La Prensa Medica Argentina

Review Article

Role of Lactic Acid Bacteria as Probiotics in Health and Disease

Mayur Sharma[1], Dinesh Raj Modi[2] and Madhukar Saxena[2*]

[1]Department of Microbiology, Hind Institute of Medical Sciences, Near Canal, Safedabad, Barabanki Road, Lucknow-226001, Uttar Pradesh, India

[2]Department of Biotechnology, Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Rai Bareilly Road, Lucknow-226025, Uttar Pradesh, India

[*]**Corresponding author:** Madhukar Saxena, Department of Biotechnology, Babasaheb Bhimrao Ambedkar University, (A Central University), Vidya Vihar Rai Bareilly Road, Lucknow-226025, Uttar Pradesh, India; Tel: +91-9839317441; E-mail: madhukarbio@gmail.com

Rec date: Mar 03, 2014 **Acc date:** Sep 22, 2014 **Pub date:** Sep 25, 2014

Abstract

In natural environment a delicate symbiosis evolves between endogenous bacteria and their host is very crucial for maintaining the internal flora of organisms. It stimulates immune system to respond rapidly to infection with pathogens and through bacterial antagonism it inhibits the colonization of the gut by harmful or pathogenic bacteria. A dominant flora represents 90% of the population, essentially composed of *Bifidobactrium* and *Lactobacilli*. In group they are called as Lactic Acid Bacteria (LAB) and are collectively called probiotics. These antibacterial effects of LAB are possible due to different antimicrobial compounds like organic acids, hydrogen peroxide (H_2O_2), carbon dioxide (CO_2), fatty acids, reuterin, bacteriocins and other low molecular mass compounds produced by them. Probiotics is playing an important role in prevention of many bacterial diseases also. Probiotic bacteria may add a low-cost, low risk layer of protection from infection and disease.

Key words

LAB; Probiotics; GI tract; Bacteriocins; Diarrhea; Biopreservative agent

Introduction

Microorganisms are ubiquitous in biosphere. We generally have more than three pounds of bacteria inside our bodies. The human intestine is habitat for more than a trillion live bacteria from about 400 species. The average adult human body contains about 20 times more bacteria than it does cells [1]. In the natural environment a delicate symbiosis evolves between these endogenous bacteria and their host.

Microflora of Gastrointestinal (GI) tract plays a crucial role in the anatomical, physiological and immunological development of the host. It stimulates the immune system to respond rapidly to infection with pathogens and through bacterial antagonism it inhibits the colonization of the gut by harmful or pathogenic bacteria [2]. It consists of species belonging to families: - *Bacteroids, Fusobacterium. Butyrivibrio, Clostridium, Bifidobacterium, Eubacterium* and *Lactobacillius, Enterococcus* and *E.coli* constitute less than 1% of all intestine micro-organism. Anaerobes dominate upon facultative anaerobes and microaerophillic at the ratio of 1000:1 [3]. A dominant flora represents 90% of the population, essentially composed of *Bifidobactrium* and *Lactobacilli.* In group they are called as Lactic Acid Bacteria (LAB). LAB was first isolated from milk and have since been found in such foods and fermented products such as meat, milk products, vegetables, beverages, bakery products, soil, water, manures and sewage [4-8]. In addition, LAB produce small organic compound that give the aroma and flavour to the fermented product and have been used as a flavouring and texturizing agents as well as a preservative in food for centuries and are now added as starters in food [9]. Antimicrobial effect of LAB is mainly due to their lactic acid and organic acid production, resulting in reduced pH of the growth environment; apart from this it also produce acetaldehydes hydrogen peroxide, diacetyl, CO_2, polysaccharides and bacteriocins [9,10].

S. no	Health-effect	Mechanism	Strain example	Reference
1	Relive lactose intolerance symptoms	Hydrolysing lactose into glucose and galactose and forming the physical appearance of milk into a thick substance,such as yogurt, that passes through the GI tract slowly reducing the lactose pulse in the colon	*Lactobacillus rhamnosus GG*	[80].
2	Control viral, bacterial and antibiotic assotiated diarrhea in humans and animals	Reinforcing the local immune defence through specific IgA response to rotavirus and to other pathogens	*L. rhamnosus GG L .reuterii Enterococcus faecium*	[15, 53, 81, 82].
3.	Prevention of allergy and atopic eczema	Prevention is partially due to serum antibodies IgG and scretory IgA and IgM immune response enhanced by probiotics	*L. rhamnosus GG Bifidobacterium lactis Bb-12*	[82, 84].
4.	Prevention of intestinal bacterial enzymes involved in the synthesis of colonic carcinogens	Enhancing host`s immune response, binding and degrading carcinogens, producing antimutagenic compounds, alteration of metabolic activities of intestinal bacteria and alteration of physio-chemical conditions in colon might work to prevent cancer	*B. bifidum* *B .infantis* *B .longum* *L. acidophillus* *L. paracasei*	[81, 85, 86].

Table 1: Selected health-promoting Lactic-acid bacteria, their impacts and mechanisms.

Members of LAB share the property of being Gram-positive that ferment carbohydrate into energy and lactic acid [11]. Depending on the organism, metabolic pathway differ when glucose is the main carbon source: Homo-fermentative bacteria such as Lactococcus and Streptococcus yield two lactate molecule from one glucose molecule, whereas the Hetero-fermentative (i.e, Leuconostoc and Weissella) transform a glucose molecule into lactate, ethanol and carbon-dioxide [10,11]. Selected health promoting Lactic acid bacteria, their impacts and mechanisms is summarized in (Table 1).

Apart from antimicrobial activity LAB is also involved in maintaining healthy Gastrointestinal (GI) micro ecology and host metabolism [12]. It also controls intestinal disorder by producing Serum antibodies IgG and Secretary IgA and IgM enhancing immune responses [13,14,15] (Figure 1). LAB is one of the major class of Probiotics which is defined as "live micro-organism which, when administered in adequate amounts confer a health benefit on the host" [16]. While probiotics is defined as non-absorable or non-digestible food components that beneficially stimulate one or more of the gut beneficial microbe groups and thus have a positive effect on human health and Synbiotic is combined administration of specific perbiotics with probiotics to provide definite health benefit by synergisitic action.

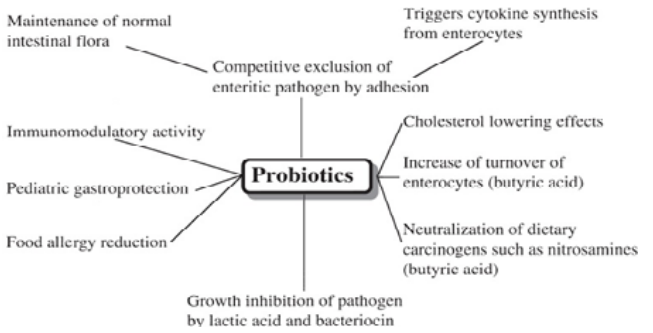

Figure 1: Potential benefits of Lactic acid bacteria

Probiotic bacteria come from two groups – *Lactobacillus* and *Bifidobacteria. Lactobacillus* (Gram-positive, facultative anaerobic bacteria) are present in vagina and GI tract. Bacteriacinogenic strains have been found among homo and hetrofermentive species of LAB. The bacteriocins of lactic acid bacteria normally kill other sensitive Gram-positive bacteria by destablizig membrance function. The antibacterial properties of bacteria are combating spoilage, pathogenic bacteria in food and as a feed supplements for animals to reduce the emergence of antibiotic resistance bacterial pathogens and as probiotics in humans for control of GI ailments caused by enteric pathogens [17].

These antibacterial effects of LAB are possible due to different antimicrobial compounds produced by them. Some of which are discussed below

Organic acids

Fermentation of LAB is characterized by the accumulation of organic acids and the accompanying reduction in pH. The levels and types of organic acids produced during the fermentation process depends on the species of organisms, culture composition and growth conditions [18]. The antimicrobial effect of organic acids lies in the reduction of pH, as well as undissociated form of the molecules [19,20]. Low external pH causes acidification of the cell cytoplasm, while the undissociated acid, being lipophilic, can diffuse passively across the membrane [21]. The undissociated acid aids by collapsing the electrochemical proton gradient or by altering the cell membrane permeability which results in disruption to substrate transport systems [22,23]. Lactic acid is the major metabolite of LAB fermentation where it is in equilibrium with its undissociated and dissociated forms. The extent of dissociation depends on pH, at low pH a large amount of lactic acid is in the undissociated form and it is toxic to many bacteria, fungi and yeasts. However, different microorganisms vary considerable towards their sensitivity to lactic acid. At pH 5.0, lactic acid was inhibitory towards spore forming bacteria but was ineffective against yeasts and moulds [24]. While stereoisomers of lactic acid also differentiated in their antimicrobial activity [25].

Acetic acid and propionic acid produced by LAB strains through hetero-fermentative pathways may interact with cell membrane and cause intracellular acidification and protein denaturation [26]. They are more antimicrobially effective than lactic acid due to their higher pKa values (lactic acid 3.08, acetic acid 4.75 and propionic acid 4.87) and higher percent of undissociated acids than lactic acid at a given pH [23]. Acetic acid was more inhibitory than lactic and citric acid towards *Listeria monocytogens* [27,28]. Acetic acid also acts synergistically with lactic acid, which decreases the pH of the medium thereby increasing the toxicity of acetic acid.

Hydrogen peroxide (H_2O_2)

Hydrogen peroxide is produced by LAB in the presence of oxygen as a result of the action of flavoprotein oxidases or nicotinamide adenine hydroxy dinucleotide (NADH) peroxidases. The antimicrobial effect of H_2O_2 may result from the oxidation of sulfhydryl groups causing denaturations of a number of enzymes and from the peroxidation of membrance lipids thus the increased membrane permeability [29]. H_2O_2 may also be as a precursor for the production of bactericidal acid free radicals such as superoxide, carbon-dioxide and hydroxyl (OH) radicals which can damage DNA [30]. The production of H_2O_2 by *Lactobacillus* and *Lactococcus* strains inhibited *Staphyloccus aureus, Pseudomanas spp.* and various psycho - trophic microorganisms in foods [31,32].

Carbon dioxide (CO_2)

CO_2 is mainly produced by heterofermentative LAB. CO_2 plays a role in creating anaerobic environment which inhibits enzymatic decarboxylations and the accumulation of CO_2 in the membrane lipid bilayer may case a dysfunction in permeability [33]. CO_2 can effectively inhibit the growth of many food spoilage microorganisms, specialty Gram-positive psychrotrophic bacteria [34,35]. The degree of inhibition by CO_2 varies considerably between the organisms.

Fatty acids

Under certain conditions some *Lactobacilli* and *Lactococci* possessing lipolytic activities may produce significant amounts of fatty acids i.e. in dry fermented sausage and fermented milk [36,37]. The unsaturated fatty acids are active against Gram-positive bacteria and the antifungal activity of fatty acids is dependent on chain length, concentration and pH of the medium [19]. The antimicrobial action of fatty acids is due to the undissociated molecule, not the anion since pH had profound effects on their activity [38].

Reuterin and other low molecular mass compounds

Reuterin is produced by *Lactobacillus reuteri*, a heterofermentative species inhibiting the GI tract of humans and animals [39]. It is formed during the anaerobic growth of *L. reuteri* by the action of glycerol dehydratase which catalyzes the conversion of glycerol into reuterin [40]. Reuterin has been chemically identified to be 3-hydroxy propanol (β-hydroxyl propionaldehyde) a highly soluble, pH- neutral compound which is in equilibrium with its hydrated monomeric and cyclic dimeric forms [41]. Reuterin exhibits a broad spectrum of antimicrobial activity against certain Gram-positive and Gram-negative bacteria, yeast, fungi and protozoa. Spoilage organisms sensitive to reuterin include species of *Salmonella, Shigella, Clostridium, Staphylocaccus, Listeria, Candida* and *Trypanosoma* [42]. Besides reuterin which has been studied, there are several reports on the production of Low molecular mass (LMM) antimicrobial compounds by different species of LAB (Table 2).

Bacteriocins

These are ribosomally synthesized, extra cellularly released bioactive peptides or peptide complexes, having a bactericidal and bacteriostatic activity. Bacteriocins are proteins peptide or proteinaccous complexes secreted by many strains of Gram positive and Gram negative bacteria that show their inhibitory action against strains of the same species or species of that are closely related to producer strains [43]. Four general classes of antimicrobial peptides or proteins (Bacteriocins) from LAB (Table 3). The detailed source and spectrum of different bacteriocins is summarized in (Table 4).

Producing Strain	Antimicrobial Compound	Anti microbial activity	Reference
Lactobacillus sp.	Mixture of small antibiotics, peptides and organic acids	*E.coli* and *Streptcoccus mutants*	[87].
Casei ssp. Casei strains	Acidolin	Entero pathogenic organisms and spore formers	[88]
Acidophilus 2181	Bulgarican	Wide spectrum	[88].
Delbruocki ssp	Non lactic compound possibly with an aromatic group	*Pseudomanas* and *Staphylococous aureus*	[89].
bulgarius DD 14	Microcin – like compound	Wide Spectrum	[90].
Delbruocki ssp	3–Hydrocy proparal and its hydrated and dries forms (reuterin)	Wide Spectrum	[40].
bulgarius –7994	Cationic Compounds	*Pseodomonas Strains* and *E.coli*	[93].
Rhamnosus GG	Contaning carbohydrates and	Wide Spectrum	[94].
Reiteuri 1063	Amines		
Streptococcus spp.			
Diacetylactis DRC -1			
Thermophilus Strain			

Table 2: Low molecules mass (LMM) antimicrobial compounds produced by lactic acid bacteria.

Classification	Remarks	Examples
CLASS-I Lanthionine containing bacteriocins/ lantibiotics	Include both single and two peptide lantibiotics; upto 11 subclasses have been proposed.	Single peptide nisin, mersacidin, lacticin481, two peptide-lactacin 3147, cytolysin
CLASS-II Non-lanthionine containing bacteriocins	Hetrogenous class of small heat stable peptides.	LeucocinA, Lactacin F, enteriocinAS-48, Lactoccocin A
CLASS-III Non-bacteriocinlytic proteins	Large heat proteins often murin hydrolysis	Lysostaphin enterolysinA
CLASS-IV Bacteriocins (non-protenacious moties)	No longer considered bacteriocin.	-

Table 3: Suggested classification scheme for Bacteriocins [95].

S.No.	Bacteriocin	Source	Spectrum
Lactococci			
1	Nisin	*Lactococcus lactis*	Inhibits Gram positive bacteria like *bacilli, Lactococci, Micrococci, Clostridium, botulinm.*
2	Diplococcic	*Lactococues lactis subsp. cremoris in milk.*	Inhibitory against closely related *Lactococcus lactis* and other strains of *Lactococcus cremoris*

3	Lectostrepsins	*L. lactis Subs, P.diacetylactis L.lactis Subsp cremoris and L.lactis Subsp lactis*	Active against other *lactococci*, group A, C and G *Streptococci, Bacillus cereus, Lactobacillus heloetius, laconastoc hesenteroides, L.lactis subsp cremoris and Leuconastoc paracitrouonum.*
4	Lactococcins	*L .lactis subsp cremorisL. lactis subsp. diacety lactis*	Inhibit other *Lactococci* and some *Clostridia*.
Lactobacilli			
5	Lactocin 27	*L. helveticins LP 27*	Inhibitory action against other *Lactobacilli*
6	Helveticins Helveticins J Helveticin V-1829	*Lactobacillus Helveticins 481 Lactobacillus Helveticins 1829*	Active against limited related *Lactobacilli Bactericidal* against other *Lactobacilli*
7	Lantacins Lantacin F	*Lactobacillus acidophilus 110088 Lactobacillus acidophilus N2*	Inhibitory against *L. delbmeckii subsp. Bulgaricus, L. delbmeckii Subsp. Lactis, L. helveticus, L. acidophilus. L. ferenturn and strain of L. feacalis.*
8	Plantaricins Plantaricin A Plantaricin B	*Lactobacillus plantorium C-11Lactobacillus plantorium NCDOC 1193*	Inhibitory to other lactic acid bacteria Inhibitory against otter strains of *L. plantarum, L. merenteroides. Pseudomonas*
9	Fermenticin	*Lactobacillus Fermenti*	Inhibitory to *Lactobacilli*
10	Lacticins	*Lactobacillus Sake 245*	Inhibitory against *Pediococcus, Leuconostac and Lactobacillus*
11	Breviciin 37	*Lactobacillus Curvatus LTH 1174*	Inhibitory against other *Lactobacilli, leuconotocs, Carnobacterium monocytogens* weak action against *Micrococci* and *Staphylococci*
12	Sakacins Sakacin A Sakacin M Sakacin P	*Lactobacillus Sake 70B Lactobacillus Sake 148 Lactobacillus Sake LTH 673*	Inhibits strains of LAB and *L. mesenteroides Inhibits Lactobacilli, leuconostocs Cynobacteria and S. aureus Inhibits Lactobacilli, leuconastocs, Casrobacteria, Enterococci, Brochothrix thermosphacta and Listeria sp.*
13	Careicin 80	*Lactobacillus Casei B-80*	Active against otter strains of L.casei
14	Curvacin A	*Lactobacillus Curvatus LTH 1174*	Inhibitory against otter *lactobacilli, Leuconastocs, Carnobacteria, L. monocytogens* as well as weak action against *Micrococci* and *Staphylocci*
Pediococci			
15	Pediocin AcH	*Pediococcus acidolactis strain H*	Active against many *Lactobacilli*, *Leuconostoc*, *S.aureus Clostridium perfringes, L. monocytogens* and *Peudomonas spp.*
16	Pediocin PA-1	*Pediococcus acidolactis strain PAC-10*	-
Leuconostacs			
17	Mesenteriocin 5	*Leuconostac mesenteroids 5*	Inhibitory to *L. monocytogens*, *S. facealis*, *Brevibacterium*
18	Leucocin A	*Leuconostac gelidum*	Inhibitory to *Leuconostoc*, *Lactobacilli*, *Pediococci*, *E .faecalis* and *L .monocytogens*
19	Leuconostac-S	*Leuconostoc paramesenteroides OX*	Inhibits *L .monocytogens*, *S. aureus*, *Aeromonas spp., Clostridum.*
20	Carnocin	*Leuconostoc carnosum LA-44A*	Inhibits *Pediococci, Enteriococci, Leuconostoc and Listeria spp*.

Table 4: Bacteriocins of Lactococci, *Lactobacilli*, Pediococci and Leuconostacs.

Why probiotic supplementation is needed?

In our modern world it is challenge to maintain a healthy quantity of good bacteria in the colon. Fermented foods including yogurt, miso, tempeh and sauerkraut can supply some healthy bacteria but, other factors in our life may be actively depleting our probiotic population. These factors can include: A diet high in sugar and refined carbohydrates which are low in probiotic containing foods. Sugars encourage the growth of yeast and bad bacteria, enemies of probiotics but vegetables and fruits contain prebiotics the building blocks of probiotics. Over exposure to antibiotics, long term use of antibiotics, chlorinated water and over use of antacids can devastate our intestinal flora. The effects can be harmful to the probiotic bacteria resulting GI tract less acidic (less friendly for good bacteria) and stress by affecting our hormone levels which stress lowers probiotic level.

Potential benefits of Probiotics

Alleviation of lactose intolerance

About 70% of the world's population has lactose intolerance to have a low amount of intestinal ß-galactosidases activity and it is a major problem and for whom lactose behaves like an osmotic nondigestible carbohydrades [44]. Lactic acid bacteria increase the lactose tolerance level in lactose intolerant individuals [45].

Cholesterol lowering

LAB removes cholesterol from culture media [46]. The cholesterol removal from culture media results precipitation of cholesterol with free bile acids, formed in the media because of the activity of the

bacterial enzyme bile salt hydrolase [47]. Enhanced bile salt hydrolase activity increases cholesterol excretion. However, consumption of a probiotic milk product increases cholesterol excretion [48].

Prevention of urinal & genital infections in women's

Almost all infections of the vagina and bladder are caused by microorganisms that originate in the bowel. There is strong correlation between presence of commensals particularly *Lactobacilli* in the healthy vagina and an absence of these microorganisms in patients with urogenital infections. Disruption of the normal vaginal flora is caused by broad-spectrum antibiotics, hormones, dietary substances and factors not as yet fully understood. There is some evidence that probiotic microorganism delivered as foods and tropical preparation have role in preventing urinal & genital tract disorders. The criteria for selection of effective probiotic strain have been proposed and should include verification of safety, colonization ability in the vagina and ability to reduce the pathogen count through competitive exclusion of adherence and inhibition of pathogen growth [49].

Bacterial vaginosis

Bacterial vaginosis (Bv) is a disease of unknown etiology resulting from the overgrowth of various anaerobic bacteria species and associated with the disappearance of *Lactobacilli*, which dominate the normal vigina. There is some clinical evidence to suggest that oral and vaginal administration of *lactobacilli* can eradicate asymptomatic and symptomatic Bv [49, 50].

Yeast vaginitis

Yeast vaginitis is common ailment often precipitated by antibiotic use, exposure to spermicides or hormonal changes as yet not fully understood. Unlike bacterial vaginosis, yeast vaginitis is not necessarily due to loss of *Lactobacilli*. Few *Lactobacillius* strains are able to inhibit the growth and adhesion of *Candida albicans* or other *Candida* species [51].

Urinary tract infections (UTI)

Several hundered million women are affected by UTI annually uropathogenic *E .coli* originating in the bowel is the responsible agent in upto 85% of cases [52]. Asymptomatic bacteruria is also common finding in women and sometimes it is followed by symptomatic UTI. It is believed that fewer pathogens can ascend into the bladder, there by blocking the infectious process.

Enhancement of immune system

Lactic acid bacteria are thought to have several presumably beneficial effects on immune system by inactivation and reduction in number of pathogenic bactaria like *E. coli, Shigella sp., Salmonella sp.,* etc. by stimulating IgA immune response, interferon - gamma production, activation of macrophages and natural killer cells, increase secretion of lysosomal enzymes and increased production of reactive oxygen, nitrogen radicals and monokines of phagocytic cells [53].

Role in reducing risk of cancer

There is some premilinary evidence that probiotic microorganisms can prevent or delay the onset of certain cancers. This stems form the knowledge that members of the gut microflora can produce carcinogens such as nitrosamines. Therefore, administration of *Lactobacilli* and *Bifidobacterium* could theoretically modify the flora leading to decrease beta – glucuronidase and carcoinogen levels [54]. Anticolon cancer effect of the probiotic bacteria has been reported through different mechanisms includes mutagen binding, carcinogen deactivation, immune response and influence on secondary bile salt concentration [55].

Prevention of disorders associated with the GI tract-

Diarrhea

Infectious diarrhea is a major world health problem responsible for several million deaths each year. While the majority of deaths occur amongst children in developing countries, it is estimated that up to 30% of the population even in developed countries are affected by food born diarrhea each year. Probiotics can potentially provide an important means to reduce these problems. The beneficial effect of proboitics using *Lactobacillus rhamnosus* and *Bifidobacterium lactis* for prevention and treatment of acute diarrhea mainly caused by rotaviruses in children [56-59].

In addition to rotavirus infection, many bacterial species cause death and morbidity in humans. Certain probiotics strains can inhibit the growth and adhesion of a range of enteropathogens and animal studies have indicated beneficial effects against pathogens such as *Salmonella* [60-63]. A major problem associated with antibiotic treatment is the appearance of diarrhea often caused by *Clostridum difficile*. The organism is not uncommon in a healthy intestinal tract but, the disruption of the indigenous microflora by antibiotics leads to an abnormal elevation of their number and subsequent symptoms related toxin administration of exogenous commensal probiotic microorganism is required to restore the microflora to one that more closely reflects the normal flora prior to antibiotic therapy [64, 65].

Helicobacter pylori infection and complication

A new development for probiotics application is activity against *Helicobacter pylori*, a Gram negative pathogen responsible for Type-B gastritis, peptic ulcers and gastric cancer. LAB inhibits the pathogen and decreases urease activity necessary for the pathogens to remain in acidic environment of the stomach [66-68].

Acute diarrhea, mainly caused by Rotavirus

Rotavirus is the main virus of study with probiotics. Rotavirus infection causes gasteroenteritis, characterized by acute diarrhea and vomiting. There are ample evidence that probiotics reduce the duration and severity of rotavirus diarrhea. Consumption of *Lactobacillus* shortened the diarrheal phase in children infected with rotavirus infection [56, 69-71].

Traveler's diarrhea

Traveler's diarrhea is defined as the passage of greater than 3 unformed stools in a 24 hour period in people who normally live in industrialized countries and travel to tropical and sub tropical countries [72]. Although it is not possible to medically recommend any probiotic at the present time to prevent traveller's diarrhea, the likehood for some agents to be effective is high and more through studies need to be performed.

Inflammatory disease and bowel syndromes

Inflammatory bowel diseases, such as Pouchitis and Crohn's disease as well as Irritable bowel disease, may be caused by alterations in the gut flora including infection [73]. A large body of evidence suggests that the enteric microbiota may be an important factor in driving the abnormal inflammatory response in the susceptible host leading to chronic inflammatory bowel diseases due to incidence of inflammation is greatest in the part of the intestine which harbours the highest concentration of bacteria (colon, caecum and terminal ileum), fecal stream has been implicated in disease activity, its interruption has been associated with the disease improvement, enhanced mucosal permeability may play a vital role in maintaining a chronic inflammatory state due to genetic predisposition or direct contact with bacterial or their products, loss of immunological tolerance to commensal bacteria in genetically susceptible patients.

The discovery of the role of the enteric microbiota is a common denominator in the pathogenesis of inflammatory bowel disease has lead to the interest and increasing scientific evaluation of the use of probiotics as a means to reconstitute microbial and immunological hemostatis [74].

Role of LAB in food preservation as a biopreservative agent

Now a day's consumers are concerned about the synthetic chemicals used as preservatives in food and there is resulting trend towards less processed foods. The untreated foods can harbour dangerous pathogen, which can multiply under refrigeration and without oxygen. A solution to this dilemma is the use of antimicrobial metabolites of fermentative microorganisms. In common fermented products such as yogurt, lactic acid is produced by the starter bacterial culture to prevent growth of undesirable microorganism [75]. LAB has contributed in the increased volume of fermented foods worldwide especially in foods containing probiotics or health promoting bacteria.

The development of novel approaches in food allows broadening the potential for using LAB in food [76,77]. The nature of genetic modification in LAB as Genetically modified organism (GMOs) can be divided into 3 groups including one-step genetic events like deletion, gene amplification, plasmid insertion and losses, mulit-step genetic rearrangements with DNA of same species and trans –species genetic modifications has emphasized the effective use of gene manipulated LAB in battle against food–spoilage and pathogenic bacteria [10,78]. An example genetically modified LAB have been utilized to improve cheese ripening [79].

Future prospects of probiotics

It includes for determining the physiological role, mechanisms of action and extent of influence of probiotics in human health using human feeding studies, used for the validating the extent of its importance in the areas of immune system, cancer and gut micro ecology and also assess the effects of probiotics on populations its activity on gut microbes and in selection of dose responses for different strains of bacteria.

Conclusion

The interest in establishing scientific credibility for probiotic effects is of high importance to companies and scientists. Research to support health claims will have to take into account the intestinal microbiota and its interaction with the host. The information gleaned from sequence data will provide opportunity to improve probiotic functionality and expand understanding of mechanisms. The health promoting benefits and efficacy of probiotics has been demonstrated in many models of gastrointestinal disease and indeed in diseases and conditions at other anatomically distinct locations. The use of probiotics in the treatment of many forms of diarrheal disease appears especially promising. The inherent physiological and technological fragility of what are often promising candidate probiotic strains can render them ineffective for clinical use. Formulation of food products with additional vitamins, non-digestible carbohydrates, soluble fiber, phytochemicals, or other bioactive ingredients could further enhance the dietary value of the product.

Acknowledgements

Mayur is thankful to department of microbiology, hind institute of medical sciences, Lucknow. Madhukar is thankful to Dr. D. S. Kothari post doctoral fellowship from university grant commission, New Delhi (BL/12-13/0317).

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