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Omnipresence of Probiotics in Diversified Clinical Practices

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Abstract

As reviewed in details about the bidirectional relationship between the positive influence of probiotics and wellness of humans. Beneficial effects of probiotics in the present scenario are recently developed very popular due to its therapeutics responsible for human health in different diseased conditions. Despite the globally popularity of health benefits of probiotics, there is only very little information available on the advantages and application of probiotics. According to the National Centre for Complementary and Alternative Medicine in connection with the American Society for Microbiology and FAO/WHO focused on account beneficial effects of probiotics in different diseased conditions of patients because of its unconstrained power in the treatment of various diseases and disorders especially gastro intestinal and cancer diseases. On the basis of accumulating data available on literature have strongly linked with human health. Hence, the present review reflected on an overview on the use of probiotics organisms as live supplements, with specific importance on *Lactobacillus acidophilus* and *Bifidobacterium spp*. Increasing knowledge on probiotics is delighting, but in the near future it must be specified that which probiotics are most effective in specific diseases conditions. Well-designed, randomized clinical trials are still required to further define the role of probiotics as preventive and therapeutic agents. The purpose of this review is to give current state of awareness about probiotics and their influence on our well-being.

Keywords: Probiotics; Live bacteria; *Bifidobacterium spp*; *Lactobacillus acidophilus*; Gut microflora

Abbreviations

FAO: Food and Agriculture Organization; WHO: World Health Organization; GRAS: Generally Recognized as Safe; GIT: Gastrointestinal Tract; CFU: Colony Forming Units; AAG: Antibiotics Associated Diarrhea; CDD: *Clostridium difficile* Disease; IBD: Inflammatory Bowel Disease; UTI: Urinary Tract Infection; IBS: Irritable Bowel Syndrome

Introduction

Over the century, the word probiotics have been used by the experimenters in different ways. Even though, the word "probiotics" was not coined before 1960's, work done by Metchnikoff [1] and Tissier [2] gave the scientific evidences towards the conceptual and unprecedented ideology of the term "probiotics". The word "probiotic" means "for life" (from the Greek), is a relatively new word and currently used to name bacteria associated with beneficial effects for humans and animals [3].

From the beginning of 19th century scientists spent a great deal of debate regarding precise and accurate definition of the term "probiotics". It was originally used to describe substances produced by one protozoan which stimulated another [3] but was later used to describe animal feed supplements which had a beneficial effect on the host animal by affecting its gut flora [4,5].

In its latter role it was defined as "organisms and substances which contribute to intestinal microbial balance". This definition is unsatisfactory because it is too imprecise; it would include antibiotics. The definition of probiotics is revised from time to time and stresses the importance of live cells as an essential component of the probiotics preparation. With advancement in the field of probiotics research, scientists continued to investigate the concept of probiotics, which changes from time to time. The following Table 1 divulges from the birth of probiotics to current applications from last few decades.

Year	Inference on the basis of evidences and observations	Reference
1953	Probiotics are common in vegetable foods	[6]
1954	Probiotics are opposite of antibiotics	[7]
1955	Deleterious effects of antibiotics can be prevented by probiotics therapy	[8]
1965	A substance secreted by one microorganism which stimulates the growth of another	[3]

1971	Tissue extracts which stimulate microbial growth	[9]
1973	Compounds that build resistance to infection in the host but do not inhibit the growth of microorganisms in vitro	[10]
1974	Organisms and substances that contribute to intestinal microbial balance	[11]
1989	Live microbial feed supplement which beneficially affects the host animal by improving microbial balance	[12]
1992	Viable mono- or mixed culture of live microorganisms which, applied to animals or man, have a beneficial effect on the host by improving the properties of the indigenous microflora	[13]
1996	Living microorganisms which, upon ingestion in certain numbers, exert health benefits beyond inherent basic nutrition	[14]
1999	Microbial cell preparations or components of microbial cells that have a beneficial effect on the health and well-being of the host	[15]
2001	A preparation of or a product containing viable, defined microorganisms in sufficient numbers, which alter the microflora (by implantation or colonization) in a compartment of the host and by that exert beneficial health effect in this host	[16]
2002	Live microorganisms that when administered in adequate amount confer a health benefit on the host	[17]
2003	Probiotics can be defined as "as live microbes which transit the gastro-intestinal tract, and benefits the health of the consumer	[18]

Table 1: Probiotics outline from the instigation to the current applications.

By evaluating, the numerous hypotheses focusing on the scientific evolution of relationship between well-being of human and intestinal micro biota rationale for this systematic review were addresses on following themes.

- To determine the advantageous effects of probiotics from the healthy aspects, use in relation to gastrointestinal disease and possible mechanisms of bacterial attachment.
- To determine the depth and breadth and limitations of probiotics.
- To explore the beneficial uses of probiotics in different diseases.

The Human Gut probiotics Contribution and Mechanism

There are number of evidences are available, which supports that microorganisms present in gastrointestinal tract affects the human health and immunity [19-23]. In fact, the GIT of foetus *in-utero* is sterile until the time of birth. But on passage through the vagina, is exposed to the microorganisms of surrounding sources i.e. mother, environment contamination and diet [23,24]. These microorganisms from the external environment are rapidly added to the new born child. During the process of addition, many microorganisms are unable to colonise and they disappear soon after the birth of child. And other is able to successfully acquire stable microflora [25]. As GIT of a human plays such a major and important role, its role cannot be neglected. So, before making understand the role of probiotics to the human health, it is very important for us to have an appropriate role of normal human intestine with respect to microbiota.

The elementary function of the human gastrointestinal tract has long been considered as digestion and absorption of nutrients and excretion of waste end products. In recent years, however it has become recognized that the gastrointestinal tract fulfills many other functions, which are essential for our well-being [26]. The gastrointestinal tract of humans is inhabited by a complex or aggregate collection of microbial species. This has been happened because of sharing of a long evolutionary history with the human beings. The term intestinal 'microflora' or 'microbiota' refer to the microbial ecosystem colonizing the gastrointestinal tract [27].

There is an interrelationship among the different microorganisms and the host within such a complex system. The co-evolution of these bacteria has resulted in complex symbiotic relationships between the host and various microbes in the gut microbiota [28]. Distal and luminal portion of mammalian intestine are packed with bacteria although other types are also found, including protozoa and fungi.

The ileum (distal portion), is a transition zone having higher bacterial densities and species diversity, but the most dense colonization is in the colon. Due to its vast diversity in intestine around 400 species of bacteria are presents belonging to more than 190 genera [29]. The number of bacteria in large intestine may reaches up to 10^{10} cells and could substantially rises to astonishing high levels (10^{11} to 10^{12} cells) [30]. In the lower intestine, anaerobes or facultative anaerobic microorganisms predominate, particularly the *bifidobacteria*, *bacteroides*, *fusobacteria* and *peptostreptococci* (each group present at approximately 10^9 per gram); including *enterobacteria* and *lactobacilli*, are present at only moderate densities(10^6-10^8 per gram) [31].

Many of the clinical studies and research in the past decade revealed the role of such natural intestinal microflora known as probiotics can play an important role in immunological [32] digestive [33] and respiratory functions [34] and could have a significant effect in alleviating a large number of diseases. The present review focuses on the various health benefits imparted by these probiotic organisms in maintaining health of an individual. Probiotics are truly a timeless concept.

Factors Affecting Induced Changes in Gut Flora

Even though, the partnership between the gut and its microbiota is harmonious. A number of studies suggested that gut flora, which itself possess protective, metabolic and trophic function [35] is very stable, but can be influenced by many negative external factors (environmental, dietary and modern treatment therapy). Well established gut flora gets disturbed, when it is exposed to antibiotics treatment. The disturbance in well-established gut flora leads to diarrheal conditions. Mucosal and sub-mucosal factors (e.g. prostaglandins, leukotrienes, cytokines, and free radicals), produced

directly or indirectly by the inflamed intestine, stimulate secretion of intestinal fluid and electrolytes [36]. Loss of brush border enzymes involved in the terminal digestion of carbohydrates and proteins may also contribute to secretion. Mitotic arrest and initiation of apoptosis in the crypts of the small intestine caused by the drugs result in a loss of absorptive (villus) surface and causes an imbalance in the number of absorptive and secretory cells. Together with the associated inflammatory cell infiltrate, these changes result in secretion of water and electrolytes which alters the osmotic gradients in the gut, thereby leading to increased secretion of fluids and electrolytes in the stool [37,38].

Under suboptimal conditions, bacteria may pass through the intestinal epithelium and are carried via the lymph to the Mesenteric Lymph Node complex (MLN) and further. This process is known as bacterial translocation [39]. Translocation of indigenous bacteria also takes place continually, at very low rates, in healthy immune competent host. These low numbers of bacteria are killed by the host immune system, leaving the MLN complex sterile. Under very adverse conditions, translocation directly into the portal blood stream is the main pathway for various systemic infections [40].

Characteristics of a Good Probiotics

There are plenty of evidences exist for most populations, which showed that probiotics consumption has beneficial, positive effects and rare chances of complications. As evidences available in literature showed that probiotics have beneficial effects on various diseases [15,41]. So, before using the probiotics, we should follow the selection criteria for good and beneficial bacteria as per available guidelines, which play a key role in specifying consumers' acceptance. FAO/WHO (2010), the International Life Sciences Institute and the European Food and Feed Cultures Association have launched the selection criteria for probiotics. Based on the safety, technological and functionality aspects an expert panel released guidelines, have recently published an updated recommendations for probiotic use [42]. These guidelines provide broad recommendations for the use of probiotics in a range of gastrointestinal and non-gastrointestinal conditions. In the selection benchmarks for probiotics one should consider safety, functional and technological aspects as follows [34,43].

- Probiotics must from the human origin
- It must be gram positive organism
- Survival after passage through acid and bile
- Adherence to the human intestinal cells
- Able to grow in the gut
- Should have defined dosage regimes and durations of use
- Antagonism action against pathogenic and carcinogenic bacteria
- It must show a specific health benefit measured by defined tests (in vitro, animal and/or human)
- Must have defined dosage regimes and durations of use
- Clinically proven documented beneficial health effects

Bifidobacterium

Henry Tissier in the year 1900 described *Bifidobacterium* first time on the basis of their unique Y-shaped morphology. This organism was earlier included in the genus *Lactobacillus* and for many years, it was referred to as *Lactobacillus bifidus* [44]. Today, they have been given separate genus *Bifidobacterium* based on the discovery of the typical enzyme fructose-6-phosphate phosphoketolase, the presence of enzymes α-galactosidase and α-glucosidase, and the absence of the enzymes aldolase and glucose-6-phosphate dehydrogenase, distinguishing them from *lactobacilli.*

The *Bifidobacterium* are gram-positive, non-motile, anaerobic, and rod-shaped with clubs or bifurcated ends, which are the natural inhabitant of the gut and help in maintaining a healthy GIT (Gastrointestinal tract). There are around twenty species of *bifidobacterium* are approved [45]. *Bifidobacteria* constitute a major part of the normal intestinal microflora in humans throughout life, which is regarded as probiotics. *Bifidobacterium* have been found to grow better in human milk than in cow milk, which may be the reason for log count more growth of *Bifidobacerium* in the faeces of breast-fed infants in comparison of bottle-fed infants. The faecal flora of formula-fed infants resembles more closely to that of adults.

The number of *bifidobacteria* in the colon of adults is 10^{10}-10^{11} cfu/gram, but this number decreases with age. They are desirable, health-promoting bacteria, with a saccharolytic and acidogenic physiology, and without involvement in putrefying or toxigenic reactions or pathogenicity [46].

Fermented or unfermented dairy foods like milk, yoghurt, ice cream and cheese, are the most popular food vehicles that are used to deliver these cultures [47]. One of the most important health properties of *bifidobacteria* is their antimicrobial activity towards pathogens. *Bifidobacteria* have been reported to inhibit *Clostridium perfringens*, *Salmonella typhimurium*, *Listeria monocytogenes*, *Campylobacter jejuni*, *Bacteroides vulgatus* and *Escherichia coli* when there is a large amount of viable cells [48].

Many authors suggest that the inhibitory effect of *bifidobacteria* on pathogens in foods is derived from the production of organic acids, hydrogen peroxide, bacteriocins and other antimicrobial compounds when a large number of viable and functional colonies are present. *Bifidobacterium adolescentis*, *B. animalis*, *B. bifidum*, *B. breve*, *B. infantis*, *B. lactis* and *B. longum* are probiotics [49]. *Bifidobacteria* can be used to treat gastrointestinal tract diseases and lactose intolerance.

These bacteria can also improve host immune system, modulate abnormal inflammatory responses in allergies, bowel disease and also improve the function of immune system against pathogens and cancer cells [50]. *Bifidobacterium longum* and *Bifidobacterium breve* were reported to prevent carcinogens from affecting DNA. *Bifidobacterium longum* reduces the creation of tumors [51,52]. Different species of *Bifidobacteria* species are distributed throughout the body are showed in Figure 1.

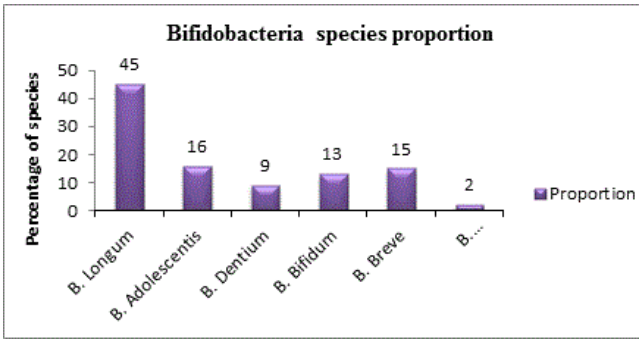

Figure 1: Different species of *Bifidobacterium.*

Lactobacillius

Lactobacilli are gram-positive, non-spore forming facultative or anaerobic rods that are ubiquitous inhabitants of the human normal microflora. As reported by several authors, lactic acid bacteria are commonly used as probiotic in animal nutrition which are *Lactobacillus bulgaricus*, *L. acidophillus*, *L. sporogenes*, *L. casei*, *L. plantarum*, and *Streptococcus thermophiles* [53-55].

These microorganisms utilize carbohydrates as the source of nutrition which helps in fermenting animals and plants products. They are both homofermentative and heterofermentative and lactic is the main metabolic acid produced. They are found where rich, carbohydrate-containing substances are available, hence in a variety of habitats such as the mucosal membranes of humans and animals (oral cavity, intestine and vagina), on plants and material of plant origin, in manure and man-made habitats such as sewage and fermenting or spoiling food.

In healthy humans, *lactobacilli* are normally present in the oral cavity (10^3-10^4 cfu/g), the ileum (10^3-10^7 cfu/g) and the colon (10^4-10^8 cfu/g), and they are the dominant microorganism in the vagina [56]. Lactic acid is an end product of glucose fermentations by *lactobacilli*, which results in a decrease of pH by one or more units. Along with lactic acid it also produces acetic acid and hydrogen peroxide. These metabolites make the environment more favorable for growth of beneficial bacteria and less unfavorable for harmful or pathogenic bacteria [57].

Bacteria belonging to the *Lactobacillus* genus are common inhabitants of human and animal intestinal tract including piglets. Different functional effects of *Lactobacillus* on the host organisms comprises protection against infections, stimulation of immune system, reduction of incidence of diarrhea, reduction of allergy and others, have been demonstrated in vitro and in animal models [58,59]. The beneficial effects of these probiotics include higher growth and feed efficiency, prevention of intestinal disorders and pre digestion of anti-nutritional factors present in the ingredients.

Saccharomyces

Saccharomyces belongs to the kingdom of fungi that includes many species of yeast. *Saccharomyces* genus includes two groups of species:

Saccharomyces sensu strict associated with the fermentation industry.

Saccharomyces sensu lato, comprising species that are more distantly related to *S. cerevisiae* [60].

There are number of researcher who used different strains of *Saccharomyces* and its effect against diarrhea of different etiologies [61].

Mechanism of Action of Probiotics

There is still much controversy as how probiotics work, but on the basis of inspired investigators and technical advances, multifactorial mechanism of probiotics is considered significant (Figure 2).

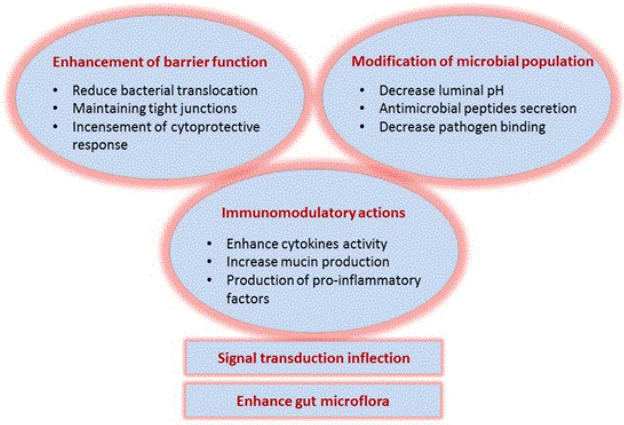

Figure 2: Mechanism of probiotics on human GUT.

Adherence and colonization of the gut

The probiotics has ability to adhere to intestinal cells, as this is the first step in colonization and may enable modification of the host immune system. A number of probiotics have been shown to strongly adhere to human cell lines, including *Lactobacillus casei GG, Lactobacillus acidophilus*, *Lactobacillus plantarum* and a variety of *Bifidobacteria* [62]. These studies also demonstrated the ability of probiotic organisms to inhibit adherence by pathogenic organisms, such as enteropathogenic *Escherichia coli* and *Salmonella typhimurium* [63].

Competition for nutrients and production of antimicrobial substances

Probiotic strains further inhibit pathogenic organisms by competing for the limited substrates required for fermentation and by secreting antimicrobial products called bacteriocins [64].

Stimulation of mucosal and systemic host immunity

There is considerable evidence from animal studies that probiotic organisms can modulate the mucosal and systemic immune systems. This stimulation of host immunity is felt to relate to the ability of microorganisms to adhere to intestinal cells and interact with the gut associated lymphoid tissue [65].

In brief mechanism of action of probiotics is described as that "probiotics" exert their beneficial effects by maintaining a normal intestinal microflora, by stimulating the immune system, by detoxifying colonic contents, by lowering serum cholesterol level and promoting lactose tolerance and by producing metabolites that maintain intestinal health [66,67].

Practical and Scientific Applications of Probiotics in Different Diseased Conditions

Although described for over a century from the different researchers and clinicians alike are only now beginning to realize the significant medical applications of probiotics cultures. Given the

increasing commercial and clinical relevance of probiotics, improving their stress tolerance profile and ability to overcome the physiochemical defences of the host is an important biological goal. Lactic acid bacteria [68] and *Bifidobacterium* [69,70] have their probiotic effects by influencing the biochemical, physiological and antimicrobial activities or changing the composition of the autochthonous intestinal micro flora.

Intestinal disorders

For the prevention of intestinal disorders, probiotics can be rendered multiple drug resistant to survive in the presence of co-administered antibiotics [70]. This generates the possibility of resistance transfer from the probiotic to human bacterial pathogens, either directly or indirectly via the commensal flora. By antibiotics, when they kill friendly bacteria in the gut along with unfriendly bacteria. Some people use probiotics to try to offset side effects from antibiotics like gas, cramping, or diarrhea. Similarly, some use them to ease symptoms of lactose intolerance [71].

Diarrheal disease

There are a number of causes with regard to one's suffering from diarrhea, including traveler's diarrhea, antibiotic-associated diarrhea, and rotavirus diarrhea in children among several others.

Antibiotics associated diarrhea (AAG)

Antibiotics associated diarrhea is the most common complication of the most antibiotics therapy [72]. Antimicrobial treatment disturbs the ecological balance of the normal microflora [73], which can result in diarrhea. 39% of the hospitalized patients receiving antibiotics therapy which disrupt the flora which cause antibiotics associated diarrhea [74]. The normal gut flora possesses a quality called colonization resistance, which prevents the overgrowth of pathogens; some of these antibacterial effects may be caused by volatile fatty acids and a decrease in pH of the luminal contents [75]. The clinical presentation varies from asymptomatic colonization to mild diarrhea to severe debilitating disease, with high fever, severe abdominal pain, paralytic ileum, colonic dilation (or megacolon), or even perforation [76,77].

Administration of certain probiotics strains before and during antibiotic treatment reduce the frequency and/or duration of episodes of antibiotic-associated diarrhea and the severity of symptoms For the treatment of (AAG) *Lactobacillus GG*, and *Enterococcus*, non-pathogenic yeast *Saccharomyces boulardii* are the most extensively studied strain of probiotics, has shown to be effective in both preventing and treating these forms of diarrhea [78,79].

Clostridium difficile associated diarrhea

Hospitalized patients exposed to antibiotics may develop to *Clostridium difficile* Disease (CDD). *Clostridium difficile* is a gram-positive, spore forming anaerobic bacillus which grows in large numbers and produces toxins and harmful substances in large number and damage the colon and cause diarrhea [80].

Clinical manifestations of *C. difficile* associated infections vary from mild diarrhea to life-threatening pseudomembranous colitis. *C. difficile* has been associated with symptomatic diarrhea since it was identified as the pathogen responsible for pseudo membranous colitis [81]. The ability of probiotics microorganisms to prevent recurrences of *C. difficile* associated diarrhea has been documented in particular regarding *Saccharomyces bouladii*, *Bacteriodes spp* [82,83].

Anti-inflammatory activities

Inflammatory Bowel Disease (IBD) is a chronic and recurrent inflammation generally affecting the colon or the small intestine and includes ulcerative colitis [84] and Crohn's disease [85]. The aetiology of IBD remains unclear although there is evidence that the immune system reacts abnormally towards the endogenous microflora. The pathogenesis consists of three interacting elements: genetic susceptibility factors, priming by injury and abnormal immune reactions. Treatment of IBD is usually aiming at altering the host response [86]. Therapeutic manipulation of the normal gastrointestinal microflora using probiotics has been regarded as a further treatment option [87]. A combination of three *Bifidobacterium* species, four *Lactobacillus* species and *S. salivarius subsp. thermophilus* has been shown to be as effective as primary therapy [88].

Irritable bowel syndrome

IBS is defined as a functional bowel disorder in which abdominal pain is associated with a change in bowel habit with features of disordered defecation and distention [89]. IBS is a chronic condition that affects quality of an individual. It is characterized by an intermittent abdominal pain, altered bowel habits may be diarrhea or constipation and gastrointestinal symptoms such as bloating and abnormalities in the intestine [90-93]. Chances of irritable bowel syndrome are 2-3 times more in female as compared to male. The restoration of the intestinal microflora may be useful therapeutic goal. The goal of restoration of normal microflora will be achieved by the use of Probiotics. It acts by modulating the immune response and reduce and cytokine production [94].

Colon cancer

The formation and growth of colonic tumor cells, as well as the generation of other carcinogens and mutagens can sometimes be attributed to bacterial enzymatic reactions in the human intestinal tract [95]. The colorectal cancer represents a major public health problem accounting for over 1 million cases and about half a million deaths worldwide [96,97].

Survival from colon cancer at 5 years has been found to vary demographically and estimated to be 65% in North America, 54% in Western Europe, 34% in Eastern Europe and 30% in India. For the treatment of colorectal cancer adjuvant therapy or treatment like chemotherapy and radiotherapy is applied which vary in success rates for local recurrence, disease- free survival and overall survival [98].

In addition, the aforementioned treatments give some side effects like diarrhea, vomiting, nausea, fatigue, hair loss and other infections [99,100]. Kubota found that colon cancer incidence rate was lowest when the colonic population of *Bifidobacterium* was highest and that of *Clostridium perfringers* was lowest [101]. Kampman reported an inverse relationship between colonic adenomas yogurt consumption [102]. The ability of *lactobacilli* and *bifidobacteria* to modify thegut microbiota and reduce the risk of cancer is in part due to their ability to decrease ß-glucuronidase and carcinogen levels [103,104].

Bingham suggested that vegetables, cereal fiber and folic acid are the important dietary factors which reduce the risk of colorectal cancer

[105]. Yogurt and fermented milk not only contain two types of lactic acid bacteria but it also contains other components with potential cancer preventing properties [106]. Probiotics has antimicrobial against carcinogen-producing microorganisms, antimutagenic properties and alteration of the tumor differentiated on processes [107]. There are number of researcher who worked on colon targeted drug delivery of 5-fluorouracil. But the side-effects like mucositis, translocation of bacteria and diarrhea was neglected. Gulati and Singh studied effects of probiotics on colon targeted drug delivery system of 5-fluorouracil for reducing its side effects [108].

Urinary Tract Infection (UTI)

Urinary tract infection is a common urogynecological problem and most commonly occurring due to bacterial Infections or anticholinergic agents. These are caused by anaerobic gram negative rods, *E. coli*, *Chlamydia* and *Candida*. Risk factors associated with an increased likelihood of UTI in women include urinary tract obstruction, urinary catheterization, neurologic malfunction, pregnancy, and use of spermicides, a diaphragm [109]. Although for the treatment of infection antibiotics therapies are used, this eradicates bacteria from the bladder and also disrupt genital flora. To overcome such problems new therapeutic agents are being used which has immune modulation or signalling effects. The development of gelatin suppositories containing freeze dried *Lactobacillus* GR-1 and B-54 or RC-14 strains into the vagina has been shown to reduce the risk of urinary tract infections, and improve the maintenance of a normal flora. Ingestion of these strains into the gut has also been shown to modify the vaginal flora to a more healthy state [110].

The presence and dominance of *Lactobacillus* in the vagina is associated with a reduced risk of bacterial vaginitis and urinary tract infections. The mechanisms appear to involve anti-adhesion factors, by-products such as hydrogen peroxide and bacteriocins lethal to pathogens. The effect of yogurt consumption on *Candida vaginitis* in a crossover trial with 33 women [111,112]. Results indicated that candida infections were decreased during yogurt consumption. The use of probiotics in urinary tract infection in the same way as in case of treatment of diarrhea [113].

Pancreatitis

Pancreatic necrosis and associated pancreatic infection are determinates of poor outcome in patients with severe acute pancreatitis, and the nature of microbial species inhabiting the intestine can influence subsequent infection rates [114].

Penner et al., in their research reported that two small randomized double-blind trials have been published by the same research group examining the effect of naso-jejunal treatment with *Lactobacillus plantarum* in patients with acute pancreatitis [115]. Both trials compared live *L. plantarum* with killed bacteria as a control, and both showed significantly lower rates of infection in the groups treated with the live probiotics. Replication of these results, ideally in larger studies, would provide excellent evidence for probiotics use in this setting [116] (Table 2).

Vaccine delivery vehicles

Recently, vaccine delivery vehicles have reached on top most of modern vaccinology due to practical and immunological applications [117,118]. Mercenier, reported the mucosal routes for vaccine delivery, in which he delivered protective antigens at the mucosal surfaces by using live bacterial vectors. As an alternative to this strategy, non-pathogenic food grade bacteria such as Lactic Acid Bacteria (LAB) are being tested for their efficacy as live antigen carriers.

Disease	Probiotic strains used	Reference
Antibiotics associated diarrhea	*Lactobacillus GG*	[119]
	Enterococcus	[76]
	Saccharomyces boulardii	[79]
Clostridium difficile associated diarrhea	*Saccharomyces bouladii*	[83]
	Bacteriodes spp	[84]
Inflammatory bowel disease	*S. salivarius subsp*	[89]
	Bifidobacterium infantis	[85]
Irritable bowel syndrome	*Bifidobacterium infantis*	[85]
Colon cancer	*Bifidobacterium*	
	Clostridium perfringers	[102]
Urinary tract infection	*Lactobacillus GR-1*	[111]
	Lactobacillus B-54	
	Lactobacillus RC-14	
Pancreatic necrosis	*Lactobacillus plantarum*	[116]

Table 2: List of different probiotic strains deliberated in order to treat different diseases.

Future prospects

The future success of probiotics clearly depends on extensive cooperation in an area requiring new ideas from food technologists, strong support from medical and nutrition scientists, and an understanding of current and future food and health needs from consumer information experts. The development of food science in the near future probably depends on the advance in functional food science, which basically deals with the treatment of diseases with the help of natural resources. Due to advancements in uses of probiotics, some suggested that there is a chance of shifting of term “probiotics” to new world of pharmabiotics [120].

Conclusion

As treatment of diseases by the use of probiotics is an emerging field of research. By taking the emerging increasingly trend of using probiotics as novel therapeutic strategies, it is concluded that its contribution in treating different diseases is safe and more effective manner. Administration of antibiotics often causes disturbances in the normal intestinal microbiota. Henceforward, it would appear that daily supplementation with viable probiotics bacteria could be too great to enable their domination. The theory of treatment with probiotics offers an approach in controlling the negative metabolic or pathogenic activities of microbes to which we are exposed daily. But the basic interference to use probiotics as a medicinal agent requires preclinical and clinical confirmations along with health benefit evidences in human volunteers. The use of probiotics in different

diseases or conditions is attractive and needs auxiliary scientific assessments.

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