Exploring the Influence of Probiotics on Human Health

Kerry B. Barbera

University of Alabama

kbbarbera@crimson.ua.edu

**Introduction**

Colonization of the intestinal microbiota begins at birth and matures over time. Found in the inner lumen of the digestive track, microbiota create a lush landscape of tens of trillions of diverse bacteria that work in harmonic balance.1 This balance is vital for absorbing key nutrients, providing a protective barrier against harmful pathogens, and producing essential vitamins. It is influenced by one’s environment, medications, diet, disease, genetics, lifestyle and illness, all of which can disrupt this delicate homeostatic balance of healthy bacteria, permitting potentially harmful bacteria to overpopulate in the digestive track. This can set off inflammatory processes responsible for digestive disorders such as inflammatory bowel disease (IBD), colitis, and diarrhea.2

Probiotics are live non-pathogenic bacteria that, when consumed in sufficient amounts, help maintain the intestinal microbiota homeostasis and improve one’s overall health.3 They are beneficial in preventing or decreasing the side effects of many chronic diseases. This review examines the use of probiotics as a possible treatment option for diabetes and H. pylori, and it also explores how probiotics can improve the immune function in the aging population.

**Science Behind Probiotics**

Probiotics are available as supplements and must be implemented slowly to prevent gastrointestinal upset. They occur naturally in fermented foods such as Kimchi, tempeh, sauerkraut, miso, yogurt, kefir, and kombucha tea, a fermented drink. Fermentation is an anaerobic metabolic process that converts pyruvate, from glycolysis, to lactic acid. Probiotics predominantly contain bacteria, but can contain yeast or a combination of both.2 Kefir, for example, uses a combination of both yeast and bacteria.

The two most common bacteria used are *Lactobacillus* and *Bifidobacteria*; *Lactobacillus* is a strict fermenter microorganism that produces lactic acid and *Bifidobacteria* is an anaerobic microorganism that produces both lactic acid and acetic acid.4The bacteria use carbohydrates as a food source, converting sugars to lactic acid. In yogurt, for example, the bacteria convert lactose to lactic acid. This imparts the sour taste of yogurt and causes the milk to coagulate, thickening the product. It may affect texture, aroma, flavor, and the viability of vitamins naturally contained in the food. These are some of the characteristics food manufacturers might have to counterbalance and keep in mind when incorporating probiotics into food.

Probiotics are live bacteria and must remain viable to promote their health benefits. This is the biggest production issue that arises when they are incorporated into any food product. Probiotics must endure the manufacturing process and ingestion by the host where they must withstand the low pH environment of the stomach and bile salts of the small intestine, and have the ability to adhere to the mucosal epithelial cells.5 Here they colonize with the host bacteria to provide their health benefits and begin the symbiotic relationship with the intestinal microbiota.

Probiotics’ diverse range of protection is dependent upon the strain of bacteria.1 They resist over colonization of pathogenic bacteria by lowering luminal pH, providing a hostile environment where pathogenic bacteria cannot proliferate. They reinforce the barrier protection by increasing mucus production from the goblet cells in the intestinal lining, which inhibits adherence of pathogenic bacteria.6 Studies have found that the interaction of the intestinal microbiota can assist in T regulatory lymphocyte development, stimulate the development of the T helper cells, and signal cell receptors that up regulate proteins responsible for inflammatory responses.6 Recently, probiotics have been found to increase the short chain fatty acid butyrate which may prove beneficial in treatment of diabetes and obesity.7

**Highlighting Primary Research – Article 1**

 Oxidative stresses from the production of reactive oxygen species play a role in inflammatory response and may be responsible for increasing insulin resistance and glucose intolerance.8 Asemi, et al. conducted a randomized, double-blind, placebo-controlled clinical trial to test the effects of multispecies probiotics on oxidative stresses associated with type-2 diabetics.8 The study measured the effects of probiotics on participants’ lipid profiles, as well as levels of high sensitivity C-reactive protein (hs-CRP), fasting plasma glucose (FPG), and total glutathione (GSH).

Diabetic patients who were selected based on the study’s strict inclusion and exclusion criteria were randomly assigned either a placebo or a multispecies probiotic supplement taken once a day for 8 weeks. The supplement consisted of 7 different strains of probiotics: *lactobacillus acidophilus*, *L.casei, L.rhamnosus, l.bulgaricus, Bifidobacterium breve, Streptoccoccus thermophiles, B. longum, and* fructo-oligosaccharide with lactose as the carrier substance.

All study subjects participated in a 2-week pre-intervention phase where they were instructed to refrain from ingesting any other probiotic foods and to continue with their normal diet and exercise routine. After the 2 weeks, fasting blood samples were taken at baseline and again post-trial for comparison. Compliance was measured weekly via phone interview and 3-day food records completed throughout the study. Results showed no improvement in serum insulin, insulin resistance or lipid panel. However, the probiotic reduced hs-CRP levels and increased the levels of the antioxidant GSH that can significantly reduce the inflammatory and oxidative stress associated with type 2 diabetes.Probiotics may provide a viable treatment for diabetic patients.

**Highlighting Primary Research – Article 2**

Zojaji, et al. conducted a randomized controlled trial evaluating the probiotic *Saccharomyces boulardii*’s effect on the elimination of *H. pylori,9* which is considered a type 1 cancer by the World Health Organization (WHO).9 *H. pylori* is a Gram-negative bacteria found in the stomach that has been associated with chronic gastritis, ulcers, and even stomach cancer.Standard treatment consists of antibiotics and a proton pump inhibitor (PPI),which can cause numerous side effects.

The study by Zojaji, et al was performed on180 patients who were selected base on strict inclusion and exclusion criteria determined for this study and randomized into two groups. Both groups received the same antibiotics and PPI regimen; group A also received *Saccharomyces boulardii* probiotic. The results of this study found the eradication rates were insignificant between the control group and treatment group; however, the side effects associated with H. pylori were significantly lowered in the treatment group. The decrease in the side effects of bloating, nausea, abdominal discomfort and diarrhea could be key in treatment compliance of H. pylori patients, though it may not help with elimination of the disease.

**Highlighting Primary Research – Article 3**

Aging adults have a decrease in immune function that in turn, increases their vulnerability to infection and their mortality rate. This is primarily due to the decrease in the number of T lymphocyte (T cells), natural killer (NK) cells, phagocytic activity in innate immunity, and a decrease in antibody responses. Honglin et al. conducted a randomized placebo-controlled, single-blind crossover study on the effects of probiotic drink on the immune function of older adults.10 Thirty volunteers were selected based on strict inclusion and exclusion criteria for this study. The volunteers consumed a drink containing either *Lactobaccillus casei* or skim milk for 4 weeks followed by a 4-week washout period before crossing over to the other treatment. Blood and saliva samples were collected at the start and end of the study for comparison. No results were found that indicated improved cholesterol, triglycerides, glucose, and C-reactive protein (CRP) levels. These finding are in agreement with article 1’s findings except for the CRP levels. This study noted improvement in the immunity of the aging population due to the increase of NK cells and Interluken-10 (IL-12) / Interluken-12 (IL-12) ratio. These are important factors in innate immunity, providing a viable treatment for use of probiotics by this population.

**Future Research**

**Background**: *The Journal of Biological Chemistry* published a recent study supporting the use of probiotics to prevent and treat obesity and disease in mice.7 The probiotic VSL# 3, which is available commercially, inhibited body weight gain and insulin resistance by influencing the intestinal microbiota. VSL#3 stimulated changes that resulted in increased levels of butyrate, a short chain fatty acid responsible for stimulating the hormone glucagon like peptide 1 (GLP-1). GLP-1 is an anti-hyperglycemic hormone that improves satiety and glucose tolerance and may reduce food intake. Further human studies are needed to see the effect of VLS#3 on obesity and diabetes. The first article highlighted in this paper found that the multispecies probiotics did not have an effect in reducing insulin resistance of fasting plasma glucose levels. This is most likely from the strains of probiotics used.

**Aim of the study**: The purpose of this study is to determine if VSL#3 probiotics provide a viable treatment for human subjects with diabetes. The independent variable is VSL#3’s probiotic effect, and the dependent variable is patient glucose levels.

**Methods:** Conduct a double-blind study on diabetic patients who are randomly assigned probiotic VSL#3 supplement or a placebo for 8 weeks after a 4-week lead-in phase and concluding with a 4-week post phase where both groups receive the placebo. The participants will be asked to follow the diabetic exchange diet and to refrain from taking any probiotic containing foods or supplements during the 16-week trial. This should prevent the influence of previous diet on study results. The final 4-week phase will prevent any influence from knowledge of the study ending. HbA1C samples will be obtained at baseline, 8 weeks post-treatment and again at the conclusion of the study. Fasting plasma glucose levels will be taken at baseline and once weekly until conclusion of the trial. Patients’ compliance with their diet and supplement will be validated via 4-day food records and weekly phone interviews.

**Results:** If study results with human subjects corroborate the previous study results on mice, it may provide substantial motivation for future studies and promote the use of probiotic supplement in the treatment for diabetes. This could lead to a future market of diabetic foods that contain probiotics and possibly lead to eradication of Type 2 diabetes or at least reduce its prevalence.

**Summary**

 Probiotics, when consumed in sufficient amounts, improve and help maintain the intestinal flora balance and one’s overall health. This balance is vital for absorbing key nutrients, providing a protective barrier against harmful pathogens, and producing essential vitamins. It is influenced by one’s environment, medications, diet, disease, genetics, lifestyle and illness. These factors can disrupt this delicate balance of healthy bacteria, and may provide the key to the pathology of many chronic diseases. Probiotics’ positive influence on health and their potential use in the treatment of chronic diseases demand further studies and will influence the marketing of both probiotic functional foods and their incorporation into new products.

**References**

1. Wallace, T.C., Guamer, F., Madsen, K., Cabana, M.D., Gibson, G., Hentges, E. & Sanders, M.E. (July 2011) Human Gut Microbiota and It’s Relationship to health and Disease. *Nutr Rev.*, 69(7):392-403. DOI: 10.1111/j.1753-4887.2011.00402.x.

2. Williams, N.T. Probiotics: clinical review (March 2010) *Am J Health-Syst Pharm.* 67(6): 449-458. DOI: 10.2146/ajhp090168.

3. Backhed, F. Fraser, C.M., Ringel, Y., Sanders, M.E., Sartor, R.S., Sherman, P.M.,…& Finlay, B.B., (November 2012) Defining a Healthy Human Gut Microbiome: Current Concepts, Future Directions, and Clinical Applications. *Cell Host & Microbe*. 12(5):611-22. DOI: 10.1016/j.chom.2012.10.012.

4. Vondnar, D.C., Paucean, A., Dulf, F.V., & Socaciu, C. (2010) HPLC Characterization of Lactic Acid Formation and FTIR Fingerprint of Probiotic Bacteria during Fermentation Process. *Notulae Botanicae Horti Agrobotanici Cluj-napoca,* 38 (1): 109-113. ISSN 0255-965X.

5. Sanders, M.E., & Marco, M.L (April 2010) Food Formats for Effective Delivery of Probiotics. *Food Sci.Technol*. 1: 65-85. DOI: 10.1146/annurev.food.080708.100743.

6. Ng, S.C., MRCP, Hart, A.L., Kamm, M.A, Stagg, A.J., & Knight, S.C. (2009) Mechanisms of Action of Probiotics: Recent Advances. *Inflamm Bowel Dis.*15 (22) 300-310.

7. Yadav, H., Lee, J., Lloyd, J., Walter, P., & Rane, S. (July 2013) Beneficial metabolic Effects of a Probiotic Via Butyrate Induced GLP-1 Secretion: Mechanism of Action of the Probiotic VSL#3.*J.Biol.Chem.* Infinity Series.DOI: 10.1074/jbc.M113.452516.

8. Asemi, Z., Zare, Z., Shakeri, H., Sabihi, S., & Esmaillzadeh, A., (July 2013) Effect of Multispecies Probiotic Supplements on Metabolic Profiles, hs-CRP, and Oxidative Stress in Patients with Type 2 Diabetes. *Ann Nutr Metab.* 63: 1-9. DOI: 10.1159/000349922.

9. Zojaji, H., Ghobakhlou, M., Rajabalinia, H., Ataei, E., Sherafat, S.J., Moghimi-Dehkordi, B., & Bahreiny, R., (May 2013) The Efficacy and Safety of Adding the Probiotic *Saccharomyces boulardii* to Standard Triple Therapy for Eradication of *H. pylori* : a Randomized Control Trial. *Gasteroenterol Hepatol.* 6:88-104.

10.Honglin, D., Rowland, I., Thomas, L.V., & Yaqoob, P., (January 2013) Immunomodulatory effects of a probiotic drink containing *Lactobacillus casei* Shirota in healthy older volunteers. *Eur J Nutr.* 52:1853-1863. DOI: 10.1007/s00394-012-0487-1.