

Probiotics in Health and Disease: New Approach to Healthier Living

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Abstract: Recent times have witness antibiotic resistance and increase in diseases, hence the trend these days is that people are turning towards natural products. Hence probiotics have come under the scanner for its uses as nutritional supplements. Their benefits to human and animal health have been proven in hundreds of Scientific Articles. *Lactobacillus* and *Bifidobacterium* are the main probiotic groups; However, there are reports on other probiotic potential of *Pediococcus*, *Bacillus*, *Lactobacillus* and yeasts. Some of the identified probiotics strains exhibit powerful anti-inflammatory, anti-allergic and other important properties. In this article, we have reviewed several articles on the use of probiotics in improving human health and describe the origin of probiotics, their potential uses in disease improvement or disease reduction. Our earlier work on Cholesterol lowering probiotics and other works has prompted us to take up this review where we have tried to represent elaborately the various aspects of the role of some popular strains of useful bacteria, which are being termed as probiotics.

Keywords: Probiotics, *Lactobacillus*, *Bifidobacterium*, *L. casei*, *Pediococcus*, *L. sirota*, Benefits, gut microflora, Yoghurt, Yakult, uses of probiotics

1. Introduction

Probiotics, as defined by the Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) in 2006, comprise live microorganisms which, when administered in adequate amounts, confer a health benefit on the host⁽¹⁾. In human medicine, much research has been performed, and the list of documented health benefits is growing, ranging from amelioration of irritable bowel symptoms in children to improvement of oral health or prevention of recurrent urinary tract infections in adults⁽²⁾. Probiotics are defined as “living microorganisms, which upon ingestion in certain numbers exert health benefits on the host beyond inherent basic nutrition”⁽³⁾. The concept of Probiotics arose at the turn of the 20th century from a hypothesis first proposed by Noble Prize winning Russian scientist Elie Metchnikoff, who suggest that the long, healthy life of Bulgarian peasants resulted from their consumption of fermented milk products⁽⁴⁾. He believed that when consumed, the fermenting *Bacillus* (*Lactobacillus*) positively influenced the microflora of the colon, decreasing toxic microbial activities. The historical association of Probiotics with fermented dairy products, still true today, stems from these early observations. Investigations in the Probiotics field during the past several decades, however, have expanded beyond bacteria isolated from fermented dairy products to those of intestinal origin⁽⁵⁾.

Gut Microflora: At birth, the gastrointestinal tract is sterile and incapable of digesting food. Within hours, bacteria ingested rapidly colonizes the gut. The gastrointestinal tract soon contains about ten times as many bacteria as there are cells in the body. Hundreds of species are present, many of which are uncultivable and remain unidentified. It is these bacteria that are responsible for priming the gastrointestinal immune system⁽¹⁴⁾. This gut flora includes 100 trillion bacteria, some three pounds, which are intimately linked to the body's natural defense system⁽¹⁵⁾. Most Probiotics fall into the group of organisms known as lactic acid-producing

bacteria and are normally consumed in the form of yogurt, fermented milks or other fermented foods⁽¹⁶⁾.

There is always some debate whether or not yogurt starter bacteria should be considered as Probiotics. The starter cultures *Lactobacillus bulgaricus* and *Streptococcus thermophilus* are used for fermenting milk and turn it into yogurt. These cultures are not resistant to the conditions in the stomach and the small intestinal and generally do not reach the GI tract in high numbers. Therefore, they cannot mediate the Probiotics effects. The starter bacteria have been shown to improve lactose digestion in people lacking lactase and demonstrated the immunity enhancing effects. For these reasons, they are often considered 'Probiotics'. Most gastrointestinal organisms are relatively benign. Some are pathogenic however many are actually beneficial⁽¹⁷⁾.

2. Advantages of Probiotics

Various studies have indicated that Probiotics may alleviate lactose intolerance; have a positive influence on the intestinal flora of the host; stimulate/modulate mucosal immunity⁽⁶⁾; reduce inflammatory or allergic reactions⁽⁷⁾; reduce blood cholesterol⁽⁸⁾; possess anti-colon cancer effects⁽⁹⁾; reduce the clinical manifestations of atopic dermatitis⁽¹⁰⁾, Crohn's disease, diarrhea, constipation, candidiasis, and urinary tract infections⁽¹¹⁾; and competitively exclude pathogens Considering this impressive list of potential health-promoting benefits, it is not surprising that there continues to be considerable interest in the use of Probiotics as biotherapeutic agents⁽¹²⁾. Furthermore, given a heightened awareness among consumers of the link between diet and health and the fact that Probiotics- containing foods are generally perceived as “safe” and “natural,” the global market for such foods is on the increase, particularly dairy-based products marketed for the prophylaxis or alleviation of gastrointestinal disorders⁽¹³⁾.

Commercial Probiotics Strains

Probiotics	Commercial Product
<i>L.acidophilus</i>	LA-5;NCDO 1748
<i>Saccharomyces boulardii</i>	Florastor,Biocodex (CreswellOR)
<i>L.casei</i>	Shirota
<i>L.johnsonii</i>	LC-1 NESTLE
<i>L.reuteri ATCC 55730</i>	BioGaia
<i>Streptococcus oralis</i>	ProBiora3
<i>L.rhamnosus PBO1</i>	Bifodan (Denmark)

Approximately 90% of the total cells in the body are present as bacteria in the colon reaching 10^{12} for every gram of large

intestine. Under natural conditions, a protective gut microflora develops are there is no need for a bacterial supplement. The changing food habits, life style force us to take processed and sterile food which affects our access to colonization by certain type of bacteria⁽¹⁸⁾. Moreover, we also consume antibacterial substances ranging from antibiotics to vinegar.

Probiotics also play major role in reducing serum cholesterol levels, Probiotics play a major role in Lactose intolerance, Diarrhoea, Anti carcinogenic properties, Enhances Immune system, Atopic Dermatitis, Urinary tract infections⁽¹⁹⁾

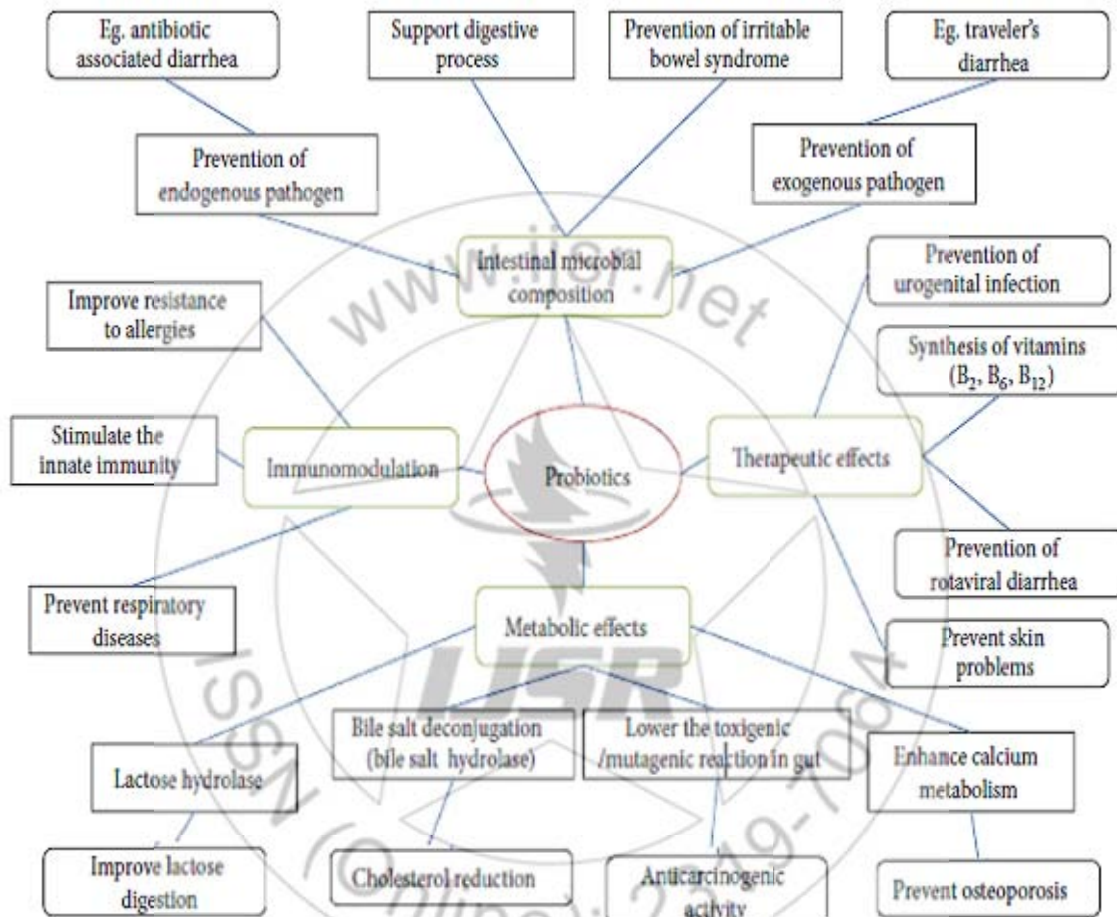


Figure: Health Benefits of Probiotics consumption

Source: <http://www.dfiles.me/probiotics-benefits.html>

3. Role of Probiotics in Preventing Diarrhoea

Normal colonic micro flora is disrupted by Antibiotics and consequently alter carbohydrate metabolism, this potentially leading to diarrhea causing by pathogenic bacteria⁽²⁰⁾. Reduced metabolism of fermentable carbohydrates leads to reduced short-chain fatty acids and increased non-absorbable carbohydrates in the lumen of the gut. As a result there is an increased rate in osmotic pressure which reduced water absorption from the gut liquefying the stools⁽²¹⁾. As a result opportunistic growth of pathogens occurs resulting in mucosal damage and inflammation leading to diarrhea. Gorbach et al demonstrated that *Lactobacillus GG* successfully eradicated *C. difficile* in five patients with relapsing colitis, when they were fed viable *Lactobacilli* in skimmed milk daily. Further reduction in incidence of traveller's diarrhoea has been reported by many studies.

Studies demonstrate that a probiotic can be effective in treating antibiotic induced diarrhoea.⁽²²⁾

4. Role of Probiotics in Lactose Intolerance

Lactose intolerance, also called lactase deficiency and hypolactasia, is the inability to digest lactose, a sugar found in milk and to a lesser extent milk-derived dairy products. This is due to a lack or depletion of the enzyme lactase, which is responsible for digesting lactose. Lactase breaks down lactose into the simpler sugar units, glucose and galactose that can be absorbed into the bloodstream⁽²³⁾. If there is none or not enough lactase produced, then lactose will remain undigested in the gut. It is this undigested lactose which causes intestinal problems including; diarrhoea, vomiting, bloating and abdominal cramps⁽²⁴⁾. Excess gas is produced when lactose is fermented by the gut

microflora and diarrhoea is thought to be caused by an osmotic response leading to excess water in the faeces. Different people may produce different amounts of lactase and will therefore be able to tolerate different amounts of lactose in their diet. The production of the enzyme lactase can be effected by digestive diseases or injuries to the small intestine. Children can also be born without the ability to produce lactase but in many cases a deficiency develops over time and people may not experience symptoms until they are older. It is a natural occurrence that a person produces less lactase as they grow older but not all will develop lactose intolerance or experience associated symptoms. People from particular countries or of a specific race may also be more likely to have a certain degree of lactose maldigestion⁽²⁵⁾.

One solution for lactose intolerance would be to avoid all dairy products but this can be difficult as many processed foods contain hidden milk ingredients. Alternatively you could increase the amount of lactase produced by the body, either in the form of an enzymatic supplement or a probiotic, whose bacterial components have a natural lactase activity. Probiotic bacteria are known to improve lactose digestion and the symptoms of lactose intolerance. Many probiotic bacteria including *Lactobacillus bulgaricus* and *Streptococcus thermophilus* actually produce lactase themselves. These lactic acid bacteria produce β -galactosidase (lactase), which can survive passage through the stomach and is released by bile salts into the small intestine, where lactose digestion occurs⁽²⁶⁾.

Various studies have shown that supplementing with probiotic bacteria improves the ability of patients to tolerate lactose. Non-fermented milk containing either *Lactobacillus acidophilus* or *Lactobacillus bulgaricus* were given to patients who were lactose mal digesters and their degree of maldigestion monitored using a breath hydrogen test. Both treatments significantly improved the symptoms of lactose intolerance and those given *Lactobacillus bulgaricus* also had significantly less hydrogen in their breath. Temporary lactose intolerance can occur in children and adults after a period of diarrhoea, which damages the gut villi and reduces the ability to produce lactase. This kind of lactose intolerance often occurs after a course of antibiotic therapy, probiotics would therefore be a useful to help to prevent diarrhoea and the associated lactose intolerance⁽²⁷⁾.

Several lines of evidence show that the appropriate strains of lactic acid bacteria, such as *S. thermophilus*, *L. bulgaricus* and other lactobacilli in fermented milk products, can alleviate symptoms of lactose intolerance by providing bacterial lactase to the intestine and stomach. Because lactose intolerance affects almost 70% of the population worldwide, consumption of these products may be a good way to incorporate dairy products and their accompanying nutrients into the diets of lactose intolerant individuals. Recent studies have also demonstrated a reduced incidence of milk allergy in toddlers given *Lactobacillus rhamnosus* during early infancy.⁽²⁸⁾

5. Role of Probiotics in Control of Gastro Intestinal Tract

Probiotics when ingested have a beneficial effect in the prevention and treatment of specific pathologic conditions⁽²⁹⁾. The principle of using harmless bacteria for conquering pathogens has been recognized for many years. In fact, Probiotics have been used for as long as people have eaten fermented foods. However, it was Metchnikoff at the turn of the century who first suggested that ingested bacteria could have a positive influence on the normal microbial flora of the intestinal tract (Metchnikoff 1907). He hypothesized that lactobacilli were important for human health and longevity, and promoted yogurt and other fermented foods as healthy.

The goal of Probiotics therapy is to increase the numbers and activities of those microorganisms suggested to possess health-promoting properties until such time that the normal flora can be reestablished⁽³⁰⁾. There are also intestinal disorders in which Probiotics have been used prophylactically and/or therapeutically in which the role of disruption of normal flora in the disease process is less clear. These diseases include traveler's diarrhea, *Helicobacter pylori* gastroenteritis and rotavirus diarrhea. The ability of *Lactobacillus salivarius* to inhibit *H. pylori* colonization of human or murine gastric epithelial cells in vitro was extended in vivo in gnotobiotic mice⁽³¹⁾ ⁽³²⁾ ⁽³³⁾ ⁽³⁴⁾, travellers' diarrhoea⁽³⁵⁾ and diarrhoea disease in young children caused by rotaviruses⁽³⁶⁾ Enhancement of innate defence mechanisms in the GI tract, such as mucin production, might be preventive or therapeutic, but this remains to be elucidated⁽³⁷⁾ ⁽³⁸⁾ ⁽³⁹⁾ ⁽⁴⁰⁾

Bifidobacterium longum has also been shown to reduce the number of times and length of antibiotic-associated diarrhea. An interesting strain, *Bifidobacterium bifidum*, is actually able to neutralize the toxins that bad microbes produce. This means that the toxins cannot damage intestinal cells and that translates into no more diarrhoea.⁽⁴¹⁾

6. Role of Probiotics in Hypercholesterimia

Mann and Spoerry (1974) were the first to report that consumption of fermented milk was associated with reduced serum cholesterol levels in the Maasai people⁽⁴²⁾. A number of studies since have found that use of Probiotics can reduce cholesterol levels by as much as 22% to 33%. Several animal studies have shown that administration of fermented milks or specific strains of lactic acid bacteria are effective in lowering blood cholesterol levels. Studies in human subjects, however, have yielded conflicting results. The most frequently used probiotics found in dairy-based food products are *Lactobacilli* and *Bifidobacteria*. Since these belong to the indigenous human microflora, they have a long history of safe use and there are evidences to support their positive roles, some of these have been designated as GRAS (generally regarded as safe) by the FDA (Food and Drug Administration) due to their long history of use in food fermentations⁽⁴³⁾.

The ability of probiotics to lower cholesterol levels is due to their ability to produce bile salt hydrolase (BSH). Bile salt

hydrolase is an enzyme that converts bile into deconjugated bile salts. Deconjugated bile salts cannot be reabsorbed by the body; thus, more bile acid is lost in the feces and less cholesterol is re-absorbed and sent to the liver⁽⁴⁴⁾. Since about 95% of bile salts are normally re-absorbed, this enzyme can have a great effect on cholesterol levels. The production of bile salt hydrolase by probiotics appears to lower cholesterol by reducing the amount of cholesterol absorbed in the gut and increasing the amount of cholesterol pulled from the blood by the liver to make bile. In recent years; interest has increased in the use of Probiotics to lower cholesterol levels. Researchers have screened more than 300 strains of bacteria for bile salt hydrolase activity⁽⁴⁵⁾. Bile salt hydrolase activity was found to be common in almost all *Bifidobacterium* and some *Lactobacillus* but not in *L. lactis* and *S. thermophilus*. Probiotics are a good addition to the diet of people with high cholesterol. Some research papers suggest that probiotics lower cholesterol levels by inhibiting the ability of the liver to make cholesterol. Another paper suggested probiotics increase the ability of low-density lipoproteins (LDL) to hold cholesterol⁽⁴⁶⁾. There appears to be evidence that Probiotics play a role in cholesterol management. Controlled clinical trials have found that Probiotics reduced cholesterol in people with hyperlipidemia (high cholesterol). A crossover study of 29 healthy women, ages 19 to 56, found that the long term daily consumption of 300 g of a plain or Probiotics-containing yogurt increased high-density lipoprotein (HDL) cholesterol⁽⁴⁷⁾. The yogurt was enriched with *Lactobacillus acidophilus* and *Bifidobacterium longum*.

Probiotics may also play a role in reducing hypertension. More research is needed before Probiotics can be used as an effective treatment for high blood pressure.

7. Role of Probiotics as Anti- Oxidants

Several Human chronic diseases are result of Oxidative stress. Oxidative stress is caused by increased activity of reactive oxidation species (ROS) through oxidation process. Reactive oxygen species (ROS) such as super oxide anion, hydrogen peroxide and hydroxyl radical consists of radical and non-radical oxygen species formed by the partial oxygen reduction.⁽⁴⁸⁾ In oxidation stress conditions there is a chance of increase of producing more free radicals which there by causes damage to nucleic acids, proteins and lipids and has been implicated in diseases like Atherosclerosis, Diabetes, aging,⁽⁴⁹⁾ Anti oxidants are the agents which interact with the free radicals generated in cells and terminate the chain reaction before damage is done to cells. As a result of this Antioxidants oxidize themselves. So there is a constant replenishment of anti oxidants in the body. It is very essential to search for non toxic, natural anti oxidants to protect human body. Due to changes in the consumer perception towards food as a source of its therapeutic values there is more demand in the market for food based ingredients and supplements which provide anti oxidants.

There is renewed interest in search of New sources of Anti oxidants which can be safely used in food. Out of the available various sources, Probiotics have been considered as an emerging sources of anti oxidants. Due to their long tradition of safe use along with the potential therapeutic

benefits role of probiotics as an anti oxidant is being investigated. Fermented milk from cow, goat and camel milk supplemented with probiotic bacteria *Pediococcus pentosus* and studied for the anti oxidative property and Fatty acid profile.⁽⁵⁰⁾ The finding showed that the probiotic fermented milk obtained from goat milk has highest DPPH radical scavenging activity followed by camel and cow milk.⁽⁵¹⁾

8. Role of Probiotics in Cancer

Cancer is a serious health global public health problem. A healthy diet and your immune system prevent cancer.

LAB play an important role retarding the carcinogenesis by possibly influencing metabolic, immunologic and protective functions in the intestine⁽⁵²⁾. The Concentrations of *Lactic acid bacteria* may increase in the intestine after consumption of foods that contain probiotics; However ingestion of prebiotics ingestion also increases the metabolic activity of LAB in the intestine of Human and Animals^{(53) (54) (55) (56) (58) (59)} Probiotics eliminate substances known to cause cancer. Probiotics stop enzymes involved in the creation of cancer causing chemicals. Probiotics have synergistic effects against colon cancer. Liver, bladder and lung cancer could be aided by Probiotics. Radiation therapy side effects may be alleviated by Probiotics.

9. Role of Probiotics as a Functional Food

The story of probiotics started with the description of lactic acid producing bacteria by Louis Pasteur in 1857 and their isolation from rancid milk by Joseph Lister in 1878. Elie Metchnikoff observed that some bacteria were beneficial to health and postulated that they could be administered to humans to replace harmful bacteria in the gut. For his foresight and pioneering work in the infancy of the study of probiotics, he has been named the "father of probiotics". Henry Tissier (1908) isolated *Bifidobacterium* from the faeces of breast fed infants and called it "*Bacillus bifidus communis*". Alfred Nissle (1917) Isolated *E.coli* from faeces of a healthy soldier and used the strain in the prevention of Shigellosis during an outbreak. Minoru Shirota (1930) cultured a strain called *Lactobacillus casei* "*shirota*". A drink incorporating it called "Yakult" was commercially released in 1935 and the concept of consuming beneficial microorganisms orally for the promotion of health started becoming widely acceptable.

Probiotics represent probably the archetypal functional food, and are defined as alive microbial supplement, which beneficially affect the host by improving its intestinal microbial balance. Kollath in 1953, first defined the term "probiotic", when he suggested the term to denote all organic and inorganic food complexes as "probiotics," in contrast to harmful antibiotics, for the purpose of upgrading such food complexes as supplements. Vergio, in his publication "Anti- und Probiotika", compared the detrimental effects of antibiotics and other antimicrobial substances with favorable factors ("Probiotika") on the gut microbiology. Lilly and Stillwell proposed probiotics to be "microorganisms promoting the growth of other microorganisms". The term probiotic was technically defined by an Expert Committee as "live microorganisms

which upon ingestion in certain numbers exert health benefits beyond inherent general nutrition". This means that the microorganisms must be alive and present in high numbers, generally more than 10⁹ cells per daily ingested dose. Each product should indicate the minimum daily amount required for it to confer specific health benefits. (Guarner and Schaafsma, 1998; FAO/WHO, 2001). The term "probiotic" meaning "for life" was first proposed by Lilly and Stillwell (1965). The term probiotics derived from the Latin prefix *pro* which means *for* and the Greek noun *βίος* (*bios*) which means "life" [Hamilton-Miller JM.*et al*]. According to the currently adopted definition by FAO/WHO, probiotics are: "Live microorganisms which when administered in adequate amounts confer a health benefit on the host". [Isolauri E.*et al*(2001), FAO/WHO(2002), Sanders ME.*et al*(2003)].

10. Role of Probiotics in Diabetic Activity

Both diabetes and high blood pressure are risk factors for the development of macrovascular and microvascular complications. Therefore, rigorous control of blood pressure and glucose are paramount to decrease the morbidity and mortality of hypertensive diabetes individuals. A wide range of anti hypertensive drugs is available in the market but not all offer beneficial effects in hypertensive diabetes.

Therefore, the development of new therapy methods is needed in order to produce an efficient method for preventing or reducing the occurrence of diabetes and hypertension with the least side effects. The consumption of probiotics is a new therapeutic strategy in preventing or delaying the onset of diabetes and subsequently reducing the incident. An induction in insulin resistance often leads to diabetic dyslipidemia, and this is highly increased by high levels of plasma total cholesterol, LDL cholesterol, and very low density lipoprotein (VLDL) cholesterol [Yadav.*et al* (2006)].

The efficacy of probiotics in reducing serum cholesterol levels as demonstrated by various in-vivo models could subsequently improve insulin resistance. It has been suggested that the consumption of probiotics can lower the onset of insulin resistance and consequently reduce the incident of hypertensive conditions that are closely related to diabetes. Past studies have also postulated that the onset of diabetes is associated with a poor inflammatory status of the individuals that have consumed high-fats diets over prolonged periods. (Cani.*et al* (2007)). The authors demonstrated that the composition of natural intestinal gut microflora often determine the degree of inflammation contributing to the onset of diabetes and obesity. The concentration of plasma lipopolysaccharides, the pro inflammatory factor, is inversely correlated with the population of *Bifidobacterium spp*.

11. Role of Probiotics in Bacterial Vaginosis

Bacterial Vaginosis is a term used to describe the disorder that cause infections/inflammation in Vagina. Probiotic bacteria are considered as an alternative choice for BV for prevention/treatment due to their capacity to produce antimicrobial compounds such as acetic acid, hydrogen

peroxide there by impeding the growth of pathogenic bacteria⁽⁵⁹⁾. *Bacillus coagulans* is found to be very effective in preventing/ minimizing the Bacterial vaginosis disease. Probiotic capsules are alluring more because of their ease of use and satisfaction rates against the creams and gels⁽⁶⁰⁾.

12. Future of Probiotics

Number of *in vivo* and *in vitro* studies have been conducted utilizing array of probiotics/prebiotics. The genetic interactions between probiotics and the native intestinal microbes have also constituted a topic of interest. The genetic materials can be exchanged via three mechanisms Conjugation, Transduction and Transformation. The transformation of intestinal microflora by DNA may be enhanced upon ingestion of bacteria leading to the genetic material rearrangements. In addition to these the transmission of antibiotic resistant genes among beneficiary bacteria and pathogens which are harmful could be associated with a complex microflora. In the gastrointestinal tract. This transmission can in turn lead to the evolution of Antibiotic-Resistant probiotics and the potential emergence of resistant pathogens.^{(61) (62) (63) (64)}

13. Conclusion

The use of Probiotics in day-to-day medicine in the treatment of gastro intestinal disorders is increasing with the discovery of the beneficial effect of these agents. There are several reports on the role of probiotics in reducing the colon cancer but the recurrence of cancer due to such treatments has not yet been established. The commercial use of probiotics, however has proceeded because essentially no risk is associated with the consumption of well-defined probiotics in foods and many benefits are possible. Perhaps the most compelling evidence for probiotic efficacy is in the areas of anti-diarrheal effects and improved digestion of lactose in lactose-intolerant people, because these findings have been substantiated in human studies.

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