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REVIEW

Role of Probiotics in health improvement, infection control and disease treatment and management

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Abstract Research which concerns the usefulness of Probiotics show increasing interest based on the rise of their publications, products and the awareness of the public of their benefits. There is increasing interest concerning Probiotics from the public, researchers, governmental organizations (such as the WHO/FAO) and medicinal and food companies. Probiotics means "let good microbes work for you in different fields get their benefits and take a rest". Such work will include, food digestion, production of useful products to destroy the bad microbes, complement the functions of the missed digestive enzymes (due to missed or defective genes), and to maintain the digestive system's pH, and so on. Probiotics will augment the efficiency of our biological fermentors, the digestive system. Many authors have described the history and the progress of Probiotics and their different applications. In this review, we will focus mainly on three points, health improvement, infection control and disease management, which could be eliminated by the use of different types of direct uses of Probiotics or by the use of foods containing Probiotics.

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1. Introduction

It became clear that intestinal microflora had metabolic functions, such as fermenting indigestible dietary residues and endogenous mucus, saving of energy, production of vitamin K, and absorption of ions (O'Sullivan et al., 1992). Probiotics have roles in epithelial cell proliferation and differentiation, and the development and the homeostasis of the immune system (Cammarota et al., 2009). Probiotics are not an invention but existed in our traditional foods such as beverages, salty fishes, yogurt, different types of cheeses and so on since olden times (Amara, 2012). Such food structures contain different types of useful bacteria. It might be that the first real use of food containing Probiotics was fermented milk (Hosono, 1992). Humans learned that fermented milk has a good taste. Later they learned how to convert it into cheese, yogurt and so on (Metchnikoff and Mitchell, 1910; Metchnikoff, 2004; Amara, 2012). Before the discovery of the microscope, humans knew how to prepare different types of milk products with different tastes and structures (Amara, 2012). This is a result of the action of different microbial reactions induced by different microbes (Bourdichon et al., 2012). The public, globally transfer such information for producing such foods from generation to generation till today. We really did not know the starting point for the first use of food containing Probiotics particularly for medicinal applications. However, by one way or the other Probiotics collectively are a part of the fermented food if the active microbes are useful and able to colonize the digestive system. Fermentation using microbes is known from ancient times. One could see the fungi growing in the food by the naked eye. The public knew how to produce Bakery and alcoholic products from times immemorial. They knew how to maintain the product quality and testing by maintaining a seed culture from the most successful fermentation processes to use in the next process (Amara, 2012). However, scientists were interested to give such honor to Van Leeuwenhoek and Hooke in 1665 (Gest, 2004). For more details about the fermented foods, refer to Bourdichon et al. (2012) and the references within.

It might be that Probiotics have been discovered by the first human who used milk products, or, might be with substances other than milk! such as the other different types of the fermented foods. However, climatic conditions, for sure, favored traditional sour milk or cultured dairy products such as Kefir, Koumiss, Leben and Dahi as claimed by Hosono (1992). Public distribute stories about the origin of some types of Probiotics and that some have religious origin, such as the origin of Kefier. Amara, 2012, describe some of the Probiotics used by the Pharaonic civilization, which the Egyptians still use nowadays. They include milk, seeds, fish and some other products. However, it might be that Ilya Ilyich Metchnikoff, the Nobel Prize winner in Medicine in 1908, at the Pasteur Institute was the first who spotted the effect of what is called now Probiotic. He linked the health and longevity to the ingestion of bacteria present in yogurt (Metchnikoff and Mitchell, 1910; Metchnikoff, 2004). In 1907, he postulated that bacteria were involved in yogurt fermentation, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, suppress the putrefactive-type fermentations of the intestinal flora and that consumption of these yogurts was important in maintaining health. He correlated the long life of Bulgarian peasants and their good health to yogurt intake which contained the *Lactobacillus species* and he simplified his conclusions to the public that, Probiotics could do an extra-job by digesting unusual components exactly like what happens in the ruminant animals which eat rough food composed of bulky vegetables. In Japan, in the early 1930s, Shirota succeeded in isolating strains existing in healthy individuals' intestinal bacteria. Such strains are able to survive and to passage through the gut. He has used such strains to develop fermented milk and test such milk effects on patients. He introduced his first products into the market, which have been given the name Shirota (later named *Lactobacillus casei* Shirota). The producer company's name was the Yakult Honsha Company. Probiotics can be defined as living microorganisms administered in an adequate number that continue to exist in the intestinal bionetwork, to perform a health positive effect (Gismondo et al., 1999). Probiotics as a term was first used by Lilly and Stillwell (1965) to describe the 'substances secreted by one microorganism that stimulate the growth of another'. Parker (1974), proposed that Probiotics are 'organisms and substances which contribute to intestinal microbial balance'. Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO, 2001) endorsed by the International Scientific Association for Probiotics and Prebiotics (Reid et al., 2003), defined Probiotics as 'Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host'.

1.1. Common microbes used as Probiotics

The microbes used as Probiotics represent different types such as bacteria, yeast or mold. However, there are more common species of each such as: 1 – Bacteria: (i) *Lactobacillus*: *acidophilus*, *sporogenes*, *plantarum*, *rhamnosum*, *delbrueck*, *reuteri*, *fermentum*, *lactus*, *cellobiosus*, *brevis*, *casei*, *farciminis*, *paracasei*, *gasseri*, *crispatus*; (ii) *Bifidobacterium*: *bifidum*, *infantis*, *adolescentis*, *longum*, *thermophilum*, *breve*, *lactis*, *animalis*; (iii) *Streptococcus*: *lactis*, *cremoris*, *alivarius*, *intermedius*, *thermophilis*, *diacetylactis*; (iv) *Leuconostoc mesenteroides*; (v) *Pediococcus*; (vi) *Propionibacterium*; (vii) *Bacillus*; (viii) *Enterococcus*; (ix) *Enterococcus faecium*; 2 – Yeast and molds: *Saccharomyces cerevisiae*, *Saccharomyces bourlardii*, *Aspergillus niger*, *Aspergillus oryzue*, *Candida pintolopesii*, *Sacaromyces boulardii*.

The type of the microbes used as Probiotics increased due to the increase in the research concerning the subject as well as by the increase of the newly discovered and identified microbes, which could be used as Probiotics. One should update his microbial flora from time to time and follow the research and the published data about Probiotics to gain more knowledge and ideas.

1.2. Probiotic for health improvement

One of the points described in this review about Probiotics is their role in health improvement. In fact, this is the most important point, where we expected that healthy persons will be the first in need to use Probiotics which will lead to improve their general health and as a result will protect them from different kinds of illness. Improving health will be an intelligent step for protecting us from different types of illness. Nevertheless, how could Probiotics do that? The following paragraphs will highlight the concept of how Probiotics could improve our health directly or indirectly.

1.3. Good and bad microbes

Our bodies have groups of microbes each working collectively to perform different functions. The most important ones are those existing in our digestive system (Gismondo et al., 1999; Fioramonti et al., 2003). They improve food digestion and consumption. They are able to complement many deficiencies in our digestive system. They decrease the steps needed in our bodies to change complicated food structures to simpler ones. Alternatively, many bad variants of different microbes will take their positions and will digest our food incorrectly. They will even add some toxins to our food during the digestive process. Hence, each food cycle will lead to a real deterioration to our health (Amara, 2012). Many diseases are diagnosed incorrectly while their main actual elevating purpose is due to the existence of bad microbes in the digestive system, mainly due to the leakage in the feeding processes, the life style or even diseases which will direct the balance toward the bad microbes. The affected ones are humans because they did not follow the correct steps to protect themselves from losing the useful strains and gaining harmful ones. In such cases, Probiotics are needed to be given in higher dosages (Amara, 2012; Reid et al., 2003).

1.4. Probiotic, the good against the bad microbes

If harmful microbes colonized our digestive system they will ferment food in incorrect ways and toxins, which will affect our health, might be produced. *What could Probiotics do*? Probiotics are able to regenerate our digestive system with good microbes that will neutralize the harmful ones. Useful microbes will ferment our food correctly and improve our health. *Why must we use Probiotics*? During our lives, we are exposed to different types of microbes, which are unsuitable for our health. Antibiotic treatment could destroy our useful microflora. In such cases, Probiotics should be used to regenerate our microflora. If our daily food contains Probiotics, that will be the best and the cheapest way to recover any losses in our digestive system microflora and to improve our health. In olden civilizations, the public used to include food-containing Probiotics in their daily food (Amara, 2012). However, when our microflora has been affected severely due to any reasons, Probiotics should be given in large dosage as tablets or in any other suitable forms (Reid et al., 2003). A healthy intestine is one that maintains a significant balance of bacteria such as lactobacilli, streptococci, clostridia, coliform, and bacteroides. Conditions such as stress, excessive alcohol use, high fat diets, meat, sugar, genetic disorders, chlorine and fluoride in drinking water, antibiotics, inadequate food, exposure to environmental toxins and many others factors could change the balance of our intestinal flora (Hosono, 1992). In fact, our health is affected by many exogenous and endogenous factors that could change our microflora position. Useful microflora guarantees good health. One cannot hear the sound of the daily battles between the good and the bad microbes in our bodies or see how they enter our bodies with each breath, talk and with each food consumed. Actually, they are essential for our health. They build our immune system slowly to be ready for the pathogens (Bandyopadhyay and Das Mohapatra, 2009; Cammarota et al., 2009). Those that live far away from such a lifestyle are more susceptible to infections and diseases (Amara, 2012). Another side of the story, that such microbes and mainly those which are non-pathogenic, are like workers working in a big firm (our body), they do various jobs to support and assist us all the times. Mainly, they do that spontaneously. By doing such work, they save for us energy and power, or they even do what we could not do. Complementing the Lactose digestion deficiency is such an example (Hawrelak, 2003). The existence of harmful bacteria could finding resistance in the body, so their negative effects might not appear directly, but after a considerable time. Alternatively, they are not few in number but produced in considerable amounts, at this point they will be really harmful (Amara, 2012). Bad microbes, even though apparently non existant in a healthy person, actually, exist, but cannot do a lot of harm because of the existence of good bacteria. They are under continuous pressure from good bacteria. Good bacteria, fill in the spaces existing in our body, and prevent bad ones from taking their chances. However, because of our misuse and misunderstanding of their behavior, we change the conditions usually towards the benefit of bad bacteria. By changing the balance toward the bad microbes, we will start to suffer, and our health will start to degrade. To prevent that, the bad microbes should be kept under control (Amara, 2012). Therefore, there is no better solution other than, letting good ones compete with them, take

their places and in some cases omit them or decrease them to the minimum safe amount. The intestinal tract is home to one hundred trillion (10^{14}) different types of microbe (Gismondo et al., 1999). Many of the bad microbes like to live in alkaline or natural environment, that is why our stomach is acidic to kill most of them before they pass into the long intestine. Bad microbes produce ammonia that change the intestinal tract pH to becoming more alkaline (Metchnikoff and Mitchell, 1910; Metchnikoff, 2004; Marteau et al., 2001). One might observe that upon drinking fermented milk, which is weakly acidic, he feels good and relaxed. This is because of two factors, that fermented milk contains acids, which kill pathogenic bacteria, and at the same time contains good bacteria, which will directly fill the space of the just killed bacteria (Fernandes et al., 1987; Hilton et al., 1977). Additionally, it still contains proteins that are able to reduce any extra-acidity. One of the most important strains existing naturally in milk products is Lactobacillus. The microflora in our digestive system do crucial jobs, such as filling in digestive system spaces, food digestion, killing of pathogens, and secreting vitamins (e.g. vitamin B) and some essential amino acids, enzymes help in digesting complicated fibers in the food, acid (e.g. lactic acid) helps to prevent pathogenic microflora from exceeding their number limit, and to perform many other vital activities. As well, Probiotic strains found in the colon help in digesting some forms of fiber. One should highlight that Probiotics are also able to some extent activate the immune system (Cammarota et al., 2009).

1.5. The relation of Probiotics to our health could be summarized in the following points and facts

1 – Probiotics are useful and friendly microbes.
2 – They are able to compete with the bad microbes and colonize our digestive system.
3 – They are able to ferment our food to simpler byproducts and could promote our health by many different mechanisms.
4 – Their amount could be deteriorated due to many factors, such as incorrect diet, alcohol, age and so on. This is why they should be taken through our regular diet.
5 – In particular cases such as after antibiotic treatments, where they are expected to be affected severely, they should be taken orally in considerable amounts or with food.
6 – Probiotics promote health while they:
   a. Remove the side effect of the pathogens or the harmful microbes.
   b. Supply the body with useful byproducts.
   c. Reduce the jobs of our digestive system.
   d. Reduce the effect of the first attack of harmful compounds, instead of our cells, by their biofilm, which protects our digestive system.
   e. Reduce the amount of food needed by our bodies due to the correct digestion and metabolism of any amount of food.
   f. Probiotics in some cases could complement the deficiency in our genetic materials by helping us to borrow the products of their genes (such as in case of the lactose fermentation deficiency).

Here we should highlight that, Probiotics or anything in our lives should not exceed a certain limit and should be used wisely to give the best expected results (Salminen et al., 1998).

1.6. Infection control

The mechanisms by which Probiotics exert their effects are largely unknown, and there are still many open research points. However, Probiotics are involved in modifying gut pH, antagonizing pathogens through the production of antimicrobial compounds, competing for pathogen binding and receptor sites as well as for available nutrients and growth factors, stimulating immunomodulatory cells, and producing lactase (Table 1). The most important point of Probiotics is that they are proven to be safe, cost effective, and could interfere with the microbial infection. In 1994, the World Health Organization deemed Probiotics to be the next-most important immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance (Kailasapathy and Chin, 2000; Levy, 2000). The use of Probiotics in antibiotic resistance is termed as microbial interference therapy (Botes et al., 2008; Fukao et al., 2009; Zhou et al., 2005).

2. Examples

2.1. Diarrheal diseases

Probiotics are proving to have roles in diarrhea prevention and control after antibiotic treatment. *Lactobacillus GG*, *Lactobacillus reuteri*, and *S. boulardii*, *Bifidobacteria* spp., are used for curing diarrhea (Hilton et al., 1977; Isolauri, 2004; Benchimol and Mack, 2004). Also Probiotics are able to suppress travelers' diarrhea (Hilton et al., 1977) and diarrheal diseases in young children caused by rotaviruses (Saavedra et al., 1994; Vanderhoof, 2000). The Probiotic species used with children include *Lactobacillus* spp., *L. reuteri*, *Lactobacillus casei*, *S. boulardii*, *Bifidobacterium bifidum* and *S. thermophilus* (Hilton et al., 1977; Tomas et al., 2004). Probiotics might prevent microbes that carry diarrhea by competing with pathogenic viruses or bacteria by preventing them from binding to epithelial cells (DeSimone, 1986; O'Sullivan et al., 1992), or by producing bacteriocins such as nisin (del Miraglia and De Luca, 2004).

2.2. Helicobacter pylori infections

Aiba et al. (1998) showed *Lactobacillus salivarius* capable of producing high amounts of lactic acid, which can inhibit the growth of *H. pylori in vitro*. There is some preliminary evidence that Probiotic bacteria may inhibit the gastric colonization and activity of *H. pylori*, which is associated with gastritis, peptic ulcers and gastric cancer. *L. salivarius* was found to inhibit *H. pylori* colonization in the *in vitro* studies as well as in mice (Aiba et al., 1998; MacFarlane and Cummings, 2002). The use of Probiotics in the field of *H. pylori* infection has been proposed for improving the eradication rate and tolerability and for the compliance of multiple antibiotic regimens used for the infection (Bazzoli et al., 1992; Filippo et al., 2001).

Table 1 Different types of Probiotic microbial strains, and their usage.

Disease name	Strain	References
Eczema	*Escherichia coli* *Bifidobacterium bifidum* *Bifidobacterium lactis* *Lactococcus lactis*	Niers et al. (2009), Soh et al. (2009), Viljanen et al. (2005a and 2005b)
Food allergies	*Escherichia coli*	Lodinova-Zadnikova et al. (2003)
Immunity	*Bacillus circulans PB7* *Lactobacillus plantarum DSMZ 12028*	Bandyopadhyay and Das Mohapatra (2009) and Cammarota et al. (2009)
Antibiotic effect removal	*Enterococcus mundtii ST4SA* *Lactobacillus plantarum 423* *Lactobacillus brevis KB290* *Lactobacillus strains* *Bifidobacterium strains*	Botes et al. (2008), Fukao et al. (2009) and Zhou et al. (2005)
Gastroenteritis Therapeutics	*Lactobacillus casei*	Yamada et al. (2009)
Intestinal hyperpermeability	*Lactobacillus plantarum species 299 (LP299)*	Kennedy et al. (2000), Strowski and Wiedenmann (2009) and White et al. (2006)
Vaginal candidiasis (thrush)	*Lactobacillus rhamnosus GR-1* *Lactobacillus reuteri RC-14*	Martinez et al. (2009)
Urinary tract infection	*Lactobacillus rhamnosus GR-1* *Lactobacillus reuteri RC-14*	Anukam et al. (2009)
Lactose intolerance	*Lactobacillus acidophulus*	Hawrelak (2003)
Non-steroidal anti-inflammatory drug	*Escherichia coli strain Nissle 1917*	Ukena et al. (2005)
Intestinal dysbiosis	*Lactobacillus johnsonii La1* *Lactobacillus strain* *Lactobacillus GG*	Hawrelak (2003), Silva et al. (1987), and Bennett et al. (1996)
Irritable bowel syndrome	*Bifidobacterium infantis 35624* *Escherichia coli DSM17252* *Bifidobacterium infantis 35624*	Brenner and Chey (2009), Enck et al. (2009), Whorwell et al. (2006)
Traveler's diarrhea	*Lactobacillus GG* *Lactobacillus plantarum*	Hawrelak (2003), and Michail and Abernathy (2002)
Radiation-induced diarrhea	*Lactobacillus casei DN-114 001*	Giralt et al. (2008)
Crohn's disease	*Escherichia coli strain Nissle 1917*	Boudeau et al. (2003)
Prevention of colon cancer	*Enterococcus faecium M-74* *lactic acid bacteria*	Mego et al. (2005) and Thirabunyanon et al. (2009).
Ulcerative colitis	*Lactobacillus acidophilus* *Escherichia coli Nissle 1917* *Bifidobacterium*	Abdin and Saeid (2008), Adam et al. (2006), and Imaoka et al. (2008)
Peptic ulcer disease	*Lactobacillus acidophulus*	Iarovenko et al. (2007)
Prevention of atopy	*Lactobacillus rhamnosus GG*	Huurre et al. (2008) and van der Aa et al. (2008)
Hypercholesterolemia and cardiovascular diseases	*Enterococcus faecium M-74* *Lactobacillus plantarum* *Propionibacterium freudenreichii* *Lactobacillus plantarum PH04*	Hlivak et al. (2005), Kiatpapan et al. (2001) and Nguyen et al. (2007)

2.3. The role of Probiotics in disease treatment

Probiotics could not only improve our health or control pathogenic infections but could also help in real disease treatment and management (Table 1). Part of the basis for doing such tasks is based on the same concepts about Probiotic functions, which are described in the above sections. But, how could Probiotics help in real disease treatment and management. The most critical points are in understanding of the disease behavior and its causative agents. For examples, diseases which are related to genetic disorders, will cause certain sort of deficiencies like lactose intolerance. The role of Probiotics in such types of cases will be in removing such deficiencies by different mechanisms such as (i) supplying our bodies with the products of the missed gene products, (ii) supplying our bodies with suitable alternative products, (iii) supplying our bodies with the final products of a complete pathway which will be the best choice and in the case that none of the defective pathway metabolic intermediates will be accumulated in our cells in the case of a single or multiple gene deficiency which could block a certain pathway, (for more details refer to Amara, 2013 and the references within), (iv) Probiotics could

support a weak (rather than a completely defected pathway) pathway which might be due to a defect in a single allele rather than the defect in both alleles. Exactly like in the case of those who have retinoblastoma. In such a case the critical basis for the Knudson hypnosis's will be completely interfered with while a single gene will not be a subject to excessive stress that could lead to a mutation (Amara, 2013), (v) Probiotics will be the best support for us when we become old. It will reduce the load on our biological system and will enable us to do extra activity, particularly those related to improving our ability to utilize food. Here are some roles for Probiotics in maintaining our health, in disease treatment and management:

1 – Suppression of the putrefactive-type fermentation which was one of the Ilya Ilyich Metchinkoff postulations about the usefulness of Probiotics (Metchnikoff, 2004).
2 – Used to reduce the antibiotic destructive effect and to regenerate any type of loss in beneficial microflora. Some *Bacillus species* are recommended for use with antibiotics while they are resistant to them (Bandyopadhyay and Das Mohapatra, 2009; Cammarota et al., 2009).
3 – Treating of the diarrheal disorder. *Saccharomyces cerevisiae var boulardii* was used widely for treating various diarrheal disorders (Hawrelak 2003; Michail and Abernathy, 2002).
4 – Improving intestinal tract health (Vanderhoof, 2000).
5 – Enhancing the immune system, synthesis and enhancing the bioavailability of nutrients (MacFarlane and Cummings, 2002).
6 – Reducing symptoms of lactose intolerance and decreasing the prevalence of allergy in susceptible individuals (Hawrelak, 2003).
7 – Reducing the risk of certain cancers (Mego et al., 2005; Thirabunyanon et al., 2009).
8 – Control of serum cholesterol levels (Hlivak et al., 2005).
9 – Improved digestion of lactose against foods containing lactose.
10 – Probiotics may also influence the protective functions of the intestinal mucosa including the synthesis and secretion of antibacterial peptides (Cammarota et al., 2009).
11 – Hypertension (Blood pressure control) (Hlivak et al., 2005).
12 – Condition of the genitourinary tract (Martinez et al., 2009).

3. Conclusion

The health condition of the mother and the environment where the child is born determines the first species which colonizes his body and which affects his health during his life. Good microbial strain colonies of microflora will lead to good health and will give us different types of benefit. In our life, there are many factors that disturb our useful microflora, in these conditions exo-sources should be used. Such exo-sources which contain such useful microbes or what is named Probiotics could exist in many types of foods, fermented foods, milk and milk products. Also, science, the scientist and the modern companies provide us with different forms of Probiotics for different types of illness. The early human observations, the researchers and the different applications for Probiotics in their different forms highlight how much such wonderful microbes could do to promote our health, protect us and ensure treatment or management of diseases. Perhaps the most critical point of Probiotics, is that they come in natural forms and perform natural safe activities. This review, gives a compact collection of the different strains of probiotics, types, applications and some of the involved companies in such fields as well as the names of the same types of foods rich in Probiotics. The future will show increasing interest in Probiotics, the promising microbes.

References

Abdin, A.A., Saeid, E.M., 2008. An experimental study on ulcerative colitis as a potential target for probiotic therapy by *Lactobacillus acidophilus* with or without "olsalazine". J. Crohns. Colitis. 2, 296–303.

Adam, B., Liebregts, T., Holtmann, G., 2006. Maintaining remission of ulcerative colitis with the probiotic *Escherichia coli* Nissle 1917 is as effective as with standard mesalazine. Z. Gastroenterol. 44, 267–269.

Aiba, Y., Suzuki, N., Kabir, A.M., Takagi, A., Koga, Y., 1998. Lactic acid-mediated suppression of *Helicobacter pylori* by the oral administration of *Lactobacillus salivarius* as a Probiotic in a gnotobiotic murine model. Am. J. Gastroenterol. 93, 2097–2101.

Amara, A., 2012. In: Amara, A. (Ed.), Toward Healthy Genes. Schüling Verlage, Germany.

Amara, A.A., 2013. The inevitability of balanced lives: genes–foods – action-interactions. IIOBJ 4 (2), 1–27.

Anukam, K.C., Hayes, K., Summers, K., Reid, G., 2009. Probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 may help downregulate TNF-Alpha, IL-6, IL-8, IL-10 and IL-12 (p70) in the neurogenic bladder of spinal cord injured patient with urinary tract infections: a two-case study. Adv. Urol., 680363.

Bandyopadhyay, P., Das Mohapatra, P.K., 2009. Effect of a Probiotic bacterium *Bacillus circulans* PB7 in the formulated diets: on growth, nutritional quality and immunity of Catla catla (Ham.). Fish Physiol. Biochem. 35, 467–478.

Bazzoli, F., Zagari, R.M., Fossi, S., 1992. *In vivo Helicobacter pyloriclearance* failure with *Lactobacillus acidophilus*. Gastroenterology 102, A38.

Benchimol, E.I., Mack, D.R., 2004. Probiotics in relapsing and chronic diarrhea. J. Pediatr. Hematol. Oncol. 26, 515–517.

Bennett, R.G., Gorbach, S.L., Goldin, B.R., Chang, T., Laughon, B.E., Greenough, W.B., Bartlett, J.G., 1996. Treatment of relapsing *Clostridium difficile* diarrhea with *Lactobacillus GG*. Nutr. Today 31, 35S–39S.

Botes, M., Loos, B., van Reenen, C.A., Dicks, L.M., 2008. Adhesion of the probiotic strains *Enterococcus mundtii* ST4SA and *Lactobacillus plantarum* 423 to Caco-2 cells under conditions simulating the intestinal tract, and in the presence of antibiotics and anti-inflammatory medicaments. Arch. Microbiol. 190, 573–584.

Boudeau, J., Glasser, A.L., Julien, S., Colombel, J.F., Darfeuille-Michaud, A., 2003. Inhibitory effect of probiotic *Escherichia coli* strain Nissle 1917 on adhesion to and invasion of intestinal epithelial cells by adherent-invasive *E. coli* strains isolated from patients with Crohn's disease. Aliment. Pharmacol. Ther. 18, 45–56.

Bourdichon, F., Casaregola, S., Farrokh, C., Frisvad, J.C., Gerds, M.L., Hammesf, W.P., Harnett, J., Huys, G., Laulund, S., Ouwehand, A., Powell, I.B., Prajapati, J.B., Seto, Y., Schure, E.T., Van Boven, A., Vankerckhoven, V., Zgoda, A., Tuijtelaars, S., Hansen, E.B., 2012. Food fermentations: microorganisms with technological beneficial use. Int. J. Food Microbiol. 154, 87–97.

Brenner, D.M., Chey, W.D., 2009. *Bifidobacterium infantis* 35624: a novel probiotic for the treatment of irritable bowel syndrome. Rev. Gastroenterol. Disord. 9, 7–15.

Cammarota, M., De Rosa, M., Stellavato, A., Lamberti, M., Marzaioli, I., Giuliano, M., 2009. *In vitro* evaluation of *Lactobacillus plantarum* DSMZ 12028 as a probiotic: emphasis on innate immunity. Int. J. Food Microbiol. 135, 90–98.

del Miraglia, G.M., De Luca, M.G., 2004. The role of Probiotics in the clinical management of food allergy and atopic dermatitis. J. Clin. Gastroenterol. 38, S84–S85.

DeSimone, C., 1986. The adjuvant effect of yogurt on gamma interferon by Con-A stimulated human lymphocytes. Nutr. Rep. Int. 33, 419–433.

Enck, P., Zimmermann, K., Menke, G., Klosterhalfen, S., 2009. Randomized controlled treatment trial of irritable bowel syndrome with a probiotic *E. coli* preparation (DSM17252) compared to placebo. Z. Gastroenterol. 47, 209–214.

Fernandes, C.F., Shahani, K.M., Amer, M.A., 1987. Therapeutic role of dietary lactobacilli and lactobacillic fermented dairy products. FEMS Microbiol. Rev. 46, 343–356.

Filippo, C., Filippo, C., Di Caro, S., Santarelli, L., Armuzzi, A., Gasbarrini, G., Gasbarrini, A., 2001. *Helicobacter pylori treatment*: a role for Probiotics. Dig. Dis. 19, 144–147.

Fioramonti, J., Theodorou, V., Bueno, L., 2003. Probiotics: what are they? What are their effects on gut physiology? Best Pract. Res. Clin. Gastroenterol. 17, 711–724.

Food and Agriculture Organization/World Health Organization (FAO/WHO), 2001. Health and nutritional properties of Probiotics in food including powder milk with live lactic acid bacteria, Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live lactic acid bacteria, Córdoba, Argentina. Available at: http://www.who.int/foodsafety/publications/fs_management/en/probiotics.pdf.

Fukao, M., Tomita, H., Yakabe, T., Nomura, T., Ike, Y., Yajima, N., 2009. Assessment of antibiotic resistance in probiotic strain *Lactobacillus brevis* KB290. J. Food Prot. 72, 1923–1929.

Gest, H., 2004. The discovery of microorganisms by Robert Hooke and Antoni van Leeuwenhoek, Fellows of The Royal Society. Notes Records R. Soc. Lond. 58, 187–201.

Giralt, J., Regadera, J.P., Verges, R., Romero, J., de la Fuente, I., Biete, A., Villoria, J., Cobo, J.M., Guarner, F., 2008. Effects of probiotic *Lactobacillus casei* DN-114 001 in prevention of radiation-induced diarrhea: results from multicenter, randomized, placebo-controlled nutritional trial. Int. J. Radiat. Oncol. Biol. Phys. 71, 1213–1219.

Gismondo, M.R., Drago, L., Lombardi, A., 1999. Review of Probiotics available to modify gastrointestinal flora. Int. J. Antimicrob. Agents 12, 287–292.

Hawrelak, J., 2003. Probiotics: choosing the right one for your needs. J. Aust. Traditional-Med. Soc. 9 (2), 67–75.

Hilton, E., Kolakawaki, P., Singer, C., Smith, M., 1977. Efficacy of *Lactobacillus GG* as a diarrheal preventive in travelers. J. Travel Med. 4, 41–43.

Hlivak, P., Odraska, J., Ferencik, M., Ebringer, L., Jahnova, E., Mikes, Z., 2005. One-year application of probiotic strain *Enterococcus faecium* M-74 decreases serum cholesterol levels. Bratisl. Lek. Listy 106, 67–72.

Hosono, A., 1992. Fermented milk in the orient. In: Naga sawa, Y., Hosono, A. (Eds.), Functions of Fermented Milk: Challenges for the Health Sciences. Elsevier Applied Science, London, UK, pp. 61–78.

Huurre, A., Laitinen, K., Rautava, S., Korkeamaki, M., Isolauri, E., 2008. Impact of maternal atopy and probiotic supplementation during pregnancy on infant sensitization: a double-blind placebo-controlled study. Clin. Exp. Allergy 38, 1342–1348.

Iarovenko, I.I., Golofeevskii, V., Sitkin, S.I., 2007. The new possibilities for improving peptic ulcer therapy with the use of probiotic drugs. Voen. Med. Zh. 328, 17–22.

Imaoka, A., Shima, T., Kato, K., Mizuno, S., Uehara, T., Matsumoto, S., Setoyama, H., Hara, T., Umesaki, Y., 2008. Anti-inflammatory activity of probiotic Bifidobacterium: enhancement of IL-10 production in peripheral blood mononuclear cells from ulcerative colitis patients and inhibition of IL-8 secretion in HT-29 cells. World J. Gastroenterol. 14, 2511–2516.

Isolauri, E., 2004. Dietary modification of atopic disease: Use of Probiotics in the prevention of atopic dermatitis. Curr. Allergy Asthma Rep. 4, 270–275.

Kailasapathy, K., Chin, J., 2000. Survival and therapeutic potential of Probiotic organisms with reference to *Lactobacillus acidophilus* and *Bifidobacterium spp*. Immunol. Cell Biol. 78, 80–88.

Kennedy, R.J., Hoper, M., Deodhar, K., Kirk, S.J., Gardiner, K.R., 2000. Probiotic therapy fails to improve gut permeability in a hapten model of colitis. Scand. J. Gastroenterol. 35, 1266–1271.

Kiatpapan, P., Yamashita, M., Kawaraichi, N., Yasuda, T., Murooka, Y., 2001. Heterologous expression of a gene encoding cholesterol oxidase in probiotic strains of *Lactobacillus plantarum* and *Propionibacterium freudenreichii* under the control of native promoters. J. Biosci. Bioeng. 92, 459–465.

Levy, J., 2000. The effects of antibiotic use on gastrointestinal function. Am. J. Gastroenterol. 95, S8–S10.

Lilly, D.M., Stillwell, R.H., 1965. Probiotics: Growth-promoting factors produced by microorganisms. Science 147, 747–748.

Lodinova-Zadnikova, R., Cukrowska, B., Tlaskalova-Hogenova, H., 2003. Oral administration of Probiotic *Escherichia coli* after birth reduces frequency of allergies and repeated infections later in life (after 10 and 20 years). Int. Arch. Allergy Immunol. 131, 209–211.

MacFarlane, G.T., Cummings, J.H., 2002. Probiotics, infection and immunity. Curr. Opin. Infect. Dis. 15, 501–506.

Marteau, P.R., de Vrese, M., Cellier, C.J., Schrezenmeir, J., 2001. Protection from gastrointestinal diseases with the use of Probiotics. Am. J. Clin. Nutr. (Suppl.) 73, 430–436.

Martinez, R.C., Franceschini, S.A., Patta, M.C., Quintana, S.M., Candido, R.C., Ferreira, J.C., De Martinis, E.C., Reid, G., 2009. Improved treatment of vulvovaginal candidiasis with fluconazole plus probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14. Lett. Appl. Microbiol. 48, 269–274.

Mego, M., Majek, J., Koncekova, R., Ebringer, L., Ciernikova, S., Rauko, P., Kovac, M., Trupl, J., Slezak, P., Zajac, V., 2005. Intramucosal bacteria in colon cancer and their elimination by probiotic strain *Enterococcus faecium* M-74 with organic selenium. Folia Microbiol. (Praha) 50, 443–447.

Metchnikoff, I.I., 2004. The Prolongation of Life: Optimistic Studies. Springer Publishing Company, New York, NY, USA.

Metchnikoff, I.I., Mitchell, P.C., 1910. Nature of Man or Studies in Optimistic Philosophy. Kessinger Publishing, Whitefish, MT, USA.

Michail, S., Abernathy, F., 2002. *Lactobacillus plantarum* reduces the in vitrosecretory response of intestinal epithelial cells to entero-patho-genic *Escherichia coli* infection. J. Pediatr. Gastroenterol. Nutr. 35 (3), 350–355.

Nguyen, T.D., Kang, J.H., Lee, M.S., 2007. Characterization of *Lactobacillus plantarum* PH04, a potential probiotic bacterium with cholesterol-lowering effects. Int. J. Food Microbiol. 113, 358–361.

Niers, L., Martin, R., Rijkers, G., Sengers, F., Timmerman, H., van Uden, N., Smidt, H., Kimpen, J., Hoekstra, M., 2009. The effects of selected Probiotic strains on the development of eczema (the P and A study). Allergy 64, 1349–1358.

O'Sullivan, M.G., Thornton, G., O'Sullivan, G.C., Collins, J.K., 1992. Probiotic bacteria: myth or reality. Trends Food Sci. Technol. 3, 309–314.

Parker, R.B., 1974. Probiotics, the other half of the antibiotic story. Anim. Nutr. Health 29, 4–8.

Reid, G., Sanders, M.E., Gaskins, H.R., Gibson, G.R., Mercenier, A., Rastall, R., Roberfroid, M., Rowland, I., Cherbut, C., Klaenhammer, T.R., 2003. New scientific paradigms for Probiotics and prebiotics. J. Clin. Gastroenterol. 37, 105–118.

Saavedra, J.M., Bauman, N.A., Oung, I., Perman, J.A., Yolken, R.H., 1994. Feeding of *Bifidobacterium bifidum* and *Streptococcus thermophilusto* infants in hospital for prevention of diarrhea and shedding of rotavirus. Lancet 344, 1046–1049.

Salminen, S., von Wright, A., Morelli, L., Marteau, P., Brassart, D., de Vos, W.M., Fondén, R., Saxelin, M., Collins, K., Mogensen, G., Birkeland, S.E., Mattila-Sandholm, T., 1998. Demonstration of safety of Probiotics – a review. Int. J. Food Micro biol. 44, 93–106.

Silva, M., Jacobs, N.V., Deneke, C., Gorbach, S.L., 1987. Antimicrobial substance from a human *Lactobacillus* strain. Antimicrob. Agents Chemother. 31, 1231–1233.

Soh, S.E., Aw, M., Gerez, I., Chong, Y.S., Rauff, M., Ng, Y.P., Wong, H.B., Pai, N., Lee, B.W., Shek, L.P., 2009. Probiotic supplementation in the first 6 months of life in at risk Asian infants-effects on eczema and atopic sensitization at the age of 1 year. Clin. Exp. Allergy 39, 571–578.

Strowski, M.Z., Wiedenmann, B., 2009. Probiotic carbohydrates reduce intestinal permeability and inflammation in metabolic diseases. Gut 58, 1044–1045.

Thirabunyanon, M., Boonprasom, P., Niamsup, P., 2009. Probiotic potential of lactic acid bacteria isolated from fermented dairy milks on antiproliferation of colon cancer cells. Biotechnol. Lett. 31, 571–576.

Tomas, M.S., Claudia Oter, M., Ocana, V., Elena Nader-Macias, M., 2004. Production of antimicrobial substances by lactic acid bacteria I: determination of hydrogen peroxide. Methods Mol. Biol. 268, 337–346.

Ukena, S.N., Westendorf, A.M., Hansen, W., Rohde, M., Geffers, R., Coldewey, S., Suerbaum, S., Buer, J., Gunzer, F., 2005. The host response to the probiotic *Escherichia coli* strain Nissle 1917: specific up-regulation of the proinflammatory chemokine MCP-1. BMC Med. Genet. 6, 43.

van der Aa, L.B., Sprikkelman, A.B., van Aalderen, W.M., 2008. Impact of maternal atopy and probiotic supplementation during pregnancy on infant sensitization. Clin. Exp. Allergy 38, 1698, author reply 1698-9.

Vanderhoof, J.A., 2000. Probiotics and intestinal inflammatory disorders in infants and children. J. Pediatr. Gastroenterol. Nutr. 30, S34–S38.

Viljanen, M., Kuitunen, M., Haahtela, T., Juntunen-Backman, K., Korpela, R., Savilahti, E., 2005a. Probiotic effects on faecal inflammatory markers and on faecal IgA in food allergic atopic eczema/dermatitis syndrome infants. Pediatr. Allergy Immunol. 16, 65–71.

Viljanen, M., Pohjavuori, E., Haahtela, T., Korpela, R., Kuitunen, M., Sarnesto, A., Vaarala, O., Savilahti, E., 2005b. Induction of inflammation as a possible mechanism of Probiotic effect in atopic eczema-dermatitis syndrome. J. Allergy Clin. Immunol. 115, 1254–1259.

White, J.S., Hoper, M., Parks, R.W., Clements, W.D., Diamond, T., Bengmark, S., 2006. The probiotic bacterium *Lactobacillus plantarum* species 299 reduces intestinal permeability in experimental biliary obstruction. Lett. Appl. Microbiol. 42, 19–23.

Whorwell, P.J., Altringer, L., Morel, J., Bond, Y., Charbonneau, D., O'Mahony, L., Kiely, B., Shanahan, F., Quigley, E.M., 2006. Efficacy of an encapsulated probiotic *Bifidobacterium infantis* 35624 in women with irritable bowel syndrome. Am. J. Gastroenterol. 101, 1581–1590.

Yamada, T., Nagata, S., Kondo, S., Bian, L., Wang, C., Asahara, T., Ohta, T., Nomoto, K., Yamashiro, Y., 2009. Effect of continuous probiotic fermented milk intake containing *Lactobacillus casei* strain Shirota on fever in mass infectious gastroenteritis rest home outbreak. Kansenshogaku Zasshi 83, 31–35.

Zhou, J.S., Pillidge, C.J., Gopal, P.K., Gill, H.S., 2005. Antibiotic susceptibility profiles of new probiotic *Lactobacillus* and *Bifidobacterium* strains. Int. J. Food Microbiol. 98, 211–217.