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Role of Lactobacilli as Probiotics in Human Health Benefits: Current Status and Future Prospects

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Abstract
The Lactic Acid Bacteria (LAB) has extensivelybeen used in food industry for the production of varied fermented products such as yoghurt, cheese etc. These are also been used as probioticsfor animal as well as human welfare in terms of health and well being. also The present review focuses on available literature, current market status and on the characteristics of Lactic Acid Bacteria with a special emphasis on the probiotic properties of the genus Lactobacillus.The industrial scale development of Lactobacillus as commercial products has benefited the market in several facets.

Keywords: *Lactic acid bacteria, Health benefits, Probiotics, Market scope*

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I. Introduction

The awareness amongst the health conscious individuals has proved to be very useful for the food sector, particularly in the production of probiotics. Probiotics are the living microorganisms that are found in the human gut. In 1989, the concept of probiotics was coined by Fuller as, "a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance"[1] In scientific literature, the Lactic acid bacteria (LAB) is generally been reported as probiotics[2].

Probiotics play a very crucial role in proper functioning of our gastrointestinal system and forms an integral part of the humanbiological system[3]. It helpsin maintaining the healthy intestinal microbiota and thereby reducing the population of pathogenic bacteriain the intestine[4]. The literature reports suggest that, amongst lactic acid bacillus,large number of genera having beneficial effects on humans are constituted within the phylum Firmicutes. The genera constitutes, *Carnobacterium, Enterococcus, Lactobacillus, Lactococcus. Lactospharea, Leuconostoc, Melissococcus, Oenococcus, Pediococcus, Streptococcus,Tetragenococus, Vagococcus* and *Weissella*[5]. The intake of LAB in recommended dosage has shown to exert beneficial effects on host such as anti-inflammatory, immunomodulatory, antidiabetic etc,[6–8] even the non-viable microorganisms or microbial cell extracts have also shown beneficial effects on host [9].

II. Characteristics of lactic acid bacteria

The natural source for the indigenous microflora of lactic acid bacillus constitutes raw milk, yogurt etc. The first isolation of LAB has been reported from milk by Élie Metchnikoff[10]. Thereafter,these bacteria have been isolated from a variety of naturally fermented food products such as meat, milk products, vegetables, beverages and bakery products[11]. Besides this, the occurrence of LAB has also been noted from water, soil, sewage,manure, humans and animals[1,12]. LAB are categorised as 'Generally Recognized as Safe' (GRAS) organism, which are cocci or rod shaped, Gram positive, catalase negative and fastidious organisms. They have theability to convert carbohydratesinto energy and lactic acid via fermentation. LAB cultures are extensively been used in the food industry as starter cultures and have shown immense potential in determining the texture, flavour and nutritional value of feed and food products[13].

Mostly,LAB cultures are known as aerotolerant anaerobes as thesegrow under anaerobic conditions. On the other hand, these can also grow in the presence of oxygen since they possess peroxidase enzymes which protect these cells against free radicals [14].

Lactic acid bacteria (LAB)are classified intotwo major groupson the basis of the product formed during glucosefermentation. The homofermentative bacteria, ferment glucoseto produce two moles of lactic acid generatinga net of 2ATP per moles of glucose metabolized. In case of heterofermentative metabolism, 1 mole of glucose is metabolized to produce1 mole of lactic acid, 1 mole of ethanol and 1 mole of CO_2.The LAB containing products possess aroma and flavour due to the small organic compounds produced by these bacteria[15].

The lactic acid bacteriais widely used for the production of a variety of fermented food products such as cheese, chocolate, pickles, beer, sourdough bread etc. These bacteria lowers the pH of the food product thereby arresting the growth of harmful bacteria and preserving the nutritive value of food products which thereby increases theirshelflife[16]. Bacteriocins, the compoundproduced by LAB have the ability to penetrate the outer membrane of Gram negative bacteria and inhibit their growth. Apart from bacteriocins, the lactic acid bacteria produces compounds such as Nisin that have been approved by Food and Drug Administration(FDA) for use in the foodstuffs like the Nisin variants A and Z[16].The Nisins posses antimicrobial properties against spore forming diseasecausing gram negative bacteria like *Bacillus* sp. and *Clostridium* sp.The possession of these antimicrobial substances (*I.e.* bacteriocins, hydrogen peroxide,polysaccharides etc.) led to the inhibition of the growth of pathogenicorganisms[17]. The bacteriocins are protein moleculesthat possess anticholesterol and antitumor properties[15]. Reportssuggest that, highest bacteriocin production in LAB occurs during end of the exponential and early stage stationary phase [18].

The antimicrobial peptides secreted by LAB have known to possess probiotic properties that preserve food as well as beneficial for human health [19,20]. The *Lactobacillus* genus comprises of rod shaped, non spore forming, non pigmented, catalase negative and microaerophilic to strictly anaerobic bacteria,which are widely used in the production of fermented foods. LAB cultures grow optimal in temperature range of 30°C to 40°C, with an optimum pH range between 4.5-6.5[21].

Classification: Lactobacillus species can be divided into three groups on the basis of their metabolism[22].

1. **Obligate homofermentative:** *L.acidophilus, L.bulgarigus, L.salivarius, L. helveticus* etc.
2. **Facultative heterofermentative:** *L. casei, L. plantarum, L. curvatus, L. sakei*
3. **Obligate heterofermentative:** *L. brevis, L. buchneri, L. fermentum, L. reuteri etc.*

The LAB can be identified on the basis of the morphological characteristics such as colony color, size, margin andits shape. The various biochemical characteristicsforLAB culture identification are the fermentation type, carbohydrate metabolism and production of isomers of lactic acid.The phenotypictests for the identification of Lactobacilli on the basis of the characteristics are respiratory type, motility, growth, growth in sodium chloride, and temperature.

Identificationof LAB cultures on the basis of morphological and biochemical tests could further be authenticated through certain specific tests such as milk coagulation ability and enzyme specific testslike arginine dihydrolase and sugar utilization pattern tests which when subjected to software named PIBWIN gives tentative as well as confirmed identification of a lactic acid bacteria by matching it with Bergey's Manual of Determinative Bacteriology[23]. Few other important methods for the detection and characterization of LAB strains are protein fingerprinting using SDS gel electrophoresis, 16S ribosomal RNAsequencing analysis, Polymerase Chain Reaction (PCR), Restriction Fragment Length Polymorphism (RFLP) and Pulse-field gel electrophoresis (PFGE) [24,25].

III. Lactobacilli bacteria in benefiting human health

The health benefits of LAB in humans are well known. The gut bacteria interact directly with the host cells and exert their positive effects. LAB has a major role in the treatment of intestinal disorders, sincethese cultures enhances immune response due to serum antibodies, IgG and secretory IgA and IgM [26].

Thereare several mechanismswhich prevents the attachment of harmful bacteria on intestinal epithelium. Lactobacilli led to the fermentation of substratessuch as lactose, biogenicamines and other compounds into short chain fatty acids, organic acids and gases [28]. Theproduction and secretion of substances by LAB cultures such as bacteriocins and organic acids that are antimicrobial agents [3] adhere to intestinal epithelium after competing for binding sitesand thereby eliminates harmful bacteria [27]. A study for a period of two years was carried out which showed that, the micro flora of GI tract in case of infant is highly variable and changes rapidly in the first five months of infants life, while, in case of adults, the lactobacillus community is more stable [13].

The intestinal *Lactobacilli* constitutes an important effective mechanism for the metabolism and detoxification of foreign substances entering the biological system[29].

The functions of Lactobacilli are strain specific and results in different mechanisms to produce beneficial results for health. In available literature some additional information is present on the production of bacteriocin by probiotic bacteria that target pathogenic bacteria in vitro [30]. Reutericyclin, an antibiotic produced by *Lactobacillus reuteri* LTH2584, is reported to inhibitsbroad spectrum of bacteria [31],its biological activity is similar to that of Nisin. The colonized*L.reuteri* cells were recovered from the intestine of reconstituted lactobacillifree (RLF) mice in high cell counts. This strain has been investigated for its antibacterial role in the habitats of intestine[32]. Below in Table-1 is the list of probioticcultures of lactic acid bacteria and their administrative form, in line with clinical trial evidences.

Table 1. List of selected health-promoting lactic acid bacteria with clinical trail evidence

Probiotic cultures used and its form	Participants, age (yr),Gender,Case/Control (n)	Observations	Ref.
Probiotic Capsule: *Lactobacillus acidophilus,Lactobacilluscasei,L. rhamnosus, L. bulgaricus,Bifidobacterium breve,Bifidobacterium. longum,Streptococcus thermophilus*, FOS	T2DM, 35–70 yrs Both, 27/27	Reduces FBS, HOMA-IR, HbA1C,hs-CRP and IncreasesFSI,Improves oxidative stress biomarkers	33
Probiotic capsule: *Lactobacillus acidophilus, L. reuteri, L. fementum, Bifidobacteriumbifidum,*	DN (T1DM & T2DM), 45–85, NA, 30/30	Reduces FBS, HOMA-IR, HbA1C, hs-CRP, BUN, Cr,urine protein, inflammatorymarkers, oxidative stress biomarkers	34
Probiotic honey: *Bacillus coagulans* T4	DN (T1DM & T2DM), 45–85, NA, 30/30	Reduces FBS, HOMA-IR, lipid profile,hs-CRP, BUN, Cr, urineprotein, inflammatorymarkers, oxidative stressbiomarkers	35
Probiotic capsule: *Lactobacillusacidophilus, Bifidobacteriumbifidum, Lactobacillus casei, Lactobacillus fementum*	DF (T1DM & T2DM), 45–85, both, 30/30	Reduces FBS, HOMA-IR, lipid profile,hs-CRP, HbA1C, woundcharacteristics, inflammatorymarkers, oxidative stressbiomarkers	36
Probiotic capsule: *L. acidophilus, B.bifidum, L. casei, L.fementum*	T2DM, 40–85, Both,30/30	Reduces FBS, HOMA-IR,lipid profile,hs-CRP,inflammatory markers, oxidativestress biomarkers	37
ProbioticCapsule: *Lactobacillusacidophilus,Lactobacillus casei,L. rhamnosus,Lactobacillus bulgaricus,Bifidobacterium breve,B. longum,S. Thermophilus*, FOS	T2DM, 30–75 yrs. Both, 30/30	Reduces FBS, HbA1C,Increase HDL-Cholesterol,no significant changes HOMA IR, TC & TG	38
Lactobacillus casei	T2DM,30–60 yrs. Both, 20/20	Reduces FBS,HOMA-IR,Fetuin-A and Increases insulinSirtuin1	8
*Lactobacillusrhamnosus*GG *Bifidobacterium lactis* Bb-12	Prevention is partiallydue to serum antibodiesIgG and secretory IgAand IgM immuneresponse enhanced byprobiotics	Prevention ofallergies and atopiceczema	39
Lactobacillus rhamnosus GG *L. reuterii, Enterococcus faecium*	Reinforcing the localimmune defence throughspecific IgA response torotavirus and pathogens	Control viral,bacterial andantibiotic associateddiarrhea	40
Lactobacillusrhamnosus GG	Hydrolysing lactose intoglucose and galactoseand forming the physicalappearance of milk intoa thick substance, suchas yogurt, that passesthrough the GI tractslowly, reducing thelactose pulse in thecolon	Relieves lactoseintolerancesymptoms	40–42

IV. **Current scenario of the health effects of lactobacillus bacteria**:

It has been observed that, the probiotics exert beneficial effects in the biological system[43]. Recently, a large number of studies have been reported emphasizing probiotic properties of LAB[44]. The naturally fermented drinks are a rich source of lactic acid bacteria, such as fermented milk available in Indonesia named, dangke and dadih, contains lactic acid bacteria belonging to the species *Lactobacillus plantarum*, *Lactococcus lactis susp. Lactis* and *Enterococcus faecium*. These bacteria were evaluated for their probiotic potential where it was found that *Lactobacillus plantarum* S1.30 isolated from dadih showed positive effects *in vitro*, such as bile salt resistance, low pH tolerance, antimicrobial activity, antibiotic susceptibility and adherence to CaCo-2 colon cancer cells [45,46]. The Brazilian Kefir is also a rich source of lactic acid bacteria (LAB), and thirty-fourLAB isolateswere identified and characterized from Kefir. The isolated species belonged to *Leuconostoc* *mesenteroides*, *Lactococcus lactis* and *Lactococcus paracasei*. *L. paracasei* MRS59 showed adhesion to human Caco-2 epithelial cells thereby confirming their anti cancerous properties [47]. *Lactobacillus plantarum* YS2 (LP-YS2) was isolated from yak yoghurt and was studied for its probiotic properties. It showed high acid resistant activity when compared to *Lactobacillus bulgaricus* [48].The traditionally fermented Xinjiang cheese serve as a great source of lactic acid bacteria such as *Lactobacillus rhamnosus*, *Lactobacillus helveticus*, and *Enterococcus hirae*. *Lactobacillusrhamnosus* was found to be most effective probiotic as it degradecholesterol and triglyceride up to 50.97% and 28.92% respectively [49]. *L. rhamnosus* GR-1 in combination with *Streptococcus thermophilus* and *Weissella cibaria* N20 when consumed ondailybasis reduces the urinary concentration of aflatoxin[50]. The binding of *Lactobacillus rhamnosus* GG to aflatoxin B1, reduces intestinal absorption thereby reducingits pathogenicity, researchers also demonstrated its ability to prevent the growth of urogenitalinfectiousbacteria and fungi. The *Lactobacillus* strains such as *Lactobacillus rhamnosus* 4B15 and *Lactobacillus gasseri* 4M13 are known to possess antioxidant properties along with the ability to inhibit Nitric oxide (NO) production, lowering cholesterol and α-glucosidase activity inhibition[7]. Amongst the different strains *Lactobacillus rhamnosus* NCDC17 was found to show antimicrobial activity, bile salt tolerance and cell surface hydrophobicity [51]. The *Lactobacillus rhamnosus* L60 *and Lactobacillus fermentum* L23 are known to produce secondary metabolites such as bacteriocins, organic acids and hydrogen peroxide. The fungal growth of aflatoxin producing strains were inhibited completely by *L. rhamnosus* L60 *and L. fermentum* L23 [32]. The probiotic strains *L.acidophilus*, *L.rhamnosus* and *L.casei* exhibits acid resistance and tolerance of bile salts as compared to other lactic acid bacteria (LAB).*L. rhamnosus* IMC501and *L. paracasei* IMC 502 have shown protective effects against *Candida albicans*[52]andmultidrugresistance gram-negative bacteria[53],these strains showed high adherence to HT-29 cells and exhibit synergistic effects, these strains also showed resistance to antibiotics such as vancomycin and kanamycin etc. during *in vitro* studies[54]. Furthermore, probiotics have the ability to improve the protein as well as some minerals like calcium, iron, manganese, and copper absorption from the gut by making acidic pH of the intestine; regulate the production of mucous, regulate epithelial functions and increase intestinal motility[55].

V. Market scope of probiotics

Earlier in 2015, we have reported that, the probiotics marketed in India for Indians are mostly non-indigenous strains and their efficacy is debated, further we also reported that, the demand of probiotic food alone in global market was 27.9 billion USD in 2011 and is increases at a 6.8% CAGR by 2016period[56].

In the current globaleconomic scenario, the probiotic market is estimated to grow with approx 7% CAGR during 2018-2026 period. The growth of the probiotic market is majorly driven by the following factors:

1. Awareness amongst the health conscious consumers/public
2. Rise in demand for functional food products
3. Investment in the research and development sector especially in nutraceuticalfor functional foods
4. Rise in disposable income of developing nations
5. The awareness regarding health benefits of probiotics has been a major driver in the growth of the probiotics market. The probiotics are divided into different categories on the basis of the application

a) Food and Beverages
b) Dietary supplements
c) Animal feed products

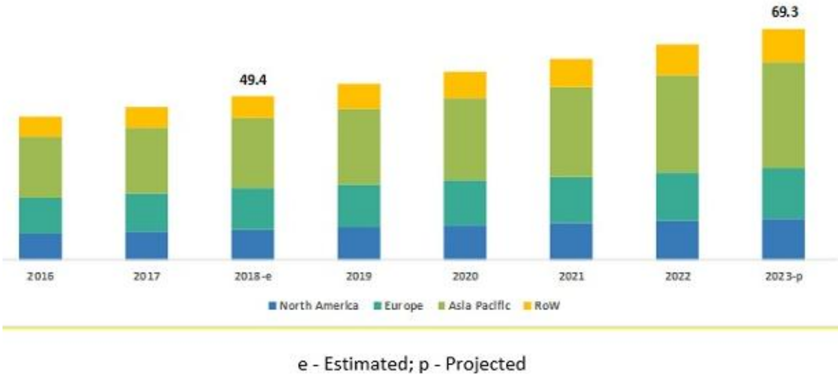

Fig.1: Probiotics Market, (Source: www.marketsandmarkets.com)

According to “MarketsandMarkets”, the probiotics market to be estimated at USD 69.3 billion by 2023, recording a CAGR of 7.0% (Probiotics Market: Published Date: Jan 2019, Report Code: FB 2269). The consumption of probioticsupplemented food has been knownto ameliorate digestive ailments, bloating and promotes strength of the immune system. The animal feed products containing probiotics market has shown a lot ofpotential in terms of growth, since a ban was imposed on synthetic antimicrobial growth promoters (AGPs) in Europe in 2006. So, now The antimicrobial drugs are not being promoted to increase the production of meat, dairy products and the growth of livestock. This paves the path for probiotics as a new entrant in the field of animal feed.

On the basis of the regional predominance of probiotics, it is the Asia Pacific region, which has shown promising market for probioticsdue to public awareness amongst these regions a high demand for functional foods as well as for dairy products has also been notedin this region.

VI. Conclusion

The Lactic acid bacteria especially bacteria of *Lactobacillus* genera shows a promising future in terms of their use as probiotics. With this in view, large number of health benefits have been explored for *Lactobacillus* bacteria, and their production as functional foods provides a great scope for the probiotics market in near future.

VII. References

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