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Do Probiotics Effectively Promote Wellbeing?

Tzvi H. Adams
Touro College

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By Tzvi H. Adams
Tzvi H. Adams will graduate in January 2016 with a BS Honors degree in Biology.

Abstract
Probiotics have been commonly ascribed many therapeutic powers. The aim of this review is to investigate these claims. While some of the claims are well supported by research, the effects of probiotics are very specific and depend on the strains used as well as the disease or condition targeted. Age and racial ethnicity may also be factors impacting the efficacy of probiotic strains.

Introduction

In recent years, probiotic supplements and probiotic yogurt have become increasingly popular pharmacy and grocery items. Proponents posit that these live cultures of beneficial bacteria counteract the negative effects of antibiotics and decreased microbial exposure of modern life, while others are skeptical of these relatively new products and claims.

Every human gut contains millions of bacteria from hundreds of species which aid in digestion and promote health. These bacteria are healthy bacteria and are very important to one's wellbeing. Western, developed countries successfully controlled infectious diseases during the last century by improving sanitation and using antibiotics and vaccines. At the same time, a rise in diseases such as allergies, autoimmune disorders, and inflammatory bowel disease has been observed in both adults and children, and it is hypothesized that improvements in hygiene, decreased microbial exposure in childhood, and decreased maintenance of microflora are responsible for this increase. In 1907, the Russian zoologist Élie Metchnikoff was the first one to suggest that gut microbes may influence human health (Britannica).

Recent studies show that ingesting oral probiotics can promote health and counteract some negative effects of antibiotics, but only in specific ways. It is necessary to understand the mechanisms and limitations of probiotic supplements in order to be an informed consumer.

Methods

This subject was researched using Touro College's online library database as well as Google Scholar. Additionally, ProQuest, EBSCO, MEDLINE, and PubMed were used to search for articles. The author had free access to these search engines through the Touro College Library. The method of research entailed reviewing published articles and studies that have been peer reviewed. Key words such as "gut bacteria", "probiotic bacteria", "health promoting bacteria", "probiotic yogurt", "human microbiome", and "microbiota" were used to find appropriate articles.

Background: Development of gut microbiome

Babies born via vaginal births are colonized by bacteria as they pass through the birth canal. The vaginal microbial communities appear to change during pregnancy to provide newborns with beneficial microbes; at the time of delivery, the vagina is dominated by Lactobacillus and Prevotella spp (Krajmalnik-Brown et al 2012). Breast milk also populates the baby's gut with additional health promoting bacteria from the Bifidobacterium family. According to very recent research, babies acquire stomach bacteria from their mothers even before birth. In healthy human fetuses, bacteria have been detected in umbilical cord blood, fetal membranes, and amniotic fluid, supporting the notion of bacterial transmission through the placental barrier. Furthermore, the meconium (ingested amniotic fluid) from newborns has been shown to be non-sterile, home to a complex community of microbes, including Enterococci and Escherichia, commonly found in the adult GI tract. Therefore, even babies born by caesarean section are born with microbiomes, despite lacking the vaginal exposure (Funkhouser and Bordenstein 2013).

Diversity between ethnic groups

While 90% of all people's gut biome is similar, the bacteria species and proportions vary between races and ethnic groups. A study published in 2010 comparing rural children of Burkina Faso, Africa, with children in the modern and developed city of Florence, Italy, showed that Bacteroidetes and Spirochaetes were abundant in the microbiota of the African children and that the specific types that were increased were well suited to extract nutrition from their herbal-rich diet. These bacteria were from the genus Prevotella and Xylanibacter (Bacteroidetes) and Treponema (Spirochaetes), which are known for their skill at cellulose and xylan hydrolysis. The diet of the rural village in Burkina Faso is low in animal protein and fat but rich in starch, fiber, and plant polysaccharides from local herbs and vegetables. These bacteria were completely lacking in the European children whose diet was high in fat, animal protein, sugars, and nutrient-rich but thoroughly cleansed foods (De Filippo et al 2010).

A recent study has shown that the Japanese possess unique bacteria in their intestines which allow them to digest red algae, commonly used to wrap fish in sushi. Japanese have a seaweed-rich diet, eating on average of 14.2 grams of sushi a day. Red algae, used in sushi, contain the polysaccharide porphyran in their cell walls. It is broken down specifically by an enzyme called porphyranase. This enzymatic activity is unique to select marine bacteria such as Zobellia galactanivorans, the bacteria that populate the gut of the Japanese, giving them the machinery they need to digest these nutritional sea plants (Hehemann et al 2010).

A similar phenomena has been detected in the guts of rodents. Desert woodrats (Neotoma lepida) of the Mojave and Great

Basin deserts have special toxin-degrading gut microbes to digest the toxic creosote and juniper bushes (Kohl et al 2014).

This diversity between ethnic groups adds a dimension of complexity to understanding the workings of the microbiome. This variation may impact the manner in which the gut responds to introduced probiotic bacteria and may result in probiotic treatments being beneficial for some people but not others.

How gut microbes affect autrient absorption and energy regulation

In a way similar to how rhizoidal fungi allow plant roots to absorb soil nutrition, the biofilm structure of the many mucosal microbiota adhering to gut epithelium facilitates benefits for the host, including nutrient exchange and stimulation of immunity (Sonnenburg et al 2004). For example, Bacteroides thetaiotaomicron is a major symbiont of the human adult gut (Hayashi et al 2013). This organism makes an important contribution to human digestion by breaking down complex plant material that innate human enzymes cannot digest. The human body can produce amylase and sucrase which break down starch, glycogen, and sucrose respectively, yet it cannot independently digest complex plant material (Microbewiki). Using the plant and fungus polysaccharides ingested by the human host as its food source, B. thetaiotaomicron is able create small sugars with its glycoside hydrolases which hydrolyze glycosidic bonds in complex sugars. It produces mucus that allows it to attach to the gut epithelial cells, avoiding washout from the microecosystem. The mucus sticks to epithelial lining as well as to undigested food particles. These aggregations serve to promote the assembly of more microbes and allow their syntrophic relationship with the gut.. Other gut bacterial species such as harmless strains of E. Coli benefit from the small sugars provided by B. thetaiotaomicron, which the E. Coli cannot produce independently. Methanogens, another family of the microbiome, use the short-chain fatty acid products of the fermentation of carbohydrates. These symbiotic relationships add productivity to the human gut (Sonnenburg et al 2004). It is clear that the many interactions between gut bacteria are extremely complex and to date only a fraction of this organization is understood. Much research is needed to fully understand the way in which introduced probiotic bacteria interrelate and network with the host gut microbiome.

Vitamins

Vitamin B12 is required for metabolism in cells and for the formation of red blood cells. The human body cannot produce vitamin B12. Only bacteria and archaea are capable of manufacturing this vitamin. Species of Pseudomonas and Klebsiella, normal residents of the human small intestine, have been shown to produce vitamin B12 (Albert et al 1980). E. coli in the large intestine produce Vitamin K2 (Bentley and Meganathan 1982). Biotin (vitamin B7), a vitamin required for production of fatty acids and cell growth, is synthesized in significant quantities by the intestinal flora (Scheinfeld et al 2015)..

Gut bacteria help prevent pathogenic infections

Lactic acid bacteria are found naturally in acidic foods such as pickles, olives, and yogurt, preventing spoilage by maintaining a low pH. In the same way, many pathogenic bacteria are deterred from growing in the human intestines due to the unfriendly acidic environment created by members of lactic acid bacteria family, Lactobacillales. Furthermore, by merely colonizing the gut, the healthy bacteria leave little real estate for pathogenic bacteria to occupy (Nester).

Having established the presence and functions of gut microbes, a question of concern is how the common use of antibiotics affects this microbiome and the life functions dependent upon it.

What happens to the bacteria when antibiotics are taken?

Studies on isolated cultured colonies of gut bacteria in a laboratory setting have shown how antibiotics impact them. In one study, 14 common gut bacterial species from the Clostridium, Bifidobacterium, and Bacteroides genera were treated in vitro with ampicillin and metronidazole, clinically prescribed antibiotics. Effects on bacterial physiology and metabolism were monitored over a 48 hour period. Bacteroides and some Clostridium species were substantially reduced by Ampicillin. On bifidobacterial species ampicillin only had a bacteriostatic effect. Metronidazole strongly affected bacteroides communities, reduced some clostridium species, but had no effect on bifidobacterial communities. This study showed that the antibiotics ampicillin and metronidazole have a real inhibitory effect on some intestinal bacteria species but not others (Newton F et al 2013).

Modeling tests have been conducted on mice as well to better understand the relationship between antibiotics and intestinal bacteria. Mice have similar gut bacterial composition to humans. Oral intake of antibiotics, streptomycin and vancomycin, was used to agitate the intestinal microbiota of the mice. Thereafter, the mice were infected with Salmonella enterica serovar Typhimurium to gauge the results of antibiotic treatment. Analysis showed that the number of intestinal bacteria was not altered significantly by the antibiotic regimen, but the microbiota composition was affected. Both vancomycin and streptomycin treatments significantly decreased lactobacilli and enterococci/group D streptococci populations and promoted the overgrowth of Enterobacteriaceae. These perturbations in the microbiota caused the mice to be more susceptible to Salmonella serovar Typhimurium intestinal colonization and infection than

before antibiotic treatment. This study demonstrates the importance of a healthy microbiota in limiting susceptibility to enteric pathogens. This study showed that the antibiotics vancomycin and streptomycin can have a detrimental effect on intestinal bacteria species, limiting host immunity (Sekirov et al 2008).

A leading expert in this field, David Relman M.D., investigated the gut bacterial communities of three healthy humans before and after treatment with ciprofloxacin, a commonly prescribed broad spectrum antibiotic of the fluoroquinolone family, by comparing stool samples before and after treatment. He monitored them for a period of ten months. Ciprofloxacin treatment eliminated about a third of the bacterial taxa in the gut, decreasing the diversity of the community. Faecalibacterium, Lachnospiraceae, Bacteroides and Alistipes are names of several genera that were reduced by ciprofloxacin. The magnitude of this effect varied to some degree between individuals. However, by 4 weeks after the end of treatment, the makeup of the community closely resembled its pretreatment state in all three individuals with the exception of several taxa which failed to recover even 6 months later. During the four week recovery period, the participants reported normal intestinal function. The rapid resurgence of the pretreatment community indicates strong bacterial community resilience. However, the fact that several bacterial species did not recover tells that even a short course of antibiotics may cause minor permanent changes to gut community flora. Though the participants did not experience any immediate obvious stomach problems from the medication, this cannot predict the possibility of long term impacts such as increased susceptibility to allergies or skin irritations (Modi S et al 2014). Relman found that a second exposure to ciprofloxacin a half year after the first treatment causes similar effects but was accompanied by incomplete recovery (Dethlefsen and Relman 2010).

Similar studies using clindamycin showed that the gut Bacteroides community never returned to its original composition even two years after antibiotic treatment (Jernberg et al 2010). Clearly antibiotics impact the bacterial gut population with possible effects on host wellness.

Which diseases result from antibiotic use?

Campylobacteriosis (stomach ulcer) has been linked with intake of antibiotics up to one year before the onset of disease (Folkhälsomyndigheten 2014). Candida glabrata, an opportunistic pathogen of the urogenital tract and bloodstream in immunocompromised persons, has been associated with taking of specific antibiotics (Ben-Ami 2012). In one large study, fluoroquinolones were found responsible for over 55% of cases of Clostridium difficile-associated diarrhea, an often fatal disease (Pepin et al 2005). Studies have demonstrated using mouse models that the two antibiotic-associated pathogens, Salmonella typhimurium and Clostridium difficile, infect their host by catabolizing mucosal carbohydrates liberated from microbiota by the antibiotic streptomycin (Katharine et al 2013). Use of antibiotics in children was significantly associated with Crohn's disease even if 6 months had elapsed between diagnosis and the latest intake of antibiotics (Virta et al 2012).

Aside for the infection of Salmonella typhimurium and Clostridium difficile, the exact biological mechanism for most of these epidemiological associations is currently unknown. However, it is logical to assume that killing off good bacteria is causative because we don't know of any other lasting effects of antibiotics, but we did see from the studies of Modi et al (2014) and Dethlefsen and Relman (2010) that some of the good bacteria decrease and don't ever reestablish themselves.

Results: Probiotic theory

To counter the adverse effects of antibiotics many have considered consuming probiotics. The theory behind probiotics is that swallowing new live bacteria will replenish the lost bacterial communities diminished by the antibiotics. Because a healthy gut microbiome is believed to promote and maintain health, probiotic yogurt and dietary supplements have been suggested even for individuals who have not taken antibiotics. First, though, it must be determined that probiotic bacteria are alive and can reach the gut when consumed orally.

Do probiotic bacteria die in the acidic pH of the stomach before they reach the intestine?

Critics of probiotics question whether the majority of the bacterial communities housed in a probiotic pill survive the acidic environment of the stomach on their journey to the intestine. Research has been done to determine the effects of the stomach's acidic environment on probiotic bacteria. It is worth noting that Lactobacilli, which are native gut bacteria and are included in most probiotic formulations, are acidophilic and are not adversely affected by stomach acid (Tannock 2004).

De Campo et al (2005) performed a double-blind study with 114 healthy volunteers. After 15 days of yogurt consumption, the participants' feces were analyzed by culture, specific PCR, and DNA hybridization for presence of the yogurt organisms L. delbrueckii and Streptococcus thermophilus. Detection of yogurt lactic acid bacteria in total fecal DNA by bacterial culture and PCR assay was consistently negative indicating that the strong acidic environment of the stomach killed microbes. However, Marina Elli et al (2006) showed that the De Campo et al's analytical detection methods were poorly set up. Elli's studies in turn confirmed that yogurt bacteria, especially L. delbrueckii subsp. bulgaricus, can be retrieved from feces of healthy

individuals after a few days of ingestion of commercial yogurt. Thus, Marina Elli's research established that many strains of probiotic bacteria do indeed survive transit through the gastrointestinal tract. It still is a possibility that though the low pH of the stomach does not destroy the entire probiotic population, it may limit the number of live bacteria that reach the intestine, reducing the effectiveness of the probiotic administration.

To overcome the possibility that a portion of the probiotic bacteria die in the stomach acid, new delivery technology has been developed to protect the strains from stomach acid. Scientists have constructed a coating for susceptible probiotics to avoid this possibility. Bifidobacterium breve, a model probiotic, was encapsulated into a multilayer alternating alginate-chitosan coating. This construction improved the endurance of B. breve during contact with stomach acid. During exposure to in vitro gastric conditions, a tremendous increase in viability from that seen in free cells was demonstrated (Cook et al 2013). Other studies have shown that capsules made of alginate, xanthan gum, and carrageenan gum increased the survival of probiotic bacteria in acidic stomach conditions (Ding and Shah 2009). Many probiotic supplements sold today include protective coatings. Though probiotic bacteria in yogurt has no such coating, the study of Marina Elli et al (2006) confirms that much of the bacteria do survive the acidic stomach environment.

Ancillary support for the survival of probiotic bacteria comes from the animal world. Coprophagy is the norm in an overwhelming number of vertebrae. Rodents, rabbits, pigs, foals and gorillas and chimpanzees all eat their feces regularly (Soave and Brand 1991). The young of elephants, pandas and hippos eat their maternal feces and thereby obtain the bacteria required to properly digest and obtain nutrition from vegetation in their diet. They are born without these necessary bacteria in their intestines (Zilber-Rosenberg 2013). The idea of sharing gut microbiota via feces has made its way to human medicine. Fecal bacteriotherapy or stool transplants have a well-entrenched place in the history of medicine of many ancient cultures. Recent studies have shown that C. difficile can be effectively treated with fecal transplants (Shultz 2014). The idea behind the consumption of feces is very similar to the reason to eat probiotics. It replenishes the microbiome with friendly bacteria.

Viability of organisms in capsules

Skeptics have questioned whether probiotic bacteria are alive and viable in their capsules or whether they die during production or storage. Many studies have been conducted proving that the bacteria are indeed alive. This is the general manufacturing process of probiotic pills as described by the Lallemand Health Solutions probiotic producer (2015): Chosen bacteria are inoculated onto a culture media and multiply. Live bacteria are then separated from the culture medium by centrifugation; they are mixed with a cryoprotectant, to help them survive the freeze-drying process. Alternatively, they are vacuum dried or spray dried. The dried bacteria form a solid cake which is milled into a fine homogeneous powder, each grain of which contains approximately 1 billion bacteria. Bacteria powders are blended with other carrier and diluent ingredients for the desired bacterial concentrations and then encapsulated and packaged.

Studies into the storage stability of spray-dried (Ananta E et al 2005), and freeze dried (Kurtmann L et al 2009) probiotics are positive. The bacteria remain alive, although dormant, and start to grow again after they reach the moist gut environment. Even higher storage stability has been found for vacuum-dried probiotic cells. Vacuum-dried cells show much higher stabilities than the freeze-dried cells (Foerst P et al 2012).

Effects of temperature on probiotic quality

Temperature has been shown to play a role in the stability of probiotics. Warmth and moisture are the ideal growing conditions for probiotic and gut bacteria. The growth and reactivation of these dormant organisms is inhibited in the presence of cold air, which holds less moisture and is not in the ideal temperature range for these bacteria to thrive. Cold air is therefore optimal for storage of probiotics as it keeps the bacteria from activating and hence dying before they have a chance to reach the human body. High heat can also degrade the viability of these organisms and care should be taken to keep them away from high temperatures. A thorough study on the effects of temperature on vacuum-dried probiotic bacteria revealed that after three months of storage at 4°C cells remained stable with a survival rate of 70%. At non-refrigerated temperatures (~37°C) only 54% of the cells survived (Foerst P et al 2012). Similarly, a study of freeze-dried common probiotic lactobacteria strains showed that stored at 4°C for three months, the survival rate was 76%, while storage at 23°C for the same length of time had only a 37% survival rate (Jalali M et al 2012). Similar effects of temperature on probiotic bacteria were determined for cells produced by spray-drying (Corcoran BM et al 2004). Based on this it would be best to store probiotics at refrigerated temperatures. Ideally, they should be kept at such temperatures in warehouses, shipment, and stores as well, though this is not currently standard.

It should be noted that as an extra measure, many manufacturers add an overage of bacteria to their probiotic products to compensate for the expected decline in numbers over time (NowFoods).

Probiotics and health

To date there has been insufficient research to prove whether probiotics counteract the many adverse effects of antibiotics

mentioned above, besides for treating antibiotic-associated diarrhea. However, a large number of studies have demonstrated the benefits of prophylactic probiotic treatment for general health benefits, preventing a variety of ailments, and curing other diseases not associated with antibiotics.

Probiotics as treatment for antibiotic-associated diarrhea

In 2012, researchers (Hempel S et al 2012) conducted an analytical search of hundreds of earlier studies and reviews about the effects of probiotics on antibiotic-associated diarrhea. This systematic review found that using the lactic acid-producing bacteria such as Lactobacillus rhamnosus, or L. casei as well as Saccharomyces boulardii [cerevisiae] may be helpful in preventing and curing antibiotic-associated diarrhea. The number-needed-to-treat value (NNT) was found to be 13. This means that statistically on average out of thirteen susceptible patients being treated with probiotics for antibiotic-associated diarrhea, one will benefit. Due to overall poor documentation of the probiotic strains, it was not clear if the efficacy of treatment was strain specific. Furthermore, the studies were spread over a vast population so more research needs to be performed to determine whether the elderly, middle-aged, or children would benefit most from adjunct probiotics therapy. Another question that requires clarity is which specific antibiotics are more likely to cause diarrhea and which probiotic strains best combat those particular antibiotics. However, the studies analyzed included patients taking a variety of antibiotics or did not specify the antibiotics used, limiting any conclusive correlation (Hempel S). Because the overall results from these studies are promising, many medical experts see no reason not to suggest probiotics when prescribing antibiotics (Kligler and Cohrssen 2008).

A more recent (2013) large study targeting 2,941 inpatients over 65 years of age exposed to broad-spectrum antibiotics found no supporting evidence that multi-strain lactobacilli or bifidobacteria probiotics were effective in prevention of antibiotic associated diarrhea in that group (Allen S et al 2013).

Studies on the effects of probiotics on the particularly dangerous condition, Clostridium difficile colitis, often caused by an impaired microbiome due to antibiotics, provide insufficient evidence to recommend probiotic therapy even merely as an adjunct treatment (Pillai A and Nelson R 2008).

Probiotics may shorten the duration of infectious diarrhea

Infectious diarrhea is often caused by shigella, E. coli, salmonella, and clostridium bacteria. A meta-analysis of almost 2000 patients from 23 studies of infectious diarrhea in both adults and children indicates that the duration of symptoms may be shortened by the use of probiotics by a mean of 30 hours (Allen SJ et al 2004). The majority of the probiotics tested in these studies were lactic acid bacteria; two studies used Saccharomyces boulardii. Though infectious diarrhea is not necessarily a result of antibiotic treatment, infectious diarrhea from Salmonella often is associated with antibiotic use. Thus, in this way probiotics may be considered to be counteracting the effects of antibiotics.

Bifidobacterium infantis 35624 reduced symptoms of irritable bowel syndrome (IBS)

In a review analyzing 16 randomized clinical trials of irritable bowel syndrome (IBS) patients who received either placebo or probiotic supplements, Bifidobacterium infantis 35624 was effective in reducing irritable bowel syndrome symptoms, such as intestinal gas, abdominal pain, bloating, and bowel function (Brenner DM et al 2009). There was no evidence of adverse results. No other probiotic, including isolated Lactobacillus species, showed significant improvement in IBS symptoms in appropriately designed randomized clinical trials.

Another systematic review of the literature revealed that probiotics succeeded in reducing irritable bowel syndrome symptoms with a number needed to treat (NNT) of 4 (Moayyedi P et al 2010). Almost all probiotic combinations contained Bifidobacteria species (Verna 2010).

Probiotics for constipation

Dr. Mary Morgan, an immunologist and researcher for probiotics companies, conducted a meta-analysis to uncover which probiotics have the best results for constipation. She found the following five are best: Bifidobacterium lactis DN-173 010, VSL#3 formula (a probiotic mix), Bifidobacterium lactis Bb-12, Lactobacillus casei Shirota, and Bifidobacterium longum (Morgan 2013).

Probiotics may prevent hepatic encephalopathy development from cirrhosis

A recent study shows that probiotics are effective in preventing the progression of liver cirrhosis to hepatic encephalopathy (Lunia MK et al 2013). Cirrhosis is an advanced liver disease characterized by replacement of healthy liver tissue with scar tissue, leading to progressive loss of liver function. It is usually caused by alcoholism, Hepatitis A or Hepatitis B. As cirrhosis is irreversible, treatment of cirrhosis focuses on preventing progression. In a progressed state, cirrhosis may lead to hepatic encephalopathy, in which an over accumulation of toxic ammonia in the blood due to loss of liver function brings the patient to an altered level of consciousness or coma. Natural members of gut flora such as Eubacterium aerofa-ciens, E. lentum, and Peptostreptococcus productus produce urease, which hydrolyzes urea into ammonia (Suzuki K et al 1979). In a healthy body,

this ammonia is absorbed from the intestine into the bloodstream then filtered out by a functioning healthy liver. Hepatic encephalopathy, the result of poor liver function, is commonly treated with the sugar, lactulose, which reduces the absorption of ammonia from the gut into the bloodstream. The usefulness of lactulose is limited by side effects such as diarrhea, bloating, and flatulence. The Lunia MK, et al study found that intake of a specific set of probiotics will alter the intestinal microbiota, preventing development of hepatic encephalopathy in patients with cirrhosis. By recolonizing the gut with non-urease producing bacteria such as those in the supplements used in this study, a buildup of ammonia is avoided, thus preventing hepatic coma.

The 86 patients in the treatment group received a regimen of probiotics which contained Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, and Streptococcus thermophilus, 110 billion colony-forming units in all, in one capsule 3 times per day. The control group included 74 patients. Patients were told to refrain from eating any commercial probiotic yogurt. The patients were followed up on each month for six months to ascertain that they were keeping to their probiotic treatment plan and to track the development of any hepatic encephalopathy symptoms. The researchers observed that the incidence of hepatic encephalopathy was significantly lower in patients treated with probiotics. No adverse effects were detected from the probiotics. These results offer a more comfortable and better-tolerated alternative to current lactulose treatments (Lunia MK).

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Probiotics as bowel movement and nutrition enhancer in the elderly

Hilla Zaharoni et al (2011) conducted a study to determine the preventive impact of probiotics on problems with bowel movement and malnutrition in the elderly (Zaharoni H et al 2011). The study included 215 elderly patients at an orthopedic rehabilitation center (107 as control, 108 as probiotic recipients), age 65 and over. Each participant received a daily dose of commercially sold probiotic bacteria. The dosage consisted of four strains of Lactobacillus – L. planturum, L. paracasei, L. bulgaris, L. acidophilus; three strains of Bifidobacterium – B. breve, B.longum, B. infantis; and one strain of Streptococcus, S. thermophiles. The control group received a daily placebo packet looking exactly like the probiotic complement. After being fed daily probiotics or placebo pills for 45 consecutive days in a randomized, double-blind, placebo-controlled trial, the patients were monitored for 45 follow-up days. The incidences of diarrhea were significantly lower among the study group (HR=0.42, p=0.04) with a more significant difference among participants age 80 and older (HR=0.32, p=0.026). The necessity to use laxatives, an indicator of constipation, also showed significant decrease in the probiotic group compared with the control group (HR=0.74, p=0.032).

Additionally, healthier levels of transthyretin, reflecting a positive nutritional intake status, and increased serum albumin levels, necessary for proper distribution of body fluids, were detected in the octogenarians of the treatment group compared with the control group (P=0.047, p=0.07, p=0.03 respectively) but not in the younger age group (between 65 and 80 years

of age). This study strongly indicates that the studied bacterial strains in commercial probiotics have a positive effect on the bowel movements of elderly patients in orthopedic rehabilitation (Zaharoni H et al 2011).

Bifidobacterium lactis (BB-12), Lactobacillus reuteri prevents occurrence of infantile fever and diarrhea, though not respiratory illness

An important study led by Weitzman Z et al (2005) shows excellent results for probiotics' prophylactic effect against fever and diarrhea in infants. A placebo-controlled, double-blind trial was conducted at 14 child care centers on healthy infants four to ten months old. Infants were assigned randomly to either no probiotics or baby formula supplemented with Bifidobacterium lactis (BB-12) and Lactobacillus reuteri 55730 for a period of 12 weeks. The infants were not breastfed prior to the study, and were fed only the assigned formula. The parents agreed not to administer any other probiotic or prebiotic supplements. The number of episodes of fever (>100.5 degrees F), diarrhea, and respiratory illness and the days of duration were measured for both groups.

Of 201 participating infants who were similar in gestational age, birth weight, and prior breastfeeding, 60 infants were controls, 73 were fed B. lactis, and 68 were fed L. reuteri. Febrile outbreaks and diarrheal episodes were nearly double in the control group compared to the recipients of B. lactis. The duration of diarrhea was also protracted in the control group. Results from the 68 infants of the L. reuteri group were even more encouraging. Compared with the controls and even B. lactis infants, the L. reuteri group had a substantial decrease in number of days with fever, doctor visits, nursery absences, and antibiotic medication prescriptions. The probiotic supplements showed no effect on the incidents of respiratory illnesses between the groups.

Bifidobacteria infantis, Streptococcus thermophilus, and Bifidobacteria bifidus for necrotizing enterocolitis

Prophylactic use of the probiotics, Bifidobacteria infantis, Streptococcus thermophilus, and Bifidobacteria bifidus, were tested by Alona Bin-Nun et al (2005) to determine their effect on the incidence and severity of necrotizing enterocolitis. Necrotizing Eterocolitis is a postnatal medical condition where portions of the bowel undergo necrosis. Primarily seen in premature infants, it is among the most common causes of mortality in premature infants. Neonates were randomized to either receive a daily feeding supplementation with a probiotic mix of 109 colony-forming units per day or to receive no probiotic supplements.

For 72 study and 73 control infants, respectively, birth weight, gestational age, and time to reach full feeds were nearly equal. The incidence of necrotizing enterocolitis was reduced in the study group (4% vs 16.4%). Additionally, necrotizing enterocolitis was less severe in the probiotic-supplemented infants. Three of 15 babies who developed necrotizing enterocolitis died, all three from the control group.

Discussion and future study

Over the past two decades there has been significant advancement in the field of probiotics since it has been first suggested in 1907 by Elie Metchnikoff. These studies have used random undirected criteria for choosing which bacteria from amongst thousands of species and strains to test for potential health benefits. They often chose strains occurring in various fermenting foods. Each trial has been like a shot in the dark hoping to find a cure. The author suggests that future studies focus on the strains unique to the gut of residents of the rural village in Burkina Faso in the De Filippo et al (2010) study and of other remote non-westernized locales for their potential probiotic qualities. Epidemiological evidence tells that the improved sanitation, sterile industrial foods, and antibiotics of westernized civilization has controlled infectious diseases but also has increased the incidence of allergic, autoimmune disorders, and inflammatory bowel disease (IBD). By selecting gut bacteria unique to isolated populations living with an environment and diet of the pre-modern era, we may discover probiotic beneficial bacteria which can restore and implant the health benefits of those primeval and rustic lifestyles into the modern urbane world. The De Filippo et al study identified bacteria from the genus Prevotella and Xylanibacter (Bacteroidetes) and Treponema (Spirochaetes) exclusive to the Burkina Faso population. These results should be verified and similar investigations should be made into the gut bacteria of other traditional societies such as remote Tibetan villages and Northern Okinawa farm towns. New randomized clinical trials for probiotic efficacy should be designed utilizing the bacterial findings of these remote searches.

Practical consumer implications; Considerations for choosing probiotic supplements

There are hundreds of probiotic supplements available on the market. Many of these products have no claim to any supporting studies. As probiotics are considered dietary supplements and not medications, they do not require certification from the Federal Department of Agriculture (FDA). There are great variations in the strains of bacteria they contain. It is best to buy products that are backed by clinical research. The wise consumer will examine the labels of the product to be certain that it contains the particular research-backed strains he or she desires. If one hopes for a particular cure or health benefit, the supplement one chooses should contain strains shown to be

Table 1

Condition	Probiotic Bacterial Species	Population*
antibiotic-associated diarrhea	Lactobacillus rhamnosus, L. casei, Saccharomyces boulardii [cerevisiae]	people younger than 65 years
infectious diarrhea caused by shigella, E. coli, and salmonella	Lactic acid bacteria species, Saccharomyces boulardii	adults and children
irritable bowel syndrome (IBS)	Bifidobacterium infantis 35624	adults
promoting bowel movements and better nutrition intake	Lactobacillus planturum, L. paracasei, L. bulgaris, L. acidophilus, Bifidobacterium breve, B.longum, B. infantis, Streptococcus thermophiles	individuals of 65 years and older
fever and diarrhea (prophylactic treatment)	Bifidobacterium lactis (BB-12), Lactobacillus reuteri 55730	infants
constipation	Bifidobacterium lactis DN-173 010,VSL#3® formula (a probiotic mix), Bifidobacterium lactis BB-12, Lactobacillus casei Shirota, Bifidobacterium longum	adults
necrotizing enterocolitis	Bifidobacteria infantis, Streptococcus thermophilus, Bifidobacteria bifidus	infants
hepatic encephalopathy (prophylactic treatment)	Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus	cirrhosis patients

**These particular populations were studied. Effects on other populations are not included unless indicated.*

Table 2

Yogurt Brands	Bacteria Strains
Yoplait	Lactobacillus bulgaricus Streptococcus thermophilus sometimes: Lactobacillus acidophilus
Chobani	Lactobacillus acidophilus Bifidobacterium bifidum Lactobacillus casei
Stonyfield Farms	Lactobacillus bulgaricus Streptococcus thermophilus Lactobacillus acidophilus Bifidobacterium bifidum sometimes Lactobacillus rhamnosus
Yakult	Lactobacillus casei Shirota
Dannon	Lactobacillus bulgaricus Streptococcus thermophilus sometimes: Lactobacillus acidophilus Bifidobacterium lactis DN-173 010 in Activia® Lactobacillus casei DN-114- 001 in DanActive®
La Yogurt	Lactobacillus bulgaricus Streptococcus thermophilus Lactobacillus acidophilus Bifidobacterium bifidum Lactobacillus casei Bifidobacterium animalis BB12

beneficial to that end. Table 1 summarizes researched bacterial strains and the conditions they benefit.

Probiotic Yogurt

Many yogurt products claim to be probiotic. Again, these claims are not backed by the FDA. Some bacterial strains in yogurt have more scientific support than others. According to the Dairy Reporter (August 2, 2013), Dannon, Yoplait, Chobani, and Stonyfield rank among the most popular brands in the United States. Table 2 lists the strains included in commonly available yogurts.

Starter bacteria

Most of the brands use Lactobacillus bulgaricus and Streptococcus thermophilus as yogurt culture starters to turn milk into yogurt. The only researched health benefits of these two species is that they boost the immune system in anorexia patients (Nova E et al 2006) and help lactose absorption those who are lactose-intolerant (Riskalla SW et al 2000).

Other added strains

Bifidobacterium animalis lactis BB-12 (LaYogurt)

The precise bacteria combination found in La Yogurt hasn't been scientifically researched. However, there have been many trials using the strain Bifidobacterium animalis lactis BB-12, which all La Yogurt probiotic products contain (*personal communication). Studies have shown BB-12 reduces incidences of fever and need for antibiotic treatment in infants (Weitzman Z et al 2005). Also, it has been demonstrated that negative immune-related effects of non-breastfed infants can be significantly reduced by including B. animalis lactis BB-12 in their diet (Holscher HD et al 2012).

Bifidobacterium lactis DN-173 010 (Activia®)

On the yogurt ingredient panel this strain is known as Bifidus regularis. This strain is well suited to treating intestinal inflammations such as colitis (Veiga P et al 2010). Studies showed that it can reduce symptoms of irritable bowel syndrome (Agrawal A et al 2009) and improve digestive comfort and symptom experience of adults from the general population (Guyonnet D et al 2009) and well as help improve constipation in children (Tabbers MM et al 2009).

Lactobacillus casei DN-114 001 (DanActive®)

L. casei DN-114 001, also known as L. casei immunitas, used in DanActive®, has great study results. Daily consumption of a product containing Lactobacillus casei DN-114 00 has been shown to reduce the risk of gastrointestinal and respiratory common infectious diseases in shift workers (Guillemard E et al 2010).

Lactobacillus casei Shirota (Yakult)

The yogurt drink Yakult's live Lactobacillus casei Shirota has been tested for effect on constipation with excellent results. Chronic constipation patients experienced a sharp reduction in symptoms after only two weeks of drinking Yakult (Koebnick C et al 2003) (Cassani E et al 2011).

Yogurt Certification

In the USA, a 'Live Active Culture Seal' (image 1) was introduced by the National Yogurt Association to identify refrigerated or frozen yoghurt products which contained at least 108 or 107 viable bacteria per gram at the time of manufacture (AboutYogurt.com). In heat-treated yogurt, a process done to prolong shelf life or decrease yogurt's natural tartness, these cultures are killed during heating after fermentation.

However, because these counts do not differentiate between true scientifically proven probiotic strains and mere starter cultures, the National Yoghurt Association's certification emblem is still not reflective of true probiotic value (Senok AC et al 2005). One must also check that the strains inside the yogurt are the well-researched bacteria discussed above.

Conclusions

While it is true that many strains of bacteria confer positive health benefits when taken orally, these bacterial strains demonstrate great specificity. Precise subspecies and strains have been shown to cure certain ailments but not others, to benefit only a particular age group, and to provide these advantages only when taken on a regular basis. The research in this paper is important because it shows the specific ways in which probiotic bacteria are effective. The widely spread beliefs about benefits of probiotic products are not ensured by any governing body. Research indicates that the functions and mechanisms of gut bacteria are very complex and therefore there is no reason to assume that random "probiotic" bacteria will offer any health benefit. In addition, considerations for form and storage of probiotics were discussed: namely that alginate coating may aid in probiotic colonization and that probiotic supplements should be stored at or below 4°C. Consumers should note that the positive results in the studies were generally observed after 2-4 weeks or more of daily probiotic consumption. Additionally, suggestions for future studies utilizing gut bacteria unique to non-modernized traditional societies have been made. This paper aids the general population by providing the necessary knowledge needed in order to be an educated consumer of probiotic products.

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