are influenced by host lifestyle and diet, with diet and dietary components shaping the microbiome to a considerable extent.[4,12,22] What people eat directly influences the gut microbiota, which, in turn, affects metabolism, immunity and neurobehavioural traits and so ultimately impacts on well-being and disease risk.[8,12,23-26] While the intake of excessive protein, fructose and saturated fats has been shown to have negative effects on the microbiome, both prebiotics and probiotics can beneficially regulate intestinal health.[4,14,27,28] It is not only the microbes themselves that impact on health but also the products of their metabolism. Fermentation supports the growth of specialist microbes that produce SCFAs and gases closely linked to specific beneficial metabolic effects,[12] with important health implications.

Lactose intolerance

The disaccharide lactose, which is the main source of energy in milk, consists of the two monosaccharides galactose and glucose linked together. The enzyme lactase is needed to hydrolyse lactose to glucose and galactose for these sugars to be absorbed and transported across the intestinal mucosa.[29] Lactase is produced in the intestinal mucosa of most mammals and full-term infants generally have sufficient lactase activity to digest milk. However, lactase activity declines after weaning in most humans (lactase non-persistence), especially those from East Asian and African heritage,[30] resulting in different degrees of lactose maldigestion.[31-34] According to Leonardi et al.[35] only about 35% of the human population can digest lactose beyond the age of about seven or eight years.

Lactose intolerance refers to the digestive symptoms associated with lactose maldigestion. Undigested lactose moves from the small intestine to the colon, where it serves as a prebiotic that is fermented by bacteria. This sometimes produces gas, which may lead to symptoms such as abdominal discomfort, nausea, cramps, bloating, flatulence and diarrhoea.[31,33] Despite this, lactose intolerance is not considered a disease, as only about 50% of lactase activity is required for the effective digestion of lactose. Most people who are lactose intolerant can eat small amounts of dairy foods without experiencing discomfort.

Those who consider themselves lactose intolerant may decrease their dairy intake, resulting in the compromised intake of the nutrients and other beneficial compounds in dairy.[36] However, total avoidance of dairy foods is unnecessary, as several easily applied strategies can assist in reducing undesirable symptoms:[31,32,34,37-39]

- A low lactose load is unlikely to cause symptoms, even in lactose-intolerant persons. Using small amounts of dairy at a time (e.g. less than one serving of milk, which contains 12 g lactose) or consuming milk with a meal slows the release of lactose into the small intestine and so reduces the load to be digested. Less discomfort is subsequently experienced.
- Dairy foods such as cheese (especially hard cheeses), active-culture yoghurt and fermented products such as buttermilk contain only small amounts of lactose and can be eaten without causing gastrointestinal discomfort. Lactic acid bacteria already convert some of the lactose to lactic acid during production of these foods.
- The semi-solid state of yoghurt slows gastric emptying and gastrointestinal transit, providing more time for lactose digestion.
- Reduced-lactose or lactose-free milk is also available. Although a more expensive dairy product, it has many health benefits over replacing dairy altogether by a substitute such as soy milk.
- Taking a lactase tablet with milk improves digestion.
- Milk and dairy products are better tolerated if consumed with other foods or incorporated in a dish. When taken with a meal, milk is digested more slowly and as a result, lactose is released more slowly into the small intestine, thereby reducing the digestive lactose load. Foods high in soluble fibre also delay gastric emptying and combining their intake with that of milk therefore provides additional time for intestinal lactase action.
- Tolerance can be built up gradually. Consuming lactose-containing foods encourages an intestinal flora population with active lactase to form. This can improve the ability of the bacteria in the gut to break down lactose and so tolerance of lactose-containing foods is gradually increased.

Effects of dairy as a prebiotic

Fermentable fibres and prebiotics have the potential to shape the diversity of the microbiome by stimulating the growth of specific genera of the gut microbiota. In addition to the prebiotic lactose, milk also contains oligosaccharides (e.g. galactooligosaccharides), which are composed of three to ten sugar molecules linked together. They do not serve as a source of energy, but rather provide nutrients to intestinal bacteria, therefore performing a major role in gut health.[29]

In persons with lactase non-persistence, lactose is not fully digested and thus proceeds to the colon. In contrast, most of the lactose will be digested in the small intestine of lactase-persistent persons, although a small amount may reach the large intestine.[6] Lactose and oligosaccharides in milk are considered to be bioactive ingredients with bifidogenic effects,[31,40] serving as a substrate for the growth of the beneficial *Bifidobacteria* and *Lactobacillus* bacteria. In inflammatory bowel disease, the bifidogenic effects of prebiotics such as lactose may prevent the growth of potential pathogens.[5,41]

Colonic microbiota ferment the lactose and oligosaccharides in dairy foods in the colon, producing metabolites such as SCFAs (primarily acetate, propionate and butyrate) and gases.[12,42] These metabolites lead to the uncomfortable symptoms experienced by persons who are lactose intolerant when they ingest large amounts of milk. The SCFAs produced when prebiotics are fermented have several important functions: they are metabolised by the colonocytes; promote colon motility; reduce inflammation; increase visceral irrigation; induce apoptosis, and inhibit tumour cell progression. Furthermore, SCFAs have been shown to protect against diet-induced obesity, probably through an effect on gut hormones that reduce appetite and food intake. SCFAs can also be absorbed into the portal circulation and transported to the liver, where they may have beneficial systemic effects.[31,43] Moreover, fermentation of lactose in the colon has a positive effect on the absorption of minerals, particularly calcium and magnesium, owing to increased mineral solubility or enhanced osmotic pressure.[44]

With regard to immune function, lactose may have beneficial effects on gut immunity in both children and adults through interactions with other carbohydrates or SCFAs.[5,6] Lactose may further promote immunity through the cathelicidin antimicrobial peptide, which ideally occurs synergistically with other colonic fermentation metabolites such as butyrate.[45]
In the presence of undigested lactose, enzymes that metabolise sugars are stimulated, leading to a decrease in harmful bacterial metabolites such as hydrogen and ammonia.[46]

Hirahatake et al.[40] have shown that the intestinal production of glucagon-like peptide (GLP-1) is influenced by components in foods that provide a substrate for colonic microbiota. In particular, prebiotics and probiotics from dairy may influence gut microbiota in such a way that insulin sensitivity and the action of GLP-1 are positively affected.[47,48] The low glycaemic index of lactose also contributes to improved glycaemic control.[49]

Probiotic effects of fermented dairy foods

In addition to beneficial fatty acids, micronutrients and bioactive peptides, fermented foods also contain live microbes (probiotics) that can influence the diversity and composition of the gut microbiota favourably.[50-52]

How fermented foods are manufactured, processed and stored determines the types and number of microbes that are present.[53] Cultured dairy products and cheese are commonly made using starter cultures chosen for specific performance characteristics. Lactic acid bacteria are preferred for milk fermentation as they do not affect the taste and nutritional value of dairy. The growth of these bacteria is furthermore enhanced by the vitamins, amino acids and nucleotides present in milk.[50]

Lactic acid bacteria such as *Lactobacillus*, *Streptococcus* and *Leuconostoc* are commonly used at levels of 107–109 colony forming units per gram lactic acid bacteria. Starter cultures of *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. bulgaricus are most often used in the production of yoghurt.[53] According to Marco et al.,[54] the food matrix of dairy can protect bacteria during their transit through the gut, improving the delivery of viable bacteria.

Although probiotics consumed in microbe-containing foods are transient components of the microbiome (they seldom persevere for more than a few days),[55,56] they have numerous beneficial effects on the diversity, structure and function of the gut microbiota, especially when they are habitually consumed.[56] Fermented dairy foods such as cultured milk products and yoghurt beneficially regulate intestinal health through direct effects on the gut and through immune effects. A recent study by González et al.[15] assessed the association between the consumption of fermented dairy foods, microbial diversity and biomarkers of health in an observational cohort. The authors found that study participants who consumed natural yoghurt had higher levels of the beneficial *Akkermansia* bacteria and lower levels of inflammation than those who did not consume natural yoghurt (although consumption of sweetened yoghurt was associated with lower levels of *Bacteroides*). These findings have been confirmed in probiotic yoghurt intervention studies,[57,58] suggesting that fermented dairy products may protect against chronic low-grade inflammation common in many chronic conditions, such as metabolic syndrome.[16,50,59] Proposed mechanisms include the possible induction of anti-inflammatory cytokines such as IL-1011,60,61 and an increase in total serum IgA to potentiate the humoral immune response.[4]

Other health benefits of fermented dairy products include improved lactose tolerance and alleviation of gastrointestinal intolerance symptoms,[50,62] accelerated intestinal transit time, inhibition of pathogen adhesion to the intestinal mucosa,[55,63] prophylactic prevention of traveller's diarrhoea[4] and improved glucose metabolism.[59] Cheese consumption is associated with increased *Bifidobacteria* counts and decreased *Bacteroides* and *Clostridium* counts (some strains are associated with intestinal infections), providing potential protection against pathogens through increased production of SCFAs and decreased production of trimethylamine oxide.[26,64,65]

Conclusion

There is substantial evidence that the human microbiome can be modified by diet and that specific dietary components are closely linked to health and disease. A balanced diet has a positive impact on the microbiome, decreasing the risk of developing metabolic and inflammatory diseases. Milk and fermented dairy foods contain microbial, nutritive and bioactive components that benefit the gut microbiome and, consequently, general health. Research related to the potential lasting impact of habitual dairy intake on the microbiome and the potential to promote shifts in microbiota species is, however, needed. This is especially important in poverty-stricken communities, where the risk for gastrointestinal infections is high.

REFERENCES

1. Rafey MF, Murphy CF, Abdalgwad R, Kilkelly K, Griffin H, Beatty N, et al. Effects of a milk-based meal replacement program on weight and metabolic characteristics in adults with severe obesity. Diabetes Metab Syndr Obes. 2020; 13:197-205.

2. Mozaffarian D. Dairy foods, obesity, and metabolic health: The role of the food matrix compared with single nutrients. Adv Nutr. 2019; 10(5):917S-923S.

3. Kongerslev Thorning T, Raben A, Tholstrup T, Soedamah-Muthu SS, Givens I, Astrup A. Milk and dairy products: good or bad for human health? An assessment of the totality of scientific evidence. Food Nutr Res. 2016; 60:32527.

4. Singh RK, Chang H, Yan D, Lee KM, Ucmak D, Wong K, et al. Influence of diet on the gut microbiome and implications for human health. J Transl Med. 2017; 15:73.

5. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health.Nutrients. 2017; 9(9):1021.

6. Lukito W, Malik SG, Surono IS, Wahlqvist ML. From 'lactose intolerance' to lactose nutrition'.Asia Pac J Clin Nutr. 2015; 24 Suppl 1:S1-8.

7. Visioli F, Strata A. Milk, dairy products, and their functional effects in humans: A narrative review of recent evidence. Adv Nutr. 2014; 5:131-143.

8. Hills RD Jr, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut microbiome: Profound implications for diet and disease. Nutrients. 2019;11(7):1613.

9. Velasquez-Manoff M. How the Western diet has derailed our evolution. Nautilus. 2019; 30.

10. Duvallet C, Gibbons SM, Gurry T, Irizarry RA, Alm EJ. Meta-analysis of gut microbiome studies dentifies disease-specific and shared responses. Nat Commun. 2017; 8:1784.

11. Plaza-Diaz J, Ruiz-Ojeda FJ, Gil-Campos M, Gil A. Mechanisms of action of probiotics. Adv Nutr.2019; 10 Suppl 1:S49-66.

12. Valdes AM. Role of the gut microbiota in nutrition and health. BMJ. 2018; 361:k2179.

13. Robertson RC, Manges AR, Finlay BB, Prendergast AJ. The human microbiome and child growth – first 1000 days and beyond. Trends Microbiol. 2019; 27(2):131-147.

14. Cerdó T, García-Santos JA, G Bermúdez M, Campoy C. The role of probiotics and prebiotics in the prevention and treatment of obesity. Nutrients. 2019;11(3):635.

15. González S, Fernández-Navarro T, Arboleya S, De los Reyes-Gavilán CG, Salazar N, Gueimonde M. Fermented dairy foods: Impact on intestinal microbiota and health-linked biomarkers. Front Microbiol. 2019; 10:1046.

16. Baothman OA, Zamzami MA, Taher I, Abubaker J, Abu-Farha M. The role of gut microbiota in the development of obesity and diabetes. Lipids Health Dis. 2016; 15:108.

17. Tuohy K, Del Rio D. Diet-microbe interactions in the gut: Effects on human health and disease. Amsterdam: Elsevier Science, 2014.

18. Eckburg PB, Lauber CL, Costello EK, Berg-Lyons D, Gonzalez A, Stombaugh J. Diversity of the human intestinal microbial flora. Science. 2005; 308:1635-1638.

19. Rivière A, Selak M, Lantin D, Leroy F, De Vuyst L. Bifidobacteria and butyrate-producing colon bacteria: Importance and strategies for their stimulation in the human gut. Front Microbiol. 2016; 7:979.

20. Amar J, Lange C, Payros G, Garret C, Chabo C, Lantieri O, et al. Blood microbiota dysbiosis is associated with the onset of cardiovascular events in a l arge general population: The DESIR Study. PLoS ONE. 2013; 8:e54461.

21. Pasolli E, Asnicar F, Manara S, Zolfo M, Karcher N, Armanini F. Extensive unexplored human microbiome diversity revealed by over 150 000 genomes from metagenomes spanning age, geography, and lifestyle. Cell. 2019; 176:649-662.

22. Wilson AS, Koller KR, Ramaboli MC, Nesengani LT, Ocvirk S, Chen C, et al. Diet and the human gut microbiome: An international review. Dig Dis Sci. 2020; 65(3):723-740.

23. Fernández-Navarro T, Salazar N, Gutiérrez-Díaz I, Sánchez B, Rúas-Madiedo P, De los ReyesGavilán CG. Bioactive compounds from regular diet and faecal microbial metabolites. Eur J Nutr.2018; 57:487-497.

24. Rothschild D, Weissbrod O, Barkan E, Kurilshikov A, Korem T, Zeevi D, et al. Environment dominates over host genetics in shaping human gut microbiota. Nature. 2018; 555:210-215.

25. Levy M, Kolodziejczyk AA, Thaiss CA, Elinav E. Dysbiosis and the immune system. Nat Rev Immunol. 2017; 17:219-232.

26. Zhang H, Sparks JB, Karyala SV, Settlage R, Luo XM. Host adaptive immunity alters gut microbiota. ISMEJ. 2015; 9:770-781.

27. David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, et al. Diet rapidly and reproducibly alters the human gut microbiome. Nature. 2014; 505:559-563.

28. Tong X, Dong JY, Wu ZW, Li W, Qin LQ. Dairy consumption and risk of type 2 diabetes mellitus: A meta-analysis of cohort studies. Eur J Clin Nutr. 2011; 65:1027-1031.

29. Pereira PC. Milk nutritional composition and its role in human health. Nutrition. 2014; 30:619-627.

30. Deng Y, Misselwitz B, Ning D, Fox M. Lactose intolerance in adults: Biological mechanism and dietary management. Nutrients. 2015; 7:8020–8035.

31. Vandenplas Y. Lactose intolerance. Asia Pac J Clin Nutr. 2015; 24(1):S9-S13.

32. Heaney RP. Dairy intake, dietary adequacy, and lactose intolerance. Adv Nutr. 2013; 4:151-156.

33. Mattar R, De Campos Mazo DF, Carrilho FJ. Lactose intolerance: Diagnosis, genetic, and clinical factors. Clin Exp Gastroenterol. 2012; 5:113-121.

34. Brown-Esters O, Mc Namara P, Savaiano D. Dietary and biological factors nfluencing lactose intolerance. Int Dairy J. 2012; 22:98-103.

35. Leonardi M, Gerbault P, Thomas M, Burger J. The evolution of lactase persistence in Europe. A synthesis of archaeological and genetic evidence. Int Dairy J. 2012; 22:88-97.

36. Bailey RK, Pozo Fileti C, Keith J, Tropez-Sims S, Price W, Allison-Ottey SD. Lactose intolerance and health disparities among African Americans and Hispanic Americans: An updated consensus statement. J Natl Med Assoc. 2013; 105(2):112-127.

37. Hodges JK, Cao S, Cladis DP, Weaver CM. Lactose intolerance and bone health: The challenge of ensuring adequate calcium intake. Nutrients. 2019;11(4):718.

38. Suchy FJ, Brannon PM, Carpenter TO, Fernandez JR, Gilsanz V, Gould JB, et al. National Institutes of Health Consensus Development Conference: Lactose intolerance and health. Ann Intern Med. 2010; 152:792-796.

39. European Food Safety Authority. Scientific opinion on the substantiation of health claims related to live yoghurt cultures and improved lactose digestion (ID 1143,2976) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA J. 2010; 8(10):1763-1781.

40. Hirahatake KM, Slavin JL, Makic KC, Adams SH. Associations between dairy foods, diabetes, and metabolic health: Potential mechanisms and future directions. Metabolism. 2014; 63:618-627

41. Szilagyi A. Review article: Lactose--a potential prebiotic. Aliment Pharmacol Ther. 2002;16(9):1591-1602.

42. Venema K. Intestinal fermentation of lactose and prebiotic lactose derivatives, including human milk oligosaccharides. Int Dairy J. 2012; 22:123-140.

43. Vulevic J, Juric A, Walton GE, Claus SP, Tzortzis G, Toward RE, et al. Influence of galactooligosaccharide mixture (B-GOS) on gut microbiota, immune parameters and metabonomics in elderly persons. Br J Nutr. 2015; 114:586-595.

44. Romero-Velarde E, Delgado-Franco D, García-Gutiérrez M, Gurrola-Díaz C, Larrosa-Haro A, Montijo-Barrios E, et al. The importance of lactose in the human diet: Outcomes of a Mexicanconsensus meeting. Nutrients. 2019; 11(11):2737.

45. Wahlqvist ML. Lactose nutrition in lactase nonpersisters. Asia Pac J Clin Nutr. 2015; 24(1):S21-S25.

46. Cederlund A, Kai-Larsen Y, Printz G, Yoshio H, Alvelius G, Lagercrantz H, et al. Lactose in human breast milk an inducer of innate immunity with implications for a role in intestinal homeostasis. PLoS One. 2013; 8(1):e53876.

47. Flint HJ, Scott KP, Louis P, Duncan SH. The role of the gut microbiota in nutrition and health. Nat Rev Gastroenterol Hepatol. 2012; 9(10):577-589.

48. Zivkovic AM, Barile D. Bovine milk as a source of functional oligosaccharides for improving human health. Adv Nutr. 2011; 2:284-289.

49. Wolever TM. Yogurt is a low-glycemic index food. J Nutr. 2017; 147(7):1462S-1467S.

50. Ghosh T, Beniwal A, Semwal A, Navani NK. Mechanistic insights into probiotic properties of lactic acid bacteria associated with ethnic fermented dairy products. Front Microbiol. 2019;10:502.

51. Severyn CJ, Bhatt AS. With probiotics, resistance is not always futile. Cell Host Microbe. 2018;24:334-336.

52. Panahi S, Doyon CY, Després JP, Pérusse L, Vohl MC, Drapeau V, et al. Yogurt consumption, body composition, and metabolic health in the Québec family study. Eur J Nutr. 2018; 57:1591-1603.

53. Rezac S, Kok CR, Heermann M, Hutkins R. Fermented foods as a dietary source of live organisms. Front Microbiol. 2018; 9:1785.

54. Marco ML, Heeney D, Binda S, Cifelli CJ, Cotter PD, Foligné B, et al. Health benefits of fermented foods: Microbiota and beyond. Curr Opin Biotechnol. 2017; 44:94-102.

55. Derrien M, Van Hylckama, Vlieg JET. Fate, activity, and impact of ingested bacteria within the human gut microbiota. Trends Microbiol. 2014; 23:354-366.

56. Zhang C, Derrien M, Levenez F, Brazeilles R, Ballal SA, Kim J. Ecological robustness of the gut microbiota in response to ingestion of transient food-borne microbes. ISME J. 2016; 10:2235-2245.

57. Burton KJ, Rosikiewicz M, Pimentel G, Bütikofer U, Von Ah U, Voirol MJ, et al. Probiotic yogurt and acidified milk similarly reduce postprandial inflammation and both alter the gut microbiota of healthy, young men. Br J Nutr. 2017; 117:1312-1322.

58. Mohamadshahi M, Veissi M, Haidari F, Shahbazian H, Kaydani GA, Mohammadi F. Effects of probiotic yogurt consumption on inflammatory biomarkers in patients with type 2 diabetes. Bioimpacts. 2014; 4:83-88.

59. Salas-Salvadó J, Guasch-Ferré M, Díaz-López A, Babio N. Yogurt and diabetes: Overview of recent observational studies. J Nutr. 2017; 147(7):1452S-1461S.

60. Pandey KR, Naik SR, Vakil BV. Probiotics, prebiotics and synbiotics – a review. J Food Sci Technol. 2015; 52:7577-7587.

61. Wang S, Zhu H, Lu C, Kang Z, Luo Y, Feng L, et al. Fermented milk supplemented with probiotics and prebiotics can effectively alter the intestinal microbiota and immunity of host animals. J Dairy Sci. 2012; 95:4813-4822.

62. Savaiano DA. Lactose digestion from yogurt: Mechanism and relevance. Am J Clin Nutr. 2014;5 Suppl:1251S-1255S.

63. Rajkumar H, Mahmood N, Kumar M, Varikuti SR, Challa HR, Myakala SP. Effect of probiotic (VSL#3) and omega-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: A randomized, controlled trial. Mediators Inflamm. 2014;2014:348959.

64. Uchida M, Mogami O, Matsueda K. Characteristic of milk whey culture with Propionibacterium freudenreichii ET-3 and its application to the inflammatory bowel disease therapy. Inflammopharmacology. 2007; 15:105-108.

65. Foligné B, Breton J, Mater D, Jan G. Tracking the microbiome functionality: Focus on Propionibacterium species. Gut. 2013; 62:1227-1228.