

Claimed Health Effect of Probiotic Feeding

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Abstract

Gut microflora consists of a complex mixture of different microorganism species which live in the digestive tract. The gut microflora is estimated to have around 100 trillion species and some have a harmful effect to the host. Probiotic feeding were advised due to the healthy effect and they can positively influence the intestinal microflora and prevent diseases from occurring in the host. This review includes lactose maldigestion, cancer, constipation, allergic disorders, helicobacter pylori infection, mental disorders, obesity and inflammatory bowel diseases.

Keywords: Probiotic, Health, Gut

1. Introduction

Gut microflora consists of a complex mixture of different microorganism species which live in the digestive tract. The gut microflora is estimated to have around 100 trillion species. Some of them have a healthy effect when some have a harmful effect to the host, however, it is interesting that some species such as streptococcus, enterococcus show not only harmful but healthy effect in the intestinal. Harmful species can be able to cause such diseases such as cancer, inflammatory bowel disease in the host while the healthy species prevent the host from these illnesses or even treat the host. The healthy species can even treat the host by using many metabolic activities such as training the immune system, preventing growth of harmful and pathogenic bacteria, production of short-chain fatty acids and so on. Therefore, the intestinal microflora is deemed as `forgotten organ` in human body (Miller et. al., 2009). Using healthy species to get rid of such diseases is a brilliant idea, human intestinal microflora, however, is not constant and some factors such as host age or environment may lead to an alteration in composition of intestinal microflora. Manipulation of intestinal microflora, hence, attracted researches` interest in this area. Probiotic feeding were advised due to the healthy effect, they can positively influence the intestinal microflora. Even if there is still a lack of researches and supportive ideas in this area, it might be possible in the future that people can be free from many diseases by diet (Miller et. al., 2009). In the current point, it was seen from the researches that probiotic feeding prevent people from many diseases or even treat the diseases of people (Tannock, 2002).

World Health Organization (WHO) defined probiotics as `living micro-organisms which upon ingestion in certain numbers exert health benefits beyond inherent general nutrition` in 2001. Recommended ingestion dose for health effects of probiotics is 10^6 colony forming unit/per day (WHO, 2001). Probiotic health effects, however, are strain, dose, and disease and host dependant. Hence, the health benefits of each specific strain of probiotics must be scientifically proven by clinical trials in human. So far, probiotics mostly used in probiotic feeding trials in human are the strains of *bifidobacterium* or *lactobacillus*. However, there are some other probiotics` strains used in human trials such as streptococcus and enterococcus. Main properties expected available in a possible probiotic used for healthy effects to the host are resistance to pancreatic enzymes, acid or bile; good adhesion to the intestinal mucosa to show probiotic healthy effects by colonizing; and safe (non-toxic or no side-effect to the host) (Lee & Salminen, 2009).

2. Lactose Maldigestion

Lactose maldigestion occurs in some people after ingestion of dairy products and the reason for lactose maldigestion is inadequate level of lactase (also known as β-galactosidase) in the gut. Lactase is an enzyme that breaks up lactose into glucose and galactose (Boushey and Coulston, 2008). Lidbeck et al. (1987) found that regular probiotic feeding, *Lactobacillus acidophilus*, can modulate the gut microflora and gut function within 7 days of the start of administration at the dose of 5 X 10^8-2 X 10^9 CFU/milliliter in 250 milliliter fermented milk product, and Vrese et al. (2001) have found that probiotic bacteria in dairy products can prevent lactose maldigestion, because, they have lactose digestion enzyme (β- galactosidase). Hence, the hypothesis is that when probiotics get the chance of entering the gut via fermented milk products, they can modulate gut flora and function by transferring their health enzyme into the gut microflora. Moreover, Antoine et. al. (2010) have found that fermented milk products can improve lactose digestion due to the effect of delaying transit time in the gut. The delayed time causes slow passage of β- galactosidase available in dairy products throughout the small intestine, then, the lactase have more time to hydrolyse lactose, which improves lactose maldigestion in the gut. Yet, to date, how fermented milk products delay transit time in gut is still unclear. It is possible that the viscosity or solid composition of fermented milk products, or the level of β- galactosidase may be able to alter transit time in the gut, because, Martini et. al. (1987) found that the viscosity of fermented milk products plays a role in lactose maldigestion, so, people with lactose maldigestion digest lactose more effectively in yogurt than in other dairy products. In addition, Evans et. al. (1988) have found that pH in small intestine is 6,4 and Gary et. al. (1969) have shown that the optimum activity of lactase is at 4.5 pH in the gut. Hence, Vrese et al. (2001) suggested a possible mechanism for how fermented milk products prevent lactose maldigestion stating that short- or long- term probiotic feeding with fermented milk products may be able to decrease the pH of gut and reduced pH hydrolyses more lactose by increasing the speed of β- galactosidase activity. However, there is a lack of study in this point and there is a crucial need for a study which investigates the link between gut pH and the speed of β- galactosidase activity in gut.

3. Cancer

Cancer is a disease, which occurs due to uncontrolled cell growth. There are many types of cancer. The current treatment methods of the cancer include surgery, medication, radiation and immunotheraphy. They are not recommended, because, these methods cause an imbalance in gut microflora, which then leads to several disorders. A good treatment for cancer should not have any side-effect (Haskell, 2001). Uccello et. al. (2012) found that colorectal cancer, which is the one of the cancer types, occurs after an imbalance in the intestinal microflora. Hence, it is hypothesised that the possible treatment or prevention method to all types of cancer should aim to positively modulate the intestinal microflora in order to balance the gut microflora. Fermented dairy products on their own were recommended for cancer treatment by Hirayama and Rafter (2000). They found that regular consumption of fermented dairy products, which include probiotics, can prevent or even treat different types of cancer including colorectal cancer. Moreover, Van`t Veer et. al. (1989) found a protective effect of fermented dairy product (consumption of 225 gram fermented milk or 60 gram fermented product on a daily basis) on breast cancer. The protective effect, also called as antitumor effect of probiotic feeding (Uccello et. al., 2012), might be associate with the link between the balance in gut microflora and enzymatic activity, because, Benno et. al. (1991) found that reduced level of *Bifidobacterium* in the intestinal microflora increases the enzymatic activity of β-glucuronidase, azoreductase, urease, nitroreductase and glycocholic acid reductase in gut. These enzymes are dangerous, because, they are able to convert procarcinogens into carcinogens, which leads to colorectal cancer. Therefore, it may be concluded that the possible treatment method of all the cancer should either positively modulate gut microflora, with increasing *Bifidobacterium* level, or, inactivate or reduce the enzymatic activity of β-glucuronidase, azoreductase, urease, nitroreductase and glycocholic acid reductase in gut. However further studies are crucial to clearly identify the minimum dosage of probiotic needed in diet to yield anti-cancer effect in host.

4. Constipation

Constipation describes infrequent bowel movements which are tough to pass. The current clinical treatment methods for constipation include laxatives and physical intervention (Hersen and Sturmey, 2002). It is observed in the study of Shimoyma et. al. In 1984 that constipated subjects have a different faecal microflora, with constipated subjects having lower level of *Bifidobacteria* and *Clostridia* ($p<0,05$), therefore, it can be assumed that an alteration (first) in gut flora composition could lead to constipation. Then, the hypothesis is that beneficial bacteria in gut microflora should be modulated for the treatment and of constipation. The hypothesis for the treatment of constipation was supported by two studies. First, Koebnick et. al. (2003) have found that a 4-week treatment of a probiotic beverage (65 milliliter/day) including *Lactobacillus casei* Shirota (also known as *LcS*) to 70 subjects shows a beneficial effect on the severity of constipation ($p<0,0001$ even after the second week of the treatment). Second, Spanhaak et. al. (1998) have found that fermented milk products containing *LcS* at the dose of 10^9 CFU/gram, which is consumed by 10 subjects three times daily 100 milliliter, increased *Bifidobacterium* (p<0,05). Therefore, fermented dairy products containing probiotics (especially *LcS*) can be recommended for the treatment in at least 65 milliliter/day (Koebnick et. al., 2003) due to probiotic effect of modulating the intestinal microflora. Further studies are needed to investigate the link between probiotic effect on constipation and gut transit time.

5. Allergic Disorders

Allergic disorders including allergic rhinitis, asthma, atopic dermatitis (also known as eczema) are very common in developed countries in various age groups. The reasons for the occurrence of allergic disorders are usually related to environmental factors and alteration of the Th1/Th2 balance in favour to Th2 (Ngoc et. al., 2005). Some claims have been made for the prevention of allergic disorders, the most noticeable one is `Hygiene Hypothesis` by Strachan (1989). The hypothesis states that if people in childhood live in a clear environment, they may get any allergic disorder later ages, because, they cannot naturally develop immune system (especially development of T_H1 response). However, the study of Paunio et. al. (2000) could not support this hypothesis, later, Kalliomaki et. al. (2001) have found that an imbalance in the intestinal microbiota happens prior to the development of allergic disease, therefore, it is assumed that the intestinal microflora have a key role in allergic disorders. My hypothesis is that if an alteration in gut microflora causes allergic disorders, then, the possible treatment or prevention method for allergic diseases should focus on gut microflora. There are two possible reasons stated for the occurrence of allergic diseases led by gut microflora and probiotic feeding is recommended for both. First, allergic disorders are associated with an alteration of the Th1/Th2 cytokine balance to a Th2 response, which causes the activation of release of interleukin-4 (IL-4), IL-5 and IL-13 with IgE production. In this environment, probiotics are able to modulate the receptors and proteoglycan recognition proteins of enterocytes in gut. This modulation leads to the production of Th1 response, then, the Th1/Th2 balance is re-established (Kraehenbuhl et. al., 2007). It is important, because, after the imbalance of the Th1/Th2 cytokine, some interleukin groups are activated and they are thought to be the main responsible for many diseases such as inflammation (Elias et. al., 1999). Regular probiotic feeding, however, can decrease lgE production and some interleukin groups, which leads to the perception that probiotic feeding have a treatment effect on people with allergic disorders, instead of a protection effect (Flinterman et. al., 2007). McCarthy et. al. (2003) analysed the first reason (allergic disorders are associated with an alteration of the Th1/Th2 cytokine balance to a Th2 response) for allergic disorders led by gut microflora and found that probiotic feeding re-balances Th1/Th2 cytokine and controls the activity of interleukin groups production ($p < 0,05$) in 10 rats which consumed fermented milk products containing *Lactobacillus salivarius* 433118 at 10^9 CFU/milliliter and Bifidobacterium *infantis* 35624 at 10^8 CFU/milliliter during 19 weeks. Even though McCarthy et. al. (2003) found a positive effect of probiotic feeding on cytokine balance, further studies are needed with large numbers of human subjects to investigate the effect of probiotic feeding on cytokine balance and the mechanism in human. Second, allergic disorders may be associated with an alteration in gut microflora composition, with higher level of *Clostridium* and lower level of *Bifidobacterium. Clostridium* is a pathogenic micro-organism in gut (but not all) and leads to several diseases such as diarrhea. In addition to increased level of *clostridium*, reduced level of *bifidobacterium* could lead to allergic disorders, because, *bifidobacteria* are considered as beneficial micro-organism in gut due to its beneficial effects such as regulation of intestinal, inhibition of pathogens or positively modulation of local and systemic immune responses. Kalliomaki[1] et. al. (2001) analysed the second reason (Regular probiotic feeding can decrease lgE production and some interleukin groups, which prevent occurrence of allergic diseases) for allergic diseases led by gut microflora and found that the level of *bifidobacterium* of 76 atopic infants subjects show differences with a significant of increased level of *clostridium* ($p < 0.05$) and a significant of reduced level of *bifidobacterium* ($p < 0.5$). The hypothesis here is that probiotic feeding is able to modulate gut microflora with increasing beneficial bacteria level and reducing pathogenic bacteria level. My hypothesis was supported by Kalliomaki[2] et. al. (2001). They analysed the hypothesis and stated that *Lactobacillus rhamnosus (Lactobacillus* GG*)* is effective at protecting the development of atopic disease (the one of allergic disorders) in 132 infant subjects. In addition to probiotic feeding's treatment effect found in the first reason, Kalliomaki[2] et. al. (2001) actually showed that probiotic feeding may also have a protective effect on allergic disorders. The review of Prescott and Bjorkste (2007), however, documented the differences of protective effect of probiotic feeding on allergic diseases, with some of researches finding protective effect of probiotic feeding when others finding no protective effect of probiotic feeding. These differences may be due to probiotic factors including strain, dose, viability; or host factors including genetic or type of the intestinal microflora; or environmental factors utilized in researches.

6. Helicobacter Pylori

Helicobacter pylori (H.pylori) infection occurs in gastrointestinal tract and can lead to several dangerous gastric diseases. The current treatment of the infection is a triple treatment including antibiotics and proton pump inhibitors. However, the current treatment causes side effects such as diarrhea, vomiting, bloating or abnormal pains, or adenocarcinoma of the stomach which occurs due to cagA (cytotoxin-associated gene A, which badly affects host) infectious *H.pylori* strains have (Bell et. al., 1992). Armuzzi et. al. (2001) analysed probiotic feeding (*Lactobacillus rhamnosus* 2 hour after breakfast and dinner with water) at the dose of $6x10^9$ CFU/milligram as adjuvant therapy with antibiotics (rabeprazole 20 milligram before breakfast and dinner; tinidazole 500 milligram half an hour after breakfast and dinner; and tinidazole 500 milligram half an hour after breakfast and dinner). The antibiotic therapy lasted 7 days while the probiotic treatment lasted 14 days in 60 *Helicobacter pylori* positive subjects (mean age 40). They found that probiotic feeding as an adjuvant therapy with antibiotics show a positive effect on *H.pylori* therapy side-effects ($p < 0.05$). The possible reasons for this positive effect of probiotic feeding on *H.pylori* infection treatment's side effects are that probiotics may inhibit the adherence of pathogens in intestinal; or probiotics may be able to produce metabolites or antimicrobial molecules which can compete with the side-effects. However, further studies are needed to clearly investigate the mechanism of the positive effect of probiotic feeding on side-effects of *H.pylori* treatment with antibiotics. There is a hypothesis that if probiotic feeding has a positive effect on current treatment methods` side-effects, it is highly possible that probiotic feeding itself can treat *H.pylori* infection (because, probiotic feeding itself is effective at preventing side-effects of *H.pylori* treatment). Three assumptions were made for my hypothesis. First, Egan et. al. (2007) and Lesbros-Pantoflickova et al. (2007) have shown that some probiotics (*Lactobacillus and Bifidobacterium*) can create antimicrobial substances, then, they can prevent the growth of *H. pylori* in gut microflora, because, the anti-microbial substances can compete with pathogenic bacteries (including *H. pylori*) by binding to the gut wall and *H. pylori* cannot colonise in the stomach. Hence, probiotics can increase the gut barrier against pathogens. Second, Lesbros-Pantoflickova et al. (2007) indicated that probiotic feeding is capable of decreasing pH in the gut, therefore, pathogenic bacteries can be deactivated due to low pH in the host(H.pylori can survive in gastric Ph, but, activation of *H.pylori* is depended upon transformation and recombination DNA repair and low pH may prevent DNA repair (Cotter and Hill, 2003). Third, if the side effects of the current treatment of *H. pylori* infection can be reduced with probiotic feeding, probiotics can positively modulate the intestinal microflora, then, probiotic feeding itself can be used as a treatment method. However, to date, there is no study which clearly shows that probiotic feeding itself can or cannot treat the infection in human subjects, because, probiotic feeding is used in studies as adjuvant therapy for the treatment of side-effects of *H. pylori* infection (Egan et. al., 2007). Therefore, studies are crucial to investigate these assumptions in human subjects even for the prevention of *H. pylori* infection.

7. Mental Disrders

Mental diseases, also known as psychiatric disorder, is the one of the most reported cases in today's developed world, and influences mood (such as anxiety and depression).

According to WHO (2000), one in every three people in the world suffer from the disease. The current treatment methods are based upon supportive therapies including Psychotherapy, Psychiatric Medication, Counselling, or Electro-convulsive therapy (Sartorius, 1993). However, in 2011, Bravo et. al. have found in mice study that probiotic feeding (*Lactobacillus rhamnosus*) can be used as treatment or prevention of such mental diseases by modulating gut microflora, because, they observed that an alteration by probiotic feeding in gut microflora reduces stress-induced corticosterone and, anxiety- and depression-related behaviour with reducing GABAAα2 mRNA expression. Reduction in GABAAα2 expression is the beneficial effect of probiotic, because, GABA (gamma-aminobutyric acid A) is believed to cause essential tremor (ET), which is a neurological disorder (Gerven et. al., 2011). Hence, my hypothesis is that any disease related to brain including mental disorders can be treated or prevented with probiotics in diet. Tillisch et. al. (2013) showed that a fermented milk product with probiotics (*Bifidobacterium lactis, Streptococcus thermophiles, lactobacillus bulgaricus and Lactococcus lactis)* at the dose of 1.25×10^{10} CFU *B.lactis* and 1.2×10^9 CFU *S.thermophilus*, *L.bulgaricus and L.lactis* per cup is able to affect the activities of brain regions (mainly mid-brain) in 12 women subjects ($p < 0.005$). The main reason of the positive effect of probiotic feeding on brain activities is highly possibly because of the probiotics` effects on the host and the ability of probiotics` on modulating the intestinal microflora. From this point, the study looks too interesting, because, it was known to the study that the brain is capable of sending signals to the gut and this is one directional, hence, when people feel stressed, the brain sends signals to gut and the individual have gastrointestinal symptoms due to that. However, Tillisch et. al.`s finding suggests that the gut is also capable of sending signals to the brain as well (probiotic feeding affected activities of brain regions). Hence, probiotic feeding may be able to positively change brain neurochemistry, so, probiotic feeding may be used for the treatment or prevention of mental diseases such as depression or stress (Karl et. al., 2004). More studies are needed to investigate the link between gut microflora and brain activity.

8. Obesity

Obesity is a medical disease and people are considered as obese when their body mass index, also known as BMI, reaches 30 kilogram/m^2. Human diet is considered as the main reason or treatment for obesity in people, since, high energy intake in diet leads to obesity and low energy intake from diet can prevent people from being obese (Rippe and Angelopoulos, 2012). However, the study of Collado et. al. (2010) showed that it may be possible that obesogenic microflora is inheritable, which means that people are born as an obese or a lean individual with regards to their gut microflora composition. 42 women participated the study, the BMI of 16 women of which is greater than or equal to 25 kg/m^2 and the rest 26 women's BMI is lower than 25 kg/m^2, and the total 42 women's infants are control subjects of the study. Collado et. al. (2010) found that lower infant weigh of lower weight mother is associated with higher level of *Bifidobacterium* ($p < 0.05$) in six-month-old-infants and higher infant weigh of higher weight mother is associated with *Bacteroides* ($p < 0.05$) in six-month-old-infants, however, no significant was found for *Bifidobacterium* level of one-month-old-infants. It shows that weight of individuals is associated with gut microflora composition (lower *bifidobacterium* and higher *bacteroides*) and the mothers` gut microflora composition shows its effect in their children weight later ages. Therefore, the hypothesis is that obesity can be prevented in people by manipulating gut microflora or in infants before the born by changing their mother's microflora, so, what is eaten by mothers during pregnancy have important for infant's future weight. Probiotics can be suggested for obesity, because, probiotics have the chance to beneficially alter gut microflora (increased level of b*ifidobacterium* with reduced level of *bacteroides*), this leads to a beneficial gut flora against obesity (Claassen, 2013). A further study investigated differences in gut microflora composition and short-chain-fatty-acid (SCFA) level among the lean and the obese plus the overweight. The study of Schwiertz et. al. (2010) used 98 human subjects (30 of which are lean, 35 of which are overweight and 33 of which are obese). First, Schwiertz et. al. (2010) supported Collado et. al. (2010) and found that the obese have a different intestinal microflora than the lean, with having higher fecal concentration of *Bacteroides* ($p = 0.145$-obese, $p = 0.002$-lean) and *firmicutes* ($p = 0.002$). Probiotic feeding can be used to reduce the level of *bacteroides* and *firmicutes* when increasing *bifidobacterium* in gut microflora. The probiotic beneficial effect on microbial activity may change energy production from diet, so, probiotic feeding can prevent obesity in individuals (Claassen, 2013). Second, SCFA proportion saw difference between the lean and others, with the obese having higher total SCFA level than the lean ($p < 0.05$). The possible reason for that may be due to the fact that the obese have higher level of *firmicutes* and *bacteroidetes*, which both are able to produce SCFA from the dietary compounds that can escape digestion in small intestine. The production of total SCFAs from *firmicutes* and *bacteroidetes* could cause an extra energy intake to the host. Therefore, it is assumed that total SCFAs and microbial activity of *firmicutes* and *bacteroidetes* leads to obesity in people, with high energy intake of human diet. Probiotic feeding, however, is able to change gut functions (microbial and mucosal activities) and composition, which leads to reduced energy intake from escaped compounds or even prevent compounds from escaping digestion with changed mucosal activity (Claassen, 2013). Third, Schwiertz et. al. (2010) found that every individual SCFAs concentration show differences between the lean and the obese. Especially, the proportion of Propionate saw difference among different weigh groups (the obese > the overweight > the lean), which causes the assumption that higher level of propionate leads to obesity and it is supported by the finding that free fatty acid receptor 3, which initiates the production of total SCFAs and especially propionate, deficiency mice show a normal body index in Lin et. al. (2012), however, Lin et. al. (2012) also found that butyrate, propionate and acetate have a protective effect on diet-induced obesity in mice by reducing food intake, which leads to the assumption that there may be additional reasons for obesity when gut microflora have high level of SCFAs, such as low mucosal absorption (then, the bacteria have higher level of compounds to produce energy) or the rate of transit (if it is too fast, the compounds can escape digestion). Probiotic feeding can affect the possible reasons for obesity (higher mucosal absorption and slower transfer in gut with a fermented milk product) (Claassen, 2013). Therefore, further studies are crucial to clearly define whether total SCFAs or any individual of SCFAs concentration would cause obesity in people and Lin`s finding of protective effect of SCFAs should be investigated in human subjects with probiotics.

9. Inflammatory Bowel Disease

Inflammatory bowel disease, IBD, is an idiopathic disease led by an unbalanced immune response to host intestinal microflora. The main types of IBD include ulcerative colitis (UC), Crohn Disease (CD) and pouchitis. The current treatment methods for IBD include targeted biological treatments, use of some drugs involving immunomodulators and 5-Aminosalicylic acid (5-ASA), and the use of Corticosteroids (Stephen and Bloomfeld, 2011). Kruis et. al. (1997) offered a new method for the prevention of IBD (with specific interest in UC). They observed that modulating the intestinal microflora with probiotic feeding in randomized 120 subjects can positively contribute the pathophysiology of UC. Campieri et. al. (2000) studied the efficiency of probiotic feeding in pouchitis to investigate the new method suggested by Kruis et. al. (1997). Probiotic compound contains 4 strains of *Lactobacillus* (*L. casei, L. plantarum, L. acidophilus* and *L. bulgaricus*), 3 strains of *Bifidobacterium* (*B. longum, B. breve, B. infantis*) and 1 starin of *Streptococcus*

(*S.thermophilus*) (the probiotic is known as VSL#3 in market) with placebo group (3 gram of maize starch). 40 subjects in this study were randomized after 1 month of antibiotic treatment (1 gram ciprofloxacin and 2 gram rifaximin daily) and administered VSL#3 (6 gram/day) (20 subjects) or placebo (20 subjects) for 9 months twice a day. Campieri et. al. (2000) found that fecal concentration of *bifidobacterium, lactobacillus* and *S. thermophilus* increased in subjects who administered VSL#3 ($p<0.01$) and oral administration of probiotics was effective at preventing pounchitis in subjects (when no effect was seen in placebo group). It is assumed by me that the beneficial effect of probiotic feeding may be related to modulation of gut microflora (increased level of protective bacteria). However, further studies are needed to clearly define beneficial effect of probiotic feeding in IBD, because, first, a very high dose (300 billion viable bacteria per gram) was used in the study of Campieri et. al. (2000) and probiotic effect is dose-dependent, so, it is possible that VSL#3 effect is due to this high dose and lower dose may also be effective at producing the same probiotic effect. Second, probiotic effect is strain-dependent so different probiotics may affect different mechanism to prevent IBD. Yet, from the study of Campieri et. al. (2000), it is just known that a mixture of probiotics (VSL#3) is effective at IBD by manipulating gut microflora (increased concentration of protective bacteria). In 2010, Hegazy and El-Bedewy showed the possible mechanism of the protective effect of probiotic feeding in IBD subjects. 30 subjects separated into two groups (one of which received sulfasalazine 2400miligram/day when the another received 2400 miligram/day sulfasalazine with probiotic (*Lactobacillus delbruekii* and *Lactobacillus fermentum*) for 8 weeks). They found that probiotic feeding as an adjuvant treatment with antibiotics can treat IBD patients by showing that in the beginning of study, UC subjects had colonic mucosal injury and inflammation with high activity of IL-6 (interleukin-6) and of TNF-α and NF- κB p65 proteins. However, these activities were seen a decrease in probiotic group of the study after an 8 week treatment of probiotic, in colonic MPO (Myeloperoxidase) activity ($p<0.05$). Therefore, beneficial effects of probiotics can be seen in activity of enzymes and proteins to prevent or even treat IBD in patients.

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Table 1. Probiotic Trials and Claimed Health Effects of Probiotics

Area	Probiotic	Study details	Main findings	Reference
Lactose maldigestion	*Lactobacillus acidophilus* NCFB (5 X 10^8 - 2X 109 CFU / millilitre in a dose of 250 millilitre twice for 7 days)	n: 10 healthy volunteers. It was a controlled study. Half of the volunteers consumed probiotic product when other half did not consume to compare their results.	Gut microflora and functions were positively modulated with probiotic feeding.	Lidback et. al. -1987
	Bifidobacterium longum ATCC 15708 B6 (5 x 10^8 CFU of *B. longum*/millilitre in 400 millilitre milk)	N = Fifteen lactose malabsorbers; it was a randomized and double blind trial.	Probiotic feeding induces a higher beta-galactosidase level in gut and increases rate of lactose uptake.	Jiang et. al. -1996
	Lactobacillus acidophilus NCFM (10^{10} CFU / millilitre in 250 millilitre milk for 8 hours)	N: 20 lactose-maldigesting children (9 boys and 11 girls, their ages were between 5 and 16 years) and a positive breath H2 test (BHT) is used	Decreased symptoms in lactose maldigestion in children subjects were observed.	Montes et. al. -1995
	A yoghurt culture containing *Streptococcus thermophilus (1010 CFU / millilitre in 250 millilitre fermented milk for 8 hours) and Lactobacillus lactic (108 CFU /millilitre in 250 millilitre fermented milk for 8 hours)or 250 millilitre of uninoculated milk with 1010 cells of Lactobacillus acidophilus.*	N: 20 lactose-maldigesting children (9 boys and 11 girls, their ages were between 5 and 16 years) were used in this controlled study. (10 subjects consumed *l.acidophilus* milk product when the other 10 digested milk product which contains the yogurt culture) and a positive breath H2 test (BHT) is used.	Decreased symptoms in lactose maldigestion in children who consumed milks inoculated with *L. acidophilus* is observed, with the same effect in children who consumed milk product containing the yoghurt culture.	Montes et. al. -1995

Area	Probiotic	Study details	Main findings	Reference
Cancer	Fermented Milk Products (probiotics not indicated) Intake of product was identified as gram (75-225 gram for fermented products and milk, 20- 60 gram for cheese). Dairy products were consumed for 12 months.	n: 289 women. A randomized, questionnaire with a case-control study was used.	A fermented milk product containing probiotic have a protective effect on breast cancer.	Van`t Veer et. al. (1989)
	Lactobacillus casei Shirota ($1x10^{10}$ CFU /gram in 1 gram *L. casei* preparation three times daily for 195 days to 350 days).	n: 138 patients who are superficial bladder cancer. A double-blind and placebo-controlled trial was used.	Oral administration of *L. casei* preparation reduced recurrence of superficial bladder cancer (p = 0.01), with comparing to placebo group.	Aso et. al. -1995
	Bifidobacterium Longum ($1 x 10^8$ CFU (around 14.0-14.5 gram/rat/day) for 13 weeks).	N = 61 male Fisher 344 weanling rats and a controlled study with lactulose (2.5% - around 15.0 gram/rat/day of the diet) were used.	*Bifidobacterium* consumption had an antitumor effect in gut, (anti-cancer effect) (p < 0.05) with comparing to the lactulose group.	Challa et. al. -1997
	Lactobacillus casei Shirota ($6.5 X 10^9$ CFU in 65 millilitre/day for 4 weeks). For placebo group, they consumed 65 millilitre/day placebo.	N = 70 patients who have symptoms of chronic constipation. It was a randomized, double-blind, placebo-controlled study (35 of the subjects consumed probiotic when other 35 consumed placebo).	Probiotic feeding is beneficial at treatment of chronic constipation (P<0.0001), with comparing to the placebo group.	Koebnick et. al. (2003)

Area	Probiotic	Study details	Main findings	Reference
Allergic disorders	Bifidobacterium Lactis Bb-12 (1 x 10^9 CFU /gram) and Lactobacillus acidophilus ATCC 53103 (3 x 10^8 CFU /gram). Treatment duration and dosage were not identified.	A total of 27 infants with mean age of 4.6 months. It was a randomized, double blind, placebo-controlled study.	These probiotics can modulate gut microflora, which positively affects allergic disorders.	Isolauri et. al. -2000
	Lactobacillus fermentum VRI-033 PCC (1×10^9 CFU /gram twice daily for 8 weeks) 16 weeks is the duration of study. Administration of probiotic was done with 5–10 millilitre of water.	Forth two children aged 6-18 months with moderate or severe AD. (Half of them consumed probiotic when the other half used placebo). It was a randomised, placebo-controlled, cross-over trial.	Probiotic feeding is effective at reducing the severity of atopic dermatitis ($p < 0.05$) with comparing to the placebo group.	Prescott et. al. -2005
	Lactobacillus rhamnosus GG (6 x 10^9 CFU /gram for 14 days) it was administered as a mixture preparation with water. (Dosage is not identical, it may be possible a capsule for probiotic was used)	N = Sixty healthy asymptomatic subjects. It was a randomized and placebo controlled study.	*Lactobacillus rhamnosus* GG supplementation showed a positive impact on *H. pylori* therapy-related side-effects and on overall treatment tolerability.	Armuzzi et. al. -2001

Area	**Probiotic**	**Study details**	**Main findings**	**Reference**
Constipation	*Lactobacillus casei rhamnosus* (8×10^{8} CFU /day orally twice daily for 4 weeks). (dosage for probiotic was not identified)	N = 45 children under 10 years old with chronic constipation. (18 of the subjects consumed probiotic, another 18 used MgO and the rest 9 used placebo). It was a randomized double-blind, placebo-controlled study.	*Lactobacillus casei rhamnosus* is effective at treating children with chronic constipation ($p < 0.05$) with comparing to the placebo group.	Bu et. al. -2007
	A probiotic mixture (*Bifidobacterium Bifidum, Bifidobacterium infantis, Bifidobacterium longum, Lactobacillus casei, Lactobacillus plantarum, Lactobacillus rhamnosus*) (a daily mix of 4 $\times 10^{9}$ CFU for 4 weeks). (dosage for probiotic was not identified)	N = 20 Children aged 4–16 years with constipation	The probiotic mixture used is effective at treating constipation	Bekkali et. al. -2007
	A probiotic mixture (*Bifidobacterium Lactis DN-173 010, Lactobacillus casei Shirota, Escherichia coli Nissle 1917, Lactobacillus casei rhamnosus, Lactobacillus casei Lcr35*) (Ranging from 8×10^{8} to 25×10^{10} CFU /day for ranging from four and eight to 12 weeks).	N = 377 subjects with constipation (266 adults and 111 children); Randomised, controlled trials (194 in the experimental group and 183 in the control group)	*L. casei* rhamnosus showed no beneficial effect on constipation in children when *L. casei Lcr35 was beneficial. And other effect on constipation in adults*	*Anna and Hania (2010)*
	Lactobacillus salivarius 433118 (10^{9} CFU /millilitre for 19 weeks) and *Bifidobacterium infantis* 35624 (10^{8} CFU /millilitre for 19 weeks) in 4–7 ml of milk per day.	N = 30 IL-10 KO mice whose ages were 7–9 weeks and a double blind, placebo-controlled trial were used.	Both *Lactobacillus salivarius* 433118 and *Bifidobacterium infantis* 35624 are effective at treating allergic disorder ($p<0.05$), with comparing to the placebo group.	McCarthy et. al. (2003)

Area	Probiotic	Study details	Main findings	Reference
Helicobacter pylori Infection	*Lactobacillus gasseri* OLL 2716 (1–1.4 × 10^7 CFU /gram in 90 gram of yogurt twice daily for 8 weeks).	N = 31 subjects; Randomized controlled study.	The probiotic used is effective at *H.pylori* infection.	Sakamoto et. al. (2001)
	Lactobacillus acidophilus LB (5 x10^9 CFU /per capsule of 80 milligram for 7 days)	N = 120 *H. pylori* -positive patients; it was a randomized controlled study.	*L. acidophilus* is effective at *H.pylori* infection nad may have a therapy effect on the disease.	Canducci et. al. -2000
	Bacillus clausii (2 x 10^9 CFU /gram for 14 days) is administered in probiotic preparation (Dosage was not identified)	N = 120 *H. pylori* -positive patients; Randomized, double-blind, placebo-controlled trial.	Probiotic used was effective at reducing the side-effect of antibiotic treatment for *H.Pylori* infection.	Nista et. al. -2004
	Lactobacillus johnsonii Lj1 (High dose (not identified) twice daily in 250 millilitre fermented milk preparation for 16 weeks)	N = 50 *H.pylori* positive healthy volunteers. It was a double-blind, placebo-controlled study.	Fermented milk products containing the probiotic used is positively effective at *H.pylori* infection ($p < 0.05$) with comparing to placebo group.	Pantoflickova et. al. (2003)
	Bifidobacterium lactis I-2494 (1.25×10^{10} CFU /gram), *Streptococcus thermophilus* I-1630 (1.2 × 10^9 CFU /gram), *Lactobacillus*	N = 36 Healthy women with no gastrointestinal or psychiatric symptoms (12 subjects consumed a fermented milk	Probiotics consumed by healthy women affected activity of brain regions that control central processing of emotion and sensation.	Tillisch et. al. -2013

Area	Probiotic	Study details	Main findings	Reference
Mental Disorders	*Lactobacillus Acidophilus* Rosell-52 and *Bifidobacterium longum* Rosell-175 (3 x 10^9 CFU per sachet stick (how many gram of a sachet was not identified) for 3 weeks)	N = adults aged 18-60 years with stress symptoms. It was a randomized, double blind placebo-controlled trial	Probiotic feeding is effective at reducing 2 stress-induced gastrointestinal symptoms (vomiting and abdominal pain). However, probiotics could not modify other physical symptoms.	Diop et. al. -2008
	Lactobacillus salivarius Ls-33 (10^{10} CFU daily for 12 weeks), Probiotic was ingested in a capsule (how many gram of a capsule was not identified).	N = 50 obese adolescents. It was a double blind placebo-controlled trial.	It was seen that probiotic feeding of Ls-33 has no beneficial effect on obesity in adolescents. It may be due to probiotic strain-specific effect.	Gobel et. al. -2012

Area	Probiotic	Study details	Main findings	Reference
Obesity	*Lactobacillus rhamnosus* ATCC 53103 (1 × 10^{10} CFU of *Lactobacillus rhamnosus* ATCC 53103 for 10 years.)	N = 159 women and controlled group of 113 children (measurements to find whether probiotic feeding is effective at obesity in children were taken at the aged of 3 and 6 months and 1, 2, 4, 7 and 10 years of the child).It was a randomized double blind and placebo-controlled study.	Early gut microbiota modulation with probiotic feeding was observed to alter the growth pattern of the child by reducing weight gain throughout the first years of life. The excessive weight gain was found to have two parts; the initial phase initiates during fetal period and continues until 24–48 months of age and the second phase startes after the age of 24–48 months. Probiotic intervention was observed to have an effect on the initial phase (especially among children who later became overweight).	Luoto et. al. -2010
	Lactobacillus Rhamnosus ATCC 53103 and *Bifidobacterium lactis* BB-12 (A capsule containing > 1x10^9 CFU of each probiotic/ per capsule once daily for 28 weeks)	N = 540 pregnant women with a BMI > 25.0 kg/m ^{2}. It was a randomized, double blind, placebo-controlled study.	Probiotics used together are effective at preventing overweight and obesity in pregnant women subjects.	Nitert et. al. -2013
	Lactobacillus gasseri SBT2055 (200 gram/day of fermented milk for 12 weeks)	N = 87 subjects with a BMI of 24.2-30.7 kg/m^2 and abdominal visceral fat area 81.2-178.5 cm^2 (43 subjects consumed the fermented milk product including probiotic, the rest 44 consumed non-fermented milk product).	The probiotic LG2055 showed a lowering effects on abdominal adiposity and obesity (P<0.001) with comparing to the results of placebo group.	Tsuchida et. al. -2010
	Lactobacillus reuteri (50 microliter of 6 × 10^7 CFU /millilitre)	2-16-week old IL-10 gene-deficient 4-8 per group mice were used. It was a placebo-controlled (oral lactulose therapy) trial. Both IL -10 gene–deficient and control animals were killed using sodium pentobarbital (160 milligram/kilogram) at 2, 4, 8, and 16 weeks of age,	IL-10 gene-deficient mice have decreased levels of *Lactobacillus* and an increase in colonic mucosal adherent and translocated bacteria. Normalizing *Lactobacillus* levels reduced colonic mucosal adherent and translocated bacteria and prevented colitis.	Madsen et. al. -1999