REVIEW ARTICLE

Probiotics- A new diabetes management tool

Rajesh Prasad Jayaswal[1], Pranav Kumar Prabhakar[2]

[1]Department of Medical Laboratory Technology, Amity University, Gurgaon, Haryana, India, [2]Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, Lovely Professional University, Phagwara, Punjab, India

Abstract

Diabetes mellitus is commonly known worldwide by the name of diabetes which occurs in all age groups. About >90% of diagnosed patient specially are Type-2 diabetes. The hallmark of Type 2 diabetes developments is increased insulin resistance, whereas Type 1 is related to less production of insulin which leads to uncontrolled hyperglycemia. Hyperglycemia slowly produces mild-to-very serious complications in patient mainly affecting vital organs such as blood vessels, eyes, neurons, nephrons, heart, and brain which increase the risk of heart attack, retinopathy, nephropathy, neuropathy, and stroke. Proper management of hyperglycemia is a key to prevent from diabetes and its complications. This concept has attracted many researchers to target various cells and tissue through special remedy so that hyperglycemia can be managed and complications can be reduced. The patient shows numerous side effects during therapy. There is craving demand for the proper cure of diabetes by sufferers. In this aspect, probiotics can be more helpful if proper research and formulation are done. Probiotics are good microorganism which can control hyperglycemia and its complications by utilizing and modifying glucose before absorption. Appropriate research is required to make strategy for searching and formulating good microorganism to be used as probiotics for the regulation of blood glucose and prevention from complexity.

Key words: Diabetes, hypeglycemia, nephropathy, neuropathy, probiotics, retinopathy

INTRODUCTION

Diabetes mellitus Type 2 (DM2) is the world's fastest growing metabolic disorder and is concerned with adult patients with obesity. The uncontrolled hyperglycemia can lead to various complications of microvascular which develop into retinopathy,[1] nephropathy,[2] as well as neuropathy.[3] Similarly, macrovascular chronic disorder emerges as coronary heart disease, hypertension, and related complications.[4] The management of hyperglycemia is quite helpful to control those various complications.[5] It is the main target of many researchers to control hyperglycemia in DM2. If we limit the absorption of glucose in the intestines, then hyperglycemia can be managed.[6] To limit the absorption of glucose in the intestine, an attempt to change the microflora of intestine can be done with those which utilize glucose only [Figure 1]. The use of probiotics in regular basis before a meal may increase the population of those microbes which may use glucose only as a sole source of energy. The microbes as probiotics may oxidize glucose through anaerobic glycolysis into lactic acid which can be absorbed in the blood. The lactic acid can be transported to the muscles, brain, liver, and kidney for energy production.[7]

The probiotics can be made in such a way that its microbes may optimally grow at intestinal environments. After they oxidize glucose into lactic acid, the pH might be changed which may suppress their own or other gut microbiota (GM) optimal growth or may be excreted out through fecal material. This review suggests researcher to prepare special probiotics that may not harm the consumer if taken orally [Figure 2]. The good probiotics that decrease the amount of glucose absorption in the intestines will be supposed to be a better way of management of hyperglycemia with respect to many drugs that have various side effects after their intake. Their use might be much economic than those of various chemical drugs.[8]

Address for correspondence:
Pranav Kumar Prabhakar,
Faculty of Applied Medical Sciences,
Lovely Professional University, Phagwara,
Punjab, India. Phone: +91-7696527883.
E-mail: prabhakar.iitm@gmail.com

Received: 23-04-2017
Revised: 12-06-2017
Accepted: 27-06-2017

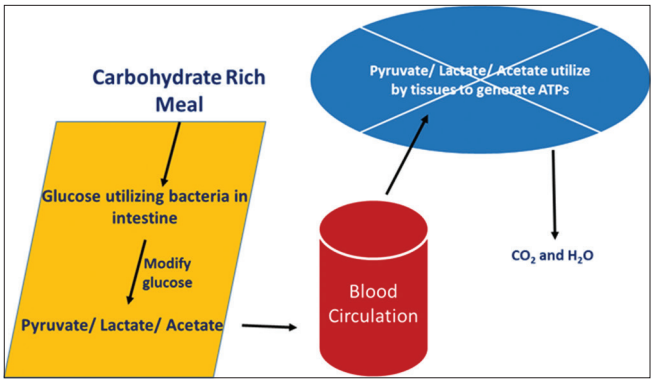

Figure 1: Effect of gut microbiota on carbohydrate digestion, absorption, and metabolism

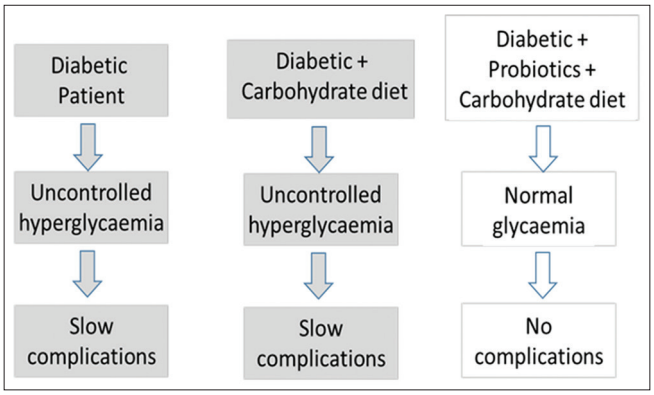

Figure 2: Model for management of hyperglycaemia in diabetes

The use of probiotics might interfere with the metabolic pathway of diabetic patients.[9] There can be enhanced partially reversed Krebs cycle, enhanced gluconeogenesis, enhanced oxidation of fatty acids, and enhanced ketogenesis. This will burn excess fat from the patient body. The blood glucose level might be normal since the dietary glucose will be utilized by probiotics before its absorption. The source of glucose in the blood will be arranged through gluconeogenesis pathway, and little amount may come through dietary absorption.

The use of probiotics may produce no harm to the patient as it would be the body normal microflora only. If anyone uses it, there may be the managed blood glucose level and fewer complications which can be further controlled by other means of treatment.

Small intestine is a house of many normal floras.[10] Bacterial population in gut varies from person to person. The reason for this variation is stress, obesity, lean, physical and mental work, intake of vegetarian and non-vegetarian food, weather, and environment.[11] The most common bacteria are the members of *Bifidobacterium* and *Lactobacillus*. More than 90% of GM has been recognized as *Bifidobacterium* ssp. in the infant's colon which gradually decreases in grown person and old-aged people.[12] Imbalance in normal flora population leads to several metabolic complications.

GM

The human gut has complex microbial ecosystems occupying 1000-1150 bacterial species.[13] Around 10^{13}-10^{14} microorganisms, mostly Gram-positive bacteria have been reported in human gut which can affect human health if their population is changed.[14]

Research reports suggest that human gut colonization with microorganism occurs only during delivery of the baby which is supposed to be less diverse, but the microbial population become more complex and significantly diverse when it slowly grows up to older age.[15] Various host factors such as age, sex, inheritance, hygiene, and environmental condition such as stress, infections, diseases, toxic agents, and food availability have been observed to influence the composition of GM.[16] Similarly, dietary components specific in fatty acids, carbohydrates, protein, and micronutrients can promote the growth of specific microbial population in the human gut. This type of changes may alter gene expression, especially in particular cells of the body mainly hepatocytes, enterocytes, adipocytes, and muscle cells which may impair the metabolic activities.[17] Colon supports the growth of many microbes in compare to unfavorable and adverse pH of the stomach and small intestine.[18] Overall, the presence of special GM can encourage or slow down human health through physiological, immunological, and metabolic process.[19] In positive aspect, GM can supply essential amino acids, short-chain fatty acids (SCFA) along with few fundamental vitamins, whereas it can also modify toxic compound to non-toxic products.[20,21] Acetate, propionate, and butyrate are the most common SCFA produced by GM from undigested food materials which on cellular oxidation has been observed to give additional calories favoring weight and fat gain in experimental animal.[22,23] Feces from obese individuals have shown elevated level of SCFA in compare to lean individuals.[24]

In a study with experimental mice, it has been found significantly less body fat in germ-free mice when fed even more calorie (29% higher) compare to control mice. However, within 2 weeks of colonization, especially with cecum-derived microbes in germ-free mice, it has been observed significant increase (~57%) in body fat along with insulin resistance which leads to development of obesity or metabolic syndrome.[25,26] GM also promotes gathering of fat in adipocytes by stimulating lipoprotein lipase (LPL) enzyme through fasting-induced adipose factor inhibition.[27] Weight loss has also been seen promoting changes in GM composition.[28] This brings to a close conclusion that changes in GM community increase intestinal permeability that activates various metabolic enzymes mostly LPL and lipogenic enzymes which increases the risk of obesity by increasing total body fat.[29]

PROBIOTICS AND ITS ROLE

The credit for describing probiotics first goes to Lilly and Stillwell who defined probiotic in 1965 that a substance like antibiotics

specially synthesized by few microorganism which has a tendency to encourage the growth of other microorganism.[30] In 1974, Parker further added his thought that probiotics represent both microorganisms and their products which promote microbial balance in the host intestine to produce health-related benefits.[31] In 1989, the probiotics were understood as microorganisms in living form but not their products which produce useful effects in the intestine.[31] In 1992, probiotics were recommended as live microorganism in mix or pure form that produces beneficial effects on the host.[32] Once more, proper explanation of probiotics was established as consumption of microbial preparation in live form can produce several useful effects on host health by improving gut microbial community.[33] This was further simplified as microbes consumed for a health effect can be considered as probiotics.[34] These days, probiotics are known as "live microorganisms, when administered in adequate amounts confer a health benefit on the host."[35]

Few research studies have claimed that regular utilization of lactic acid bacteria through fermented dairy products has potential to improve health and longevity in people.[36] At present, the use of genetically modified lactic acid bacteria has been suggested to deliver compounds of health interest.

Most common microorganism suggested to be used as probiotics are *Lactobacilli*, *Lactococci*, bifidobacteria, *Streptococci* (*Enterococci*), yeast (*Saccharomyces boulardii),* and *Escherichia coli*. These organisms should be non-pathogenic, should resist adverse pH of gastric as well as intestinal juices, and they should survive in gut for longer periods if taken orally.[37] Bifidobacteria and *Lactobacilli* spp. growth promotion in the gut has benefited many patients with allergic disorders.[38-45] GM has been getting worldwide attention day by day to recognize their specific health benefits. Their administration has been found to reduce occurrence of various unwanted complications such as eczema, dermatitis, lactose intolerance, irritable bowel syndrome, peptic ulcers, traveler's diarrhea, and autoimmune disorders in human subject.[46-49] Since there is no appropriate harmony specifying particular bacterial groups that affect individual health. Hence, more research is required to search a specific set of organism that specifically can target particular disease.

ADVERSE EFFECT OF PROBIOTICS

Many reports have shown undesirable effect of microbial preparation when used for therapeutic purpose.[50] Hence, it has become important to choose right microorganism through right protocol to make specific probiotics and propose specific dose for therapeutic point.

ROLE OF PROBIOTICS IN OBESITY

Intake of high energy diet and stagnant lifestyle are thought to be major contributors in obesity development since long time. However, recent advancement in knowledge had identified another important factor responsible for causing obesity which gradually leads to fatty liver, cardiovascular diseases, and DM2. Researchers now believe that few group of microbiota in gut has emerged as a causative agent to induce obesity in individual.[51] A study in animal model has shown that obese microbiota gathers comparatively more energy from diet than normal microbiota which are considered prime factor to cause obesity.[52] GM in obese individual promotes carbohydrates fermentation, glucose absorption, and SCFA production which ultimately increase substrates for lipogenesis in the liver and fat storage in adipose tissue. This leads to obesity.

ROLE OF PROBIOTICS IN DIABETES MANAGEMENT

Bifidobacteria and *Lactobacilli* have been thought to pretense efficacy for the management of hyperglycemia in DM. *Bifidobacterium* genus is Gram-positive, rod shape, non-motile, non-spore forming and anaerobic organism. Several species of bifidobacteria colonize intestinal tract in many animal species.[53] Most of the complex carbohydrates if not digested properly in the small intestine usually reach intact in the colon. On the contrary, after proper digestions, simple sugars and disaccharides are absorbed in small intestine. Bifidobacteria are able to use galacto, manno-, and fructo-oligosaccharides, at different levels and with different intensities. These differences can be due to the individual nature of each strain, since strains belonging to the same species, and originated from different culture source, have different patterns of carbohydrate fermentation.

Bifidobacterium degrades hexoses only and exclusively by the fructose 6-phosphate pathway.[54] The "bifid shunt" generates acetyl phosphate and erythrose 4-phosphate. The final product of the fermentation generates glyceraldehyde 3-phosphate that further enters to the Embden-Meyerhof-Parnas pathway.[55] The organic acid that produces at the end always differs between the exponential and the stationary phase and between different members of the genus. For example, in *Bifidobacterium animalis*, acetic acid production is similar in both phases, but lactic acid production is remarkably high in the early stages of the fermentation, and later it decreases.

It has been recorded that most of the strains which belong to *Bifidobacterium* species are able to degrade D-glucosamine, D-galactosamine, amylose, and amylopectin. Similarly, *Bifidobacterium bifidum* and *Bifidobacterium infantis* can ferment D-glucuronic acid, whereas *B. longum* ferment arabinogalactans and gums. *B. infantis, Bifidobacterium Breve,* and *Bifidobacterium pseudocatenulatum* have been found fermenting L-fucose effectively. However, few strains which are isolated from animals have shown less fermentation activity. These showed the diversity in the

capacity of carbohydrate catabolism within the species of *Bifidobacterium* genus.

Recent studies have forwarded the idea of combination therapies for effective treatment of metabolic diseases.[56] This concept can be used in probiotics preparations by selecting multiple microorganisms which show unique metabolic property. This may help in the development of new therapeutic agent for efficient hyperglycemic management in DM along with benefiting other lifestyle diseases.

DISCUSSION

It has been suggested that depletion of normal flora of human body may trigger health-related issue. When the microbial ecosystem become imbalance (dysbiosis) in human gut, unwanted microorganism is believed to grow more that may create situations of illness and complications. Dysbiosis may slowly lead to metabolic disorders such as DM, cardiovascular diseases, and stroke, in which most affected part will be nephrons, neurons, and retina.[57] There are no medications available in the market to counteract these complications. New treatment strategies need to be developed to overcome these health-related issues.[58] Hence, selection of novel microorganism and its preparations for using as probiotics has become a critical demand in health care which has attracted attention of many researchers to identify and study their biological effect.[59]

CONCLUSION

The available antidiabetics have some serious side effects, and there are no medicines available to manage the secondary complications. No mechanism of action has been reported for a number of pure phytochemicals, and it is essential to understand the antidiabetic effect as well as their mode of action. Phytochemicals might be a good alternative to chemically synthesized drugs to overcome these problems because of their natural origin. Free radicals play a major role in the secondary complications of diabetes. There are very few reports available on the performance of a combination of probiotics. Combination therapy using probiotics along with few drugs is a new therapeutic strategy for managing diabetes and its complications. The antidiabetic effects of probiotics alone and in combination can be validated in an animal model to make effective remedies for diabetes.

REFERENCES

1. Azad N, Agrawal L, Emanuele NV, Klein R, Bahn GD, Reaven P; VADT Study Group. Association of blood glucose control and pancreatic reserve with diabetic retinopathy in the Veterans Affairs Diabetes Trial (VADT). Diabetologia 2014;57:1124-31.
2. Fragiadaki M, Hill N, Hewitt R, Bou-Gharios G, Cook T, Tam FW, *et al.* Hyperglycemia causes renal cell damage via CCN2-induced activation of the TrkA receptor implications for diabetic nephropathy. Diabetes 2012;61:2280-8.
3. Wang L, Chopp M, Szalad A, Jia L, Lu X, Lu M, *et al.* Sildenafil ameliorates long term peripheral neuropathy in Type II diabetic mice. PLoS One 2015;10:e0118134.
4. Tahergorabi Z, Khazaei M. Imbalance of angiogenesis in diabetic complications: The mechanisms. Int J Prev Med 2012;3:827-38.
5. Kohnert KD, Heinke P, Vogt L, Salzsieder E. Utility of different glycemic control metrics for optimizing management of diabetes. World J Diabetes 2015;6:17-29.
6. Tahrani AA, Barnett AH, Bailey CJ. SGLT inhibitors in management of diabetes. Lancet Diabetes Endocrinol 2013;1:140-51.
7. Nieuwdorp M, Gilijamse PW, Pai N, Kaplan LM. Role of the microbiome in energy regulation and metabolism. Gastroenterology 2014;146:1525-33.
8. Panwar H, Rashmi HM, Batish VK, Grover S. Probiotics as potential biotherapeutics in the management of Type 2 diabetes-prospects and perspectives. Diabetes Metab Res Rev 2013;29:103-12.
9. Panwar H, Calderwood D, Grant IR, Grover S, Green BD. *Lactobacillus* strains isolated from infant faeces possess potent inhibitory activity against intestinal alpha-and beta-glucosidases suggesting anti-diabetic potential. Eur J Nutr 2014;53:1465-74.
10. Sekirov I, Russell SL, Antunes LC, Finlay BB. Gut microbiota in health and disease. Physiol Rev 2010;90:859-904.
11. Hooper LV, Gordon JI. Commensal host-bacterial relationships in the gut. Science 2001;292:1115-8.
12. Gerritsen J, Smidt H, Rijkers GT, de Vos WM. Intestinal microbiota in human health and disease: The impact of probiotics. Genes Nutr 2011;6:209-40.
13. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, *et al.* A human gut microbial gene catalog established by metagenomic sequencing. Nature 2010;464:59-65.
14. Flint HJ, Duncan SH, Scott KP, Louis P. Links between diet, gut microbiota composition and gut metabolism. Proc Nutr Soc 2015;74:13-22.
15. Palmer C, Bik EM, DiGiulio DB, Relman DA, Brown PO. Development of the human infant intestinal microbiota. PLoS Biol 2007;5:el77.
16. Frazier TH, DiBiase JK, McClain CJ. Gut microbiota, intestinal permeability, obesity-induced inflammation, and liver injury. J Parenter Enterai Nutr 2011;35:14S-20.
17. Romeo J, Nova E, Warnberg J, Gómez-Martínez S, Ligia LE, Marcos A. Immunomodulatory effect of fibres, probiotics and synbiotics in different life-stages. Nutr Hosp 2010;25:341-9.
18. Montalto M, D'Onofrio F, Gallo A, Cazzato A, Gasbarrini G. Intestinal microbiota and its functions.

Dig Liver Dis 2009;3:30-4.
19. Stappenbeck TS, Hooper LV, Gordon JI. Developmental regulation of intestinal angiogenesis by indigenous microbes via paneth cells. Proc Natl Acad Sci U S A 2002;99:15451-5.
20. Guarner F, Malagelada JR. Gut flora in health and disease. Lancet 2003;361:512-9.
21. Heselmans M, Reid G, Akkermans LM, Savelkoul H, Timmerman H, Rombouts FM. Gut flora in health and disease: Potential role of probiotics. Curr Issues Intest Microbiol 2005;6:1-7.
22. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, Ley RE, *et al.* A core gut microbiome in obese and lean twins. Nature 2009;457:480-4.
23. Samuel BS, Shaito A, Motoike T, Rey FE, Backhed F, Manchester JK, *et al.* Effects of the gut microbiota on host adiposity are modulated by the short-chain fatty-acid binding G protein-coupled receptor, Gpr41. Proc Natl Acad Sci U S A 2008;105:16767-72.
24. Schwiertz A, Taras D, Schäfer K, Beijer S, Bos NA, Donus C, *et al.* Microbiota and SCFA in lean and overweight healthy subjects. Obesity (Silver Spring) 2010;18:190-5.
25. Li JV, Ashrafian H, Bueter M, Kinross J, Sands C, le Roux CW, *et al.* Metabolic surgery profoundly influences gut microbial-host metabolic cross-talk. Gut 2011;60:1214-23.
26. Bäckhed F, Manchester JK, Semenkovich CF, Gordon JI. Mechanisms underlying the resistance to diet-induced obesity in germ-free mice. Proc Natl Acad Sci U S A 2007;104:979-84.
27. Murphy EF, Cotter PD, Healy S, Marques TM, O'Sullivan O, Fouhy F, *et al.* Composition and energy harvesting capacity of the gut microbiota: Relationship to diet, obesity and time in mouse models. Gut 2010;59:1635-42.
28. Fleissner CK, Huebel N, Abd El-Bary MM, Loh G, Klaus S, Blaut M. Absence of intestinal microbiota does not protect mice from diet-induced obesity. Br J Nutr 2010;104:919-29.
29. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006;444:1027-31.
30. Lilly DM, Stillwell RH. Probiotics: Growth-promoting factors produced by microorganisms. Science 1965;147:747-8.
31. Fuller R. Probiotics in man and animals. J Appl Bacteriol 1989;66:365-78.
32. Havenaar R, Huis In't Veld JH. Probiotics: A general view. Lactic Acid Bacteria. London: Elsevier; 1992. p. 151-70.
33. Sanders ME. Effect of consumption of lactic cultures on human health. Adv Food Nutr Res 1993;37:67-130.
34. Conway PL. Selection criteria for probiotic microorganisms. Asia Pac J Clin Nutr 1996;5:10-4.
35. Sanders ME. Probiotics: Definition, sources, selection, and uses. Clin Infect Dis 2008;46:S58-61.
36. Marteau P. Living drugs for gastrointestinal diseases: The case for probiotics. Dig Dis 2006;24:137-47.
37. Isolauri E, Rautava S, Salminen S. Probiotics in the development and treatment of allergic disease. Gastroenterol Clin North Am 2012;41:747-62.
38. Nermes M, Kantele JM, Atosuo TJ, Salminen S, Isolauri E. Interaction of orally administered *Lactobacillus rhamnosus* GG with skin and gut microbiota and humoral immunity in infants with atopic dermatitis. Clin Exp Allergy 2011;41:370-7.
39. Kuitunen M. Probiotics and prebiotics in preventing food allergy and eczema. Curr Opin Allergy Clin Immunol 2013;13:280-6.
40. Foolad N, Brezinski EA, Chase EP, Armstrong AW. Effect of nutrient supplementation on atopic dermatitis in children: A systematic review of probiotics, prebiotics, formula, and fatty acids. JAMA Dermatol 2013;149:350-5.
41. Pessi T, Sütas Y, Hurme M, Isolauri E. Interleukin-10 generation in atopic children following oral *Lactobacillus rhamnosus* GG. Clin Exp Allergy 2000;30:1804-8.
42. Lim LH, Li HY, Huang CH, Lee BW, Lee YK, Chua KY. The effects of heat-killed wild-type *Lactobacillus casei* Shirota on allergic immune responses in an allergy mouse model. Int Arch Allergy Immunol 2009;148:297-304.
43. Abrahamsson TR, Jakobsson T, Böttcher MF, Fredrikson M, Jenmalm MC, Björkstén B, *et al.* Probiotics in prevention of IgE-associated eczema: A double-blind, randomized, placebo-controlled trial. J Allergy Clin Immunol 2007;119:1174-80.
44. Masood MI, Qadir MI, Shirazi JH, Khan IU. Beneficial effects of lactic acid bacteria on human beings. Crit Rev Microbiol 2011;37:91-8.
45. Gionchetti P, Amadini C, Rizzello F, Venturi A, Poggioli G, Campieri M. Probiotics for the treatment of postoperative complications following intestinal surgery. Best Pract Res Clin Gastroenterol 2003;17:821-31.
46. McCarthy J, O'Mahony L, O'Callaghan L, Sheil B, Vaughan EE, Fitzsimons N, *et al.* Double blind, placebo controlled trial of two probiotic strains in interleukin 10 knockout mice and mechanistic link with cytokine balance. Gut 2003;52:975-80.
47. Savilahti E, Kuitunen M, Vaarala O. Pre and probiotics in the prevention and treatment of food allergy. Curr Opin Allergy Clin Immunol 2008;8:243-8.
48. Vliagoftis H, Kouranos VD, Betsi GI, Falagas ME. Probiotics for the treatment of allergic rhinitis and asthma: Systematic review of randomized controlled trials. Ann Allergy Asthma Immunol 2008;101:570-9.
49. Weston S, Halbert A, Richmond P, Prescott SL. Effects of probiotics on atopic dermatitis: A randomised controlled trial. Arch Dis Child 2005;90:892-7.
50. Besselink MG, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, Timmerman HM, *et al.* Probiotic prophylaxis in predicted severe acute pancreatitis: A randomised, double-blind, placebo-controlled trial. Lancet 2008;371:651-9.

51. Vrieze A, Holleman F, Zoetendal EG, de Vos WM, Hoekstra JB, Nieuwdorp M. The environment within: How gut microbiota may influence metabolism and body composition. Diabetologia 2010;53:606-13.
52. Wolin MJ, Zhang Y, Bank S, Yerry S, Miller TL. NMR detection of 13CH313COOH from 3-13C-glucose: A signature for *Bifidobacterium* fermentation in the intestinal tract. J Nutr 1998;128:91-6.
53. Zhang F, Ye C, Li G, Ding W, Zhou W, Zhu H, *et al.* The rat model of Type 2 diabetic mellitus and its glycometabolism characters. Exp Anim 2003;52:401-7.
54. Delcenserie V, Bechoux N, Léonard T, China B, Daube G. Discrimination between *Bifidobacterium* species from human and animal origin by PCR-restriction fragment length polymorphism. J Food Prot 2004;67:1284-8.
55. Mackenzie GM. An experimental study of blood glycolysis. The effects of thyroid and adrenal extracts and phlorhizin on glycolysis *in vitro*. J Exp Med 1915;22:757-65.
56. Fong JC, Kao YS, Tsai HY, Chiou YY, Chiou GY. Synergistic effect of endothelin-1 and cyclic AMP on glucose transport in 3T3-L1 adipocytes. Cell Signal 2004;16:811-21.
57. Miquel S, Martín R, Rossi O, Bermúdez-Humarán LG, Chatel JM, Sokol H, *et al. Faecalibacterium prausnitzii* and human intestinal health. Curr Opin Microbiol 2013;16:255-61.
58. Luna B, Feinglos MN. Drug-induced hyperglycemia. JAMA 2001;286:1945-8.
59. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermudez-Humaran LG, Gratadoux JJ, *et al. Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A 2008;105:16731-6.

Source of Support: Nil. **Conflict of Interest:** None declared.