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# EXOPOLYSACCHARIDE AS ANTIVIRAL, ANTIMICROBIAL AND AS IMMUNOSTIMULANTS: A REVIEW

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## Abstract

Microbial exopolysaccharides are defined as a polymer of biologically active substances for pharmaceutical, medicinal uses and various biological characters can be used as a viscosifier, texturizer, emulsifier and agent for syneresis-lowering, in addition to that caused by their rheological, pseudo-plastic actions and capacity of water binding, which have revealed requirement in the food industry. Probiotics -derived exopolysaccharides is of great interest. It is enhanced with biocompatibility and being non-taxability and GRAS. This makes them an option of first-line in the cure of different diseases which are chronic involving tissue engineering, a system of drug delivery, and the ability of disease healing if compared to the algal-based and plant polysaccharides. In the present review, we summarized the classification, types, importance, biological and genetics synthesis of exopolysaccharide. It also includes the biological importance exopolysaccharide for the prevention or treatment of virally-induced infectious diseases, as antiviral, antibacterial, antifungal, antioxidant, antitumor, drugs, and its target mode of action.

***Key words :*** Exopolysaccharide, Antiviral, Antimicrobial, Immunostimulants.

## Introduction

Exopolysaccharide (EPS) are polysaccharides that are long-chain formed extracellularly primarily by microalgae and bacteria especially probiotic. Probiotics are generally subjugated in traditional and medicine, dairy products, in addition to in biotechnological and processes of industrial fermentation as well recognized inoculum culture (Mahdi *et al.,* 2017; Rather *et al.,* 2013 and Kim *et al.,* 2013). Probiotics show significant implication with rising numbers of health complications includes the intestinal tract microflora (Park *et al.,* 2010), along with a production capacity of exopolysaccharides which are functional (Kim *et al.,* 2007). As well as, a vital function of probiotics which are noticed in the fermentation of food, since probiotic-resulting in foods that are fermented shows a grown rate of hygienic security, attractive sensory, and storage stability properties (Rather *et al.,* 2014).

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The risk of viral infection has dramatically increased owing to changes in human ecology. However, the efficacy of vaccines and remedies for infectious diseases is limited by the high mutation rates of viruses, especially, RNA viruses. The effectiveness of several probiotics for the prevention or treatment of virally-induced infectious diseases is increased (Kanauchi *et al*., 2018 and Mahdi *et al*., 2020).

Probiotics traditional differentiation in species can be skilled via their discovery and identification as important alternatives to detect their procedures of quality control in products of dairy (Bae *et al.,* 2005 and Koh *et al*., 2004). Because of the various microbial exopolysaccharides to work like a viscosity, texturizer, emulsifier and agent of syneresis-lowering, in addition to that caused by their rheological, pseudo-plastic actions and capacity of water binding, which have revealed demanding Industrial require particularly in industry of food (Kodali *et al.,*2009). A broad variety of dissimilar

probiotics induce different sorts of structured chemically types of exopolysaccharides. As no definite descriptions are existing on the dangerous results of probiotics until now, these can be classified as GRAS (Generally Regarded as Safe) bacteria (Yadav *et al.,* 2011 and Mahdi 2017). Exopolysaccharides Production is regarded as a sole characteristic of probiotics in the shape of starter culture for the fermentation of products of milk. As well as, EPSs show many useful health effects in humans specifically in the curing of bowel diseases, tumor, gastrointestinal diseases (Gibson and Rastall, 2003).

Probiotics -derived exopolysaccharides, although induced in a very low amount in the yogurt which is fermented, plays a vital part in improved creamy and smooth texture of yogurt, very important one aspect of quality of yogurt (Feldmane *et al.,* 2013). Also, different health benefit credits of exopolysaccharides which are derived from probiotics are definite before either as food fractions which are non-digestible (Patel and Prajapati, 2013) or becoming candidates which are natural to the treatment of immune modulation, ulcer and cancer accompanying potent capacity to decrease levels of blood cholesterol (Madhuri and Prabhakar, 2014). Probiotics plus their exopolysaccharides which are derived are having major therapeutic and economic potential for the progress of functional food products which are nutrient-rich having human health which is prolonged. Exopolysaccharides interestingly play a significant part by interaction with the system of human immunity ration as a critical part of functional foods in addition to supply bowel disease healing effects (Vinderola *et al.,* 2006). Very few chosen probiotics, the [roduction of exopolysaccharides is in the shape of fructans or glucans by using glycosyl and sucrose transferase enzymes (Tieking *et al.,* 2005).

Exopolysaccharides demonstrate a potential capacity for colonization of teeth surfaces by species of *Streptococci* (Sims *et al.,* 2011). Exopolysaccharides derived by probiotics in a composition may be present as a sole sort of monomer of sugar (homo-polysaccharides) or maybe in a combination of numerous monomers types (hetero-polysaccharides). On the other hand, differentiation in the composition of sugar, length of chain, branching degree, and linkages in sugar in the exopolysaccharides formed via various probiotics which are observed in health beneficial and rheological termination (Ruas-Madiedo *et al.,* 2002). Exopolysaccharide can be derived into homo-exopolysaccharide and hetero-exopolysaccharide depending upon their chemical composition (Harutoshi, 2013).

Advances in Biotechnology are led to biopolymers derived by probiotics or molecules of exopolysaccharide discovery with complete proofs of medical and industrial usefulness to human beings. Enhanced with biocompatibility, being non-toxic ability and GRAS of exopolysaccharides derived by probiotics which makes those a first-line option in the cure of different diseases which are chronic involving tissue engineering, a system of drug delivery, and ability of disease healing in comparison to the polysaccharides which are algal-based and plants (Otero and Vincenzini, 2003). Studies have defined that some biopolymers may be decomposed *in vivo*. Since, there may be a feasible substitute to synthetic biopolymers for the use in replacement of tissue and strategies of controlled drug release (Rehm, 2010).

The present study gives new advancements on the acquaintance of functional possessions of Probiotics-derived exopolysaccharides, their chemical characters, characterization of molecules, and genetic construction. It also summarized its application in the industrial and medical sectors with particular prominence on their projection in the future.

**Exopolysaccharide from lactic acid bacteria**

Exopolysaccharide (EPS) are polysaccharides which are long-chain formed extracellularly primarily by microalgae and bacteria. EPS is consisting of repeating branched units of sugars or derivatives of sugar. These units of sugar are chiefly N-acetyl glucosamine, rhamnose, N-acetyl galactosamine, galactose, glucose, mannose in varying ratios. Not EPS are enduringly joined to the microbial cell surface and are generated into their environments as loose slime during growth. This differentiates them from the structures like capsular polysaccharides, they live permanently joined to the surface of the microbial cell. A critical role is played by EPS in the microbes defense from difficult conditions as drying, shortage of nutrients, antagonists, bacteriophages, toxic compounds, osmotic stress. It also involved in the firm anchorage and initial adhesion of the bacteria to solid surfaces, sequestration of cations, the formation of biofilm, pathogenicity, and cellular recognition (Patel *et al.,* 2012). Lactic acid bacteria (LAB) are gram-positive, generally non-motile, catalase-negative, cocci, or non-spore-forming rods. The LAB may only get ATP by using fermentation, generally from sugars. These organisms are tolerant anaerobes (Michaela *et al.,* 2009). Lactic acid bacteria refer to a large number of bacteria. It produces lactic acid like a by-product after digestion of carbohydrates. Accumulation of lactic acid to food fermentation and LAB are accomplished of survival in low pH (acidic) environments. LAB are prevalent in the environment in

the digestive system and are useful as probiotics. Which are amid the most significant classes of microorganisms utilized in fermentation of food, which contributes to the texture and taste of products which are fermented and which inhibits the spoilage of food caused due to another bacteria (Nordqvist, 2004). A broad variety of various lactic acid bacteria produces various sorts of chemically-engineered shapes of exopolysaccharides (Yadav *et al.,* 2011).

Classification of LAB genera was depended on morphology, mode of glucose fermentation, and range of sugar consumption (Jin *et al.,* 2009). For some of the newly described genera, it depends on the growth at varying temperatures and produced lactic acid configuration, capability for growth at high concentrations of salt, and alkaline or acid tolerance (Pilar *et al.,* 2008).

Identification of exopolysaccharides as potentially practical and polymer of biologically active substances for pharmaceutical, medicinal uses, and various biological characters (Liu *et al.,* 2004). Newly discover lactic acid bacteria (LAB) have arisen engrossment for their capacity of secretion of extracellular polysaccharides. These 'exopolysaccharides' (EPS) or extracellular polysaccharides have huge commercial value because of their industrially functional Physico-chemical characters. LAB's Capacity for production of a wide range of EPS having different functionality and composition is increasing their applications in industry. The different EPS utilities are relied on their composition, linkages type present, branching degree plus molecular weight. LAB derived EPS plays a vital role in enhancing the mouthfeel, texture, rheology of formulations of fermented food, and providing advantageous physiological effects on the health of human beings, for example, immunomodulating bioactivity, anticarcinogenic, antitumor activity (Patel *et al.,* 2012).

**Chemical composition and Classification of exopolysaccharides**

From lactic acid bacteria, the microbial exopolysaccharide may be separated into two large groups such as hetero-exopolysaccharides and homo-exopolysaccharides. The classification of exopolysaccharides which are derived from lactic acid bacteria is summarized in Fig. 1.

In bacterial cells, homo- and some hetero-polysaccharides are secreted and synthesized into the extracellular environment. Even though homo-polysaccharide synthesis occurs cells outside after release of specific enzymes (Donota *et al.,* 2012). Homo-exopolysaccharides are consisting of four sub-classes representing poly-Galatians, β -D-glucans, α-D-glucans, fructans (Harutoshi, 2013). The α-D-glucans, homo-exopolysaccharides for example dextrans created from *Leuconostoc mesenteroides* sub sp. *mesenteroides* and *L. mesenteroides* subsp. *dextranicum*, from *L. mesenteroides* alternans and *Streptococcus mutants* and *S. sobrinus* mutants, are mainly composed of α-1,6 and α-1,3-linked molecules of glucose with varying branching degrees at 3rd position. Even though it may be present at 2nd or 4th position but rarely (de Vuyst and Degeest, 1999; Harutoshi, 2013). homo-exopolysaccharides for example β-D-glucans generated by *Streptococcus* and *Pediococcus* species are consisting of molecules of glucose linked to β-1,3 residual position along with β-1,2 position branching.

Mono-polysaccharides, fructans generated from *Streptococcus salivarius* are joined to molecules of β-fructose at the β-2,6 residual position along with β-2,1-branching at site O1. The polygalactans sorts of homo-exopolysaccharides are consisting of the same sugar units which are repeating having the same structures od chemicals and are joined together with different glycosidic bonds. The hetero-exopolysaccharides are constructed by the thermophilic and mesophilic lactic acid bacteria. The chief mesophilic lactic acid bacteria represent *L.rhamnosus*, *L. lactis* sub-sp. *cremoris*, *L. lactis* sub-sp. *lactis*, *L. casei, L. sakei,* and main thermophilic lactic acid bacteria include *L. acidophilus*, *S. thermophiles, L. delbrueckii* sub-sp. *bulgaricus*, *L.helveticus*. Selected lactic acid bacteria-derived exopolysaccharides Sugar linkage pattern is given in fig. 2.

**Homo-exopolysaccharide (HoPS)**

The lactic acid bacteria are having the capacity to create exopolysaccharide either as a cell adhered EPS in a capsular shape or as environmental secretion (Harutoshi, 2013). Homo-exopolysaccharides (HoPS) consists of one type of monosaccharide like β -D-glucans, α -D-glucans, polyglactin, and fructans,.While, hetero-exopolysaccharides are produced of dissimilar types monosaccharides represented L-rhamnose, D-galactose, D-glucose, and their derivatives (Harutoshi, 2013). Most groups of LABDEP are represented by α-glucans for instance mutants and dextrans produced by *S. mutants and* L. *mesenteroides* respectively; while fructans, for example, levans are induced by *S. salivarius* (Cerning, 1990). The enhanced salt components rate has revealed the negative impact on the formation of dextran in the medium of growth during sequential transformation. Also, species of *Leuconostoc*, for instance, L. *amelibiosum* may create dextran in the medium of growth when it is provided with tomato or orange juice (Vuyst and Degeest,

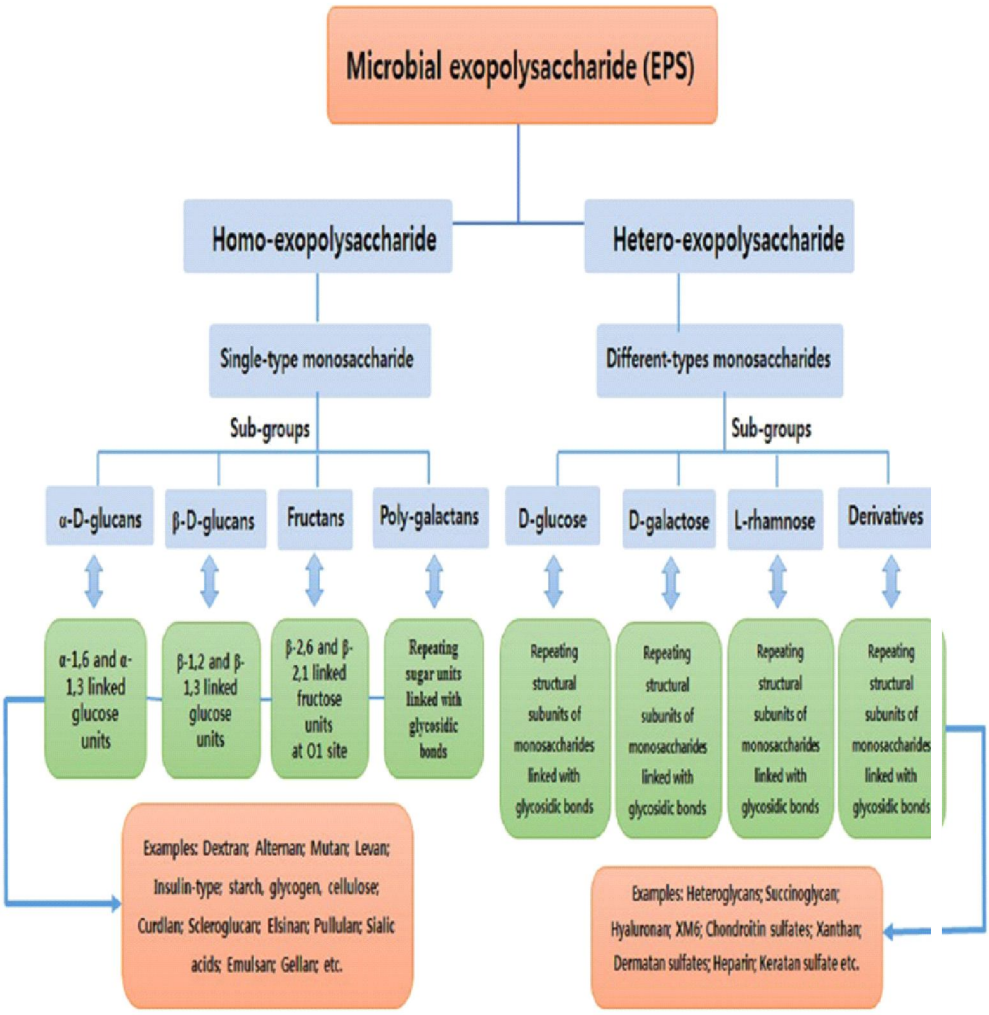


**Fig. 1:** Classification of bacterial exopolysaccharide.

1999).

Some *Streptococcus* species strains have revealed the capacity to structure mutant, a homo-exopolysaccharide glucan having α-1,3 linkages which are differing from dextran as they are highly water-soluble in addition to dextran having a high count of α-1,6 linkages (Cerning, 1990). Since mutant which is water-insoluble is useful to allow bacteria to attach on the surface of teeth, it is most extreme in tooth caries and dental cavities. Other glucan homo-exopolysaccharide, From *L. mesenteroides* NRRL B-1355 an alternate was firstly isolated with distinctive physical attributes having α-1,6 and α-1,3 alternate linkage, which makes it a component of high low viscosity and high water solubility potential to use it for industrial purposes, in particular in the food industry as a less viscosity texturizer (Harutoshi, 2013).

Levan a fructan homo-exopolysaccharide, is generated in the medium of growth which utilizes sucrose as a source of carbon, which is consisting of β-2,6-linked units of fructose having branching of β-2,1-linked (Harutoshi, 2013). For instance, insulin a fructan is consisting of β-2,1-linked sugar units of fructose also having β-2,6-linked branching. Before L. *reuteri,* L. *mesenteroides*, *S. salivarius* have revealed the capacity for synthesis of homo-EPS levan (Uchida, 1996). Fructan a homo-exopolysaccharide, also, is reported to be created from L.*sanfranciscensis* (Korakli *et al.,*2002). Chemical structures of some of the useful and industrial homo-exopolysaccharides are given in fig. 3.

**Hetero-exopolysaccharide (HePS)**

The biopolymer component of hetero-exopolysaccharide (HePS) demonstrates the varied extent of chemical separation between each other's, consist of repeating monomers of chiefly L-rhamnose, D-galactose, D-glucose (Harutoshi, 2013). The repeating structural subunits of monosaccharides and their chemical composition is used to form a polymer of hetero-EPS does not mean to confer specificity of species.

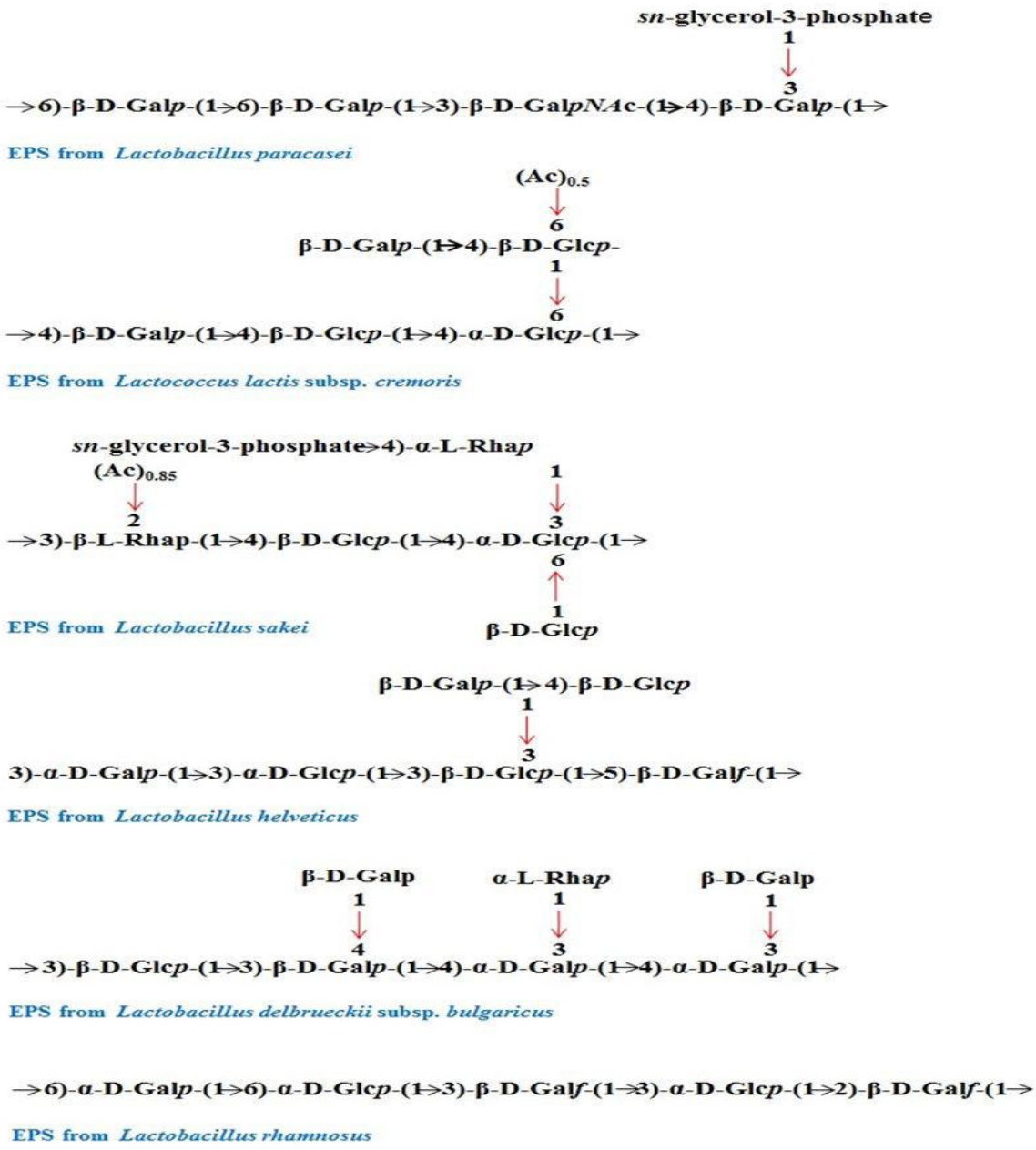


**Fig. 2:** Various EPSs Sugar linkage patterns isolated from different lactic acid bacteria (LAB) (Adopted from Landersjo *et al*., 2001).

Many species of bacteria like *Lactococcus lactis, Lactobacillus helveticus, Streptococcus thermophilus, L.delbrueckii* are well documented with a capacity to create hetero-exopolysaccharides (Mozzi *et al.,* 2006). As well as, lactic acid bacteria having a capacity of homo-fermentation are well recognized for their capability to make hetero-EPS, while, strain L. *fermentum with* a hetero-fermentative capacity is found to create exopolysaccharide having confirmed the determination of chemical nature (Leo *et al.,* 2007).

Normally, the lactic acid bacteria produce a large diversity of hetero-exopolysaccharides. However, a wide extent of variations is exposed by them. A small number of microbial isolates *viz.,* L. *casei, S. thermophiles,* L.*plantarum,* L. *delbrueckii* sub-sp. *bulgaricus,* L. *lactis* sub-sp.*cremoris* are found to create 50-60, 50-350, 60-150, 80-600, and about 140 mg/L hetero-exopolysaccharide (Miyamoto, 2010 and Harutoshi, 2013).

The great quantity of recovery of exopolysaccharide is shown for L. *kefiranofaciens* WT-2B and L.*rhamnosus* RW-9595 by 2,500 and 2275 mg/L, respectively (Maeda *et al.,* 2004). Lactic acid bacteria have revealed low capability on the production of exopolysaccharide than the bacterias of industrial

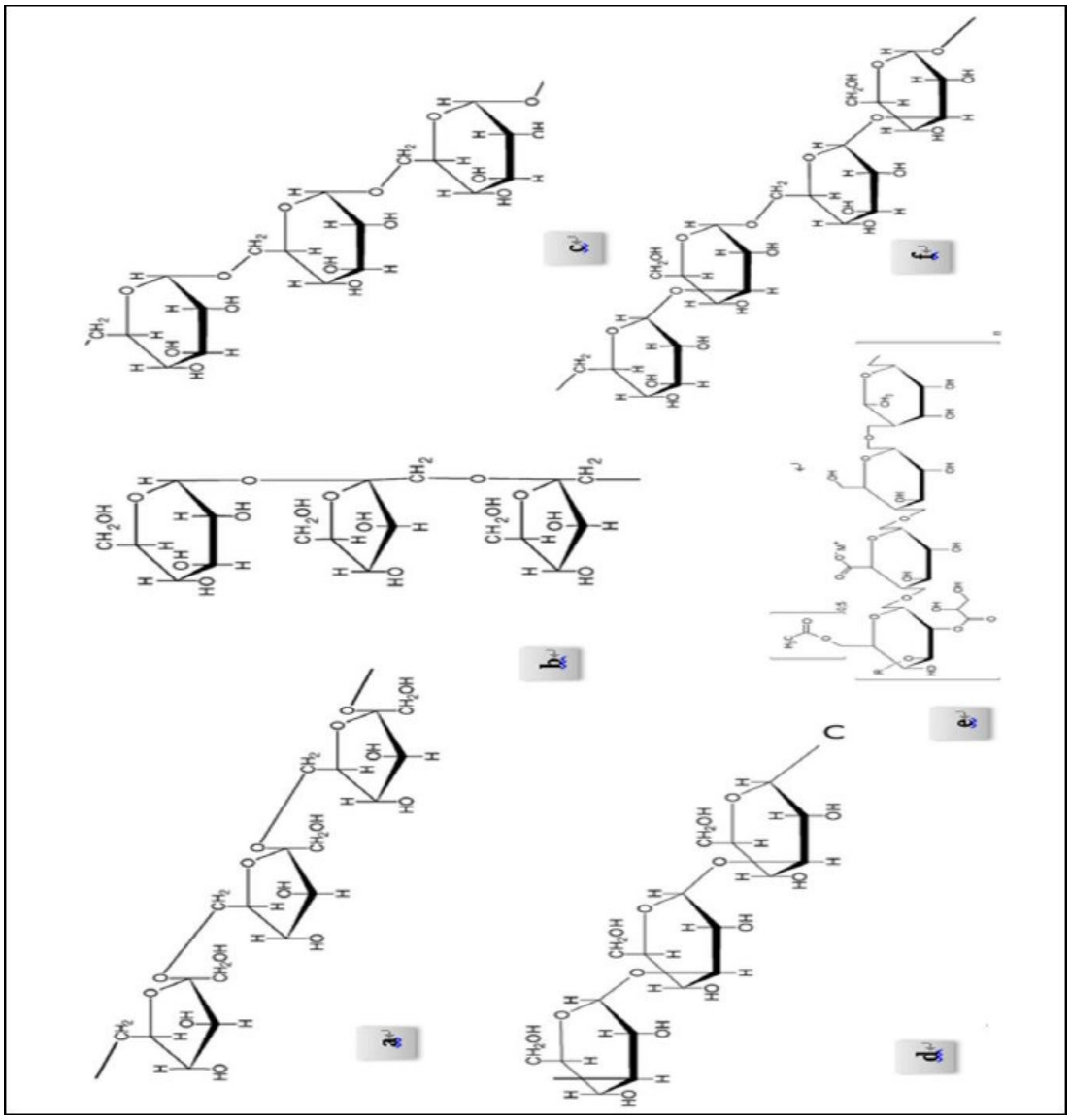

**Fig. 3:** Some selected industrial homo-exopolysaccharides chemical structures which are produced by lactic acid bacteria (LAB). a: Levan (fructans); b: Insulin-type fructan; c: Dextran (glucan); d: Mutant (glucan); e: Alternan (glucan); f: Gellan.

meaning for example *Xanthomonas campestris* Produces 30-50 g/liter xanthan exopolysaccharide (Harutoshi, 2013). But, exploitation *in situ* is achieved successfully for exopolysaccharides creation from lactic acid bacteria, which makes them be the members of choice for exopolysaccharides enhanced production with increased yields, and their practical implementations in dairy, pharma, food industries. Beneficial hetero-exopolysaccharides chemical structures are shown in fig. 4.

**Biological synthesis and genetics of exopolysaccharide in lactic acid bacteria**

Lactic acid bacteria are having a capacity for synthesis of different polysaccharides classes and helping them in constructing the cell wall's vital components. Lactic acid bacteria construct polysaccharides using various known mechanisms of biosynthesis-related with component mechanisms of the cell wall (Welman and Maddox, 2003). The biosynthesis of exopolysaccharide represents a very complex process that involves the useful capability of a numeral of genes supporting the biosynthesis of EPS. These exopolysaccharide associated genes of chromosomal and plasmid regions especially in thermophilic and mesophilic lactic acid bacteria *i.e. Lactobacilli, Streptococcus, Lactococcus* encode different proteins and enzymes and significantly participates in the biosynthesis of exopolysaccharide (Vuyst and Degeest, 1999).

The protein-encoding genes essential for EPS production originates from a plasmid in the LAB strains

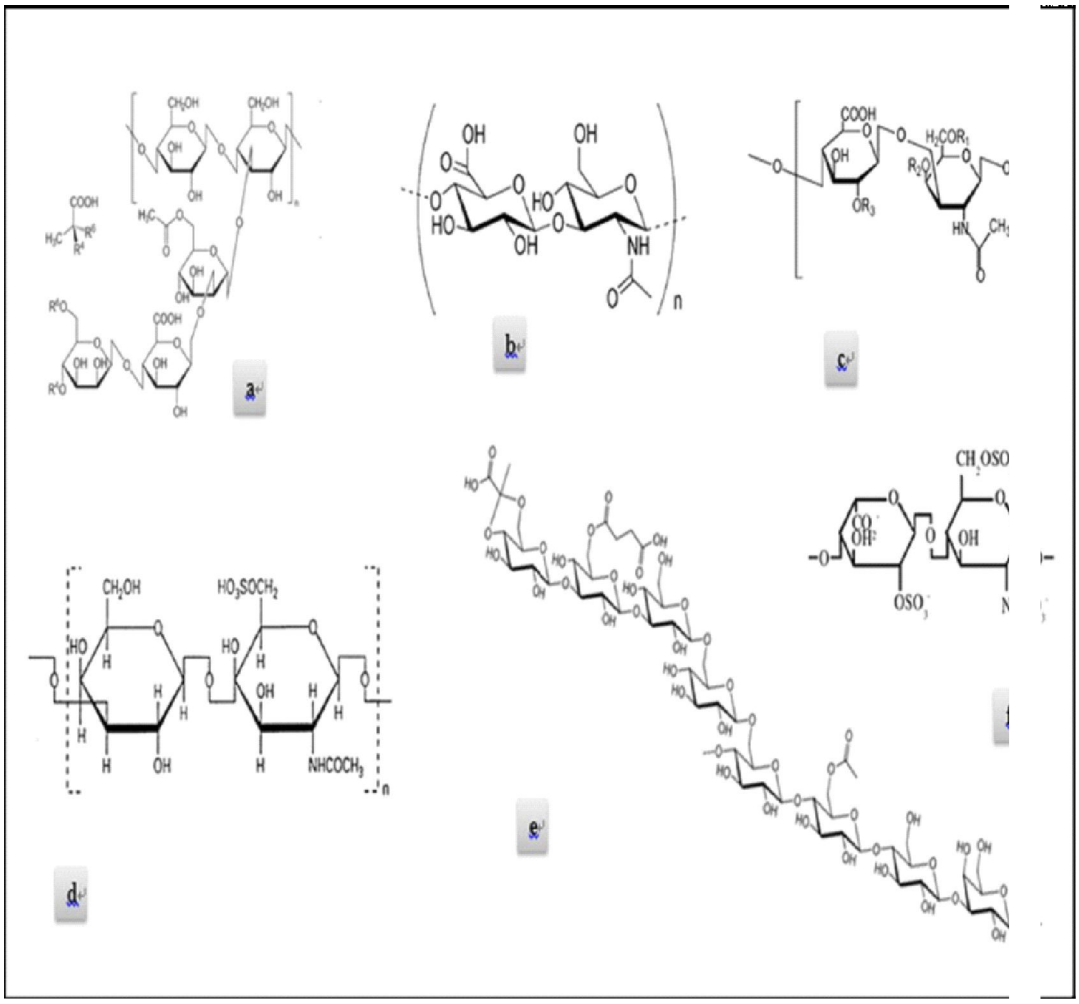

**Fig. 4:** Selected industrial hetero-exopolysaccharides produced by lactic acid bacterias (LAB) chemical structure. a: Xanthan; b: Hyaluronan; c: Chondroitin sulfate; d: Succinoglycan; e. Heparin; f: Kertan sulfate.

which are mesophilic similar to *Lactococcus* and located chromosomally in thermophilic strains of *Lactobacilli* and *Streptococcus*. Synthesis of HoPS by cell-wall bound or by extracellular glycan sucrases using substrate like sucrose. Glucosyl transferases transfer units of D-glucopyranosyl from sucrose to molecules that are acceptor, forms glycosidic bonds. The HePS biosynthesis mechanism is extra difficult in comparison with HoPS. The repeating units which form HePS are constructed in the cytoplasm by the use of precursor molecules like sugar nucleotides. Which by glycosyltransferases are translocated around the membrane of the cell where polymerization occurs via sugar nucleotide units sequential addition to the increasing chain attached to a carrier of lipid and at last, into the medium the EPS is released. The specific genes of eps and housekeeping are enrolled in the biosynthesis of sugar nucleotide. The pathway for EPS biosynthesis may be separated into four steps. These steps are (i) the reactions involved in the transport of sugar into the cytoplasm (ii) the production of sugar-1-phosphates (iii) coupling and activation of sugars and (iv) EPS export. Each of the steps is vital and may be employed to alter the quantity and EPS composition (Patel *et al.,* 2012).

## Importance of lactic acid bacterial exopolysaccharide

Molecules of microbial exopolysaccharides of the assorted composition of chemicals have revealed a multitude of useful and beneficial health impact having a huge variety of applications in agronomy, cosmetic, pharmaceutical, and food industries. Since products which are lactic acid bacteria based as certain different applications and functional properties of EPS may be used in the industries related to food having a reliable quantity of recovery and yields rate (Patel *et al.,* 2010, 2012).

Furthermore, the creation of exopolysaccharides from lactic acid bacteria may be feasible economically if creation parameters plus other components that influence the exopolysaccharide creation can be adjusted for

example cost-effective and cheaper substrates for fermentation circumstances (Patel *et al.,* 2010; 2012). Detailed information on current progress concerning different practical plus health useful characters of lactic acid bacteria and exopolysaccharides which are lactic acid bacteria-based is briefed in Table 1 and Fig. 5.

## Industrial importance

A numeral of vital applications of lactic acid bacteria-dependent exopolysaccharides are industrial for their exploitation of business, particularly having purposes of health profit and a considerable quantity of progress is made for the discovery of novel sorts of bacterial exopolysaccharides for commercial purposes (Kumar and Modi, 2009; AL Musawi *et al.,* 2017). furthermore, lactic acid bacteria-based exopolysaccharides have revealed extremely good impacts on the health of the gut, besides shows the immunomodulatory effect, cholesterol-lowering effect, antitumor effect (Madhuri and Prabhakar, 2014). The exopolysaccharide resulting from *Bacillus licheniformis* was reducing the herpes simplex virus-2 replication in the blood of the human periphery. The mononuclear cells show the antiviral result *in vivo*. Also, non-digestible oligosaccharides like prebiotics are found to invigorating the action and growth of health benefiting microorganisms represent in the colon *Bifidobacteria* and *Lactobacilli*, thereby demonstrate health profit in a host like a human (Harutoshi, 2013). Also, exopolysaccharides may ease the colonization of the gastrointestinal tract via *Bifidobacteria* and lactic acid

**Table 1:** Different EPSs list which is isolated from strains of LAB showing different functional properties.

| Name of EPS | Source strain | Application and biologicalImportance |
|---|---|---|
| Yakult | *Lactobacillus casei* | Upper respiratory tract infectionEpstein–Barr virus (EBV)Cytomegalovirus (CMV) |
| Reuteran | *Lactobacillus reuteri* LB121 *Lb. reuteri* ATCC55730 *Lb. reuteri* 35-5 | Used in bakery |
| Inulin | *Lb. johnsonii* NCC 533.*Streptococcus mutans*JC2, *Leuc. citreum*CW28 *Lactobacillusreuteri* 121 | Prebiotics, sustain cells of the gutmucosa and preventpathogens, drugdelivery targeted against cancer of the colon, fat substitute infood products |
| Kefiran | *Lb. kefirgranum Lb.parakefir Lb. kefir Lb.delbrueckii* sub sp.*bulgaricus* | Improve viscoelastic propertiesof acid milk gels, antimicrobial and woundhealing properties, ability to lower blood pressureand cholesterol in serum, capacity to retard tumorgrowth, enhance immunity of gut |
| New EPS | *Lb. johnsonii* | Immune-reactivity |
| OLL1073R-1 | *L. delbrueckii* sp. *bulgaricus* | Anti-IFV IgA, IgG1 in BALNK cell '!activity (IFV = influenza virus; BALF = bronchoalveolarlavage fluid) |
| Novel hetero-EPS | *S.phocae* PI80 | Emulsifying and flocculatingactivities, antioxidant, anti-biofilm |
| β-glucan | *Pediococcus damnosus*2.6 | Starter culture |
| New EPS | *Leuconostoc* sp. CFR2181 | Starter culture |
| Glucan | *Lactococcus lactis* 1.8 | - |
| α and β-glucans | *Lb. brevis* G-77 | Starter culture |
| Glucan | *Leuc. citreum* 1.10 | - |
| Hetero-EPS | *Lb. curvatus* 10 | - |
| Homo-EPS-3 | *Lb. plantarum*LP6 | Antioxidant |
| Neutral EPS | *Lb.fermentum*TDS030603 | - |
| EPS | *Lb. rhamnosus* KL37B | - |
| Kefiran | LAB | - |
| Neutral EPS | *Lb. johnsonii* 142 | - |
| Glucan | *Weissella cibaria* MG1 | Adjunct culture in cheese |
| ESP | *Lb. casei* C12 | Added culture in cheese |
| Glucan | *Lb. reuteri* ff2hh2 | Added culture in cheese |
| Glucan | *Lb. reuteri* cc2 | Adjunct culture in cheese |

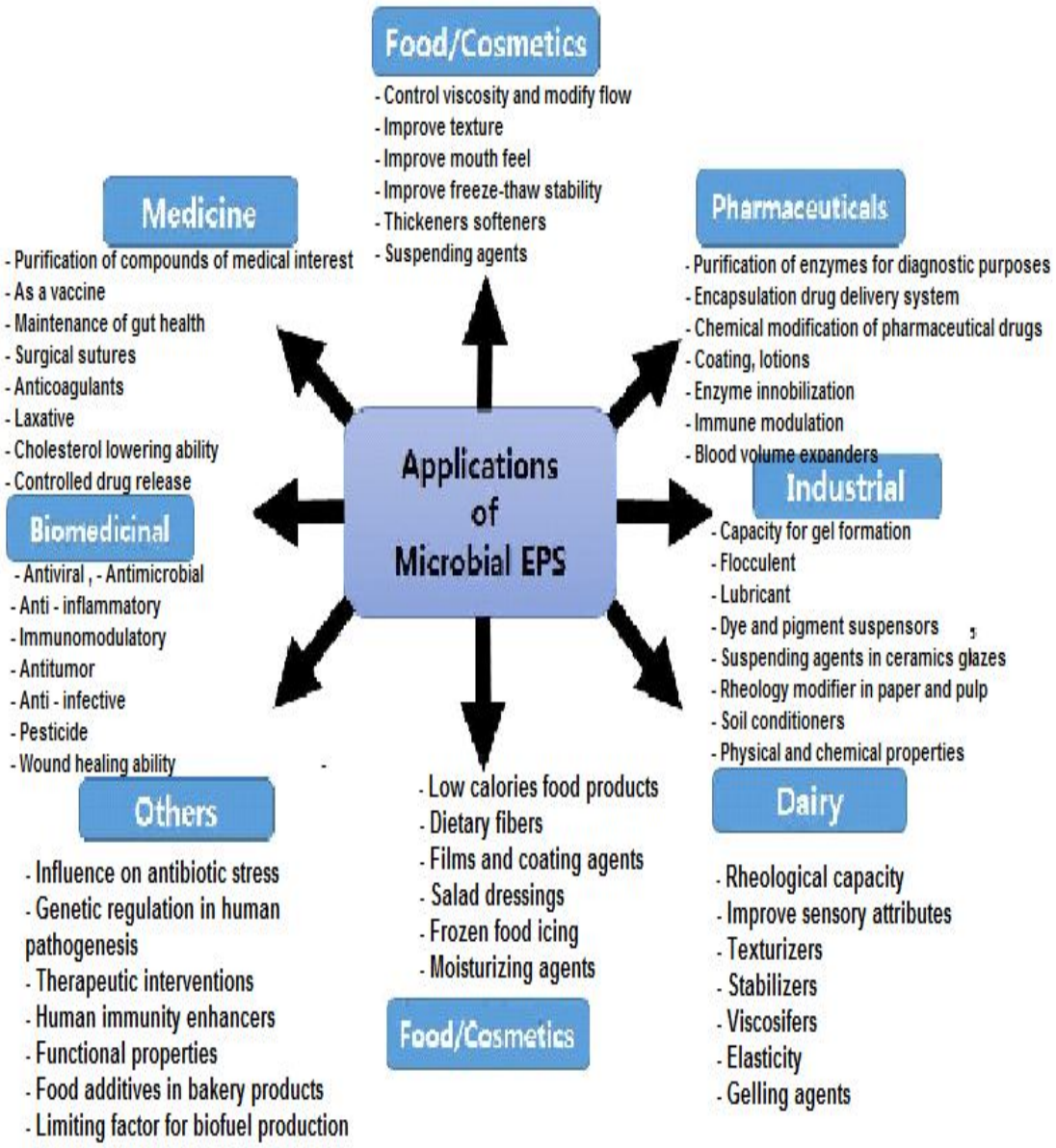


**Fig. 5:** Microbial exopolysaccharides (EPS) multifarious applications in different industries (Adopted from Bajpai *et al*., 2016).

bacteria because of their continued living capability in the tract of gastrointestinal. Further, exopolysaccharides render sole skin, involving the suffering of intolerance of lactose, enhancement of immunity against pathogens which are harmful and decrease of enzymes which are mutagenic for example β-glucuronidase, nitroreductase, β-glucuronidase (de Roos and Katan, 2000).

Also to exopolysaccharides capability as additives of food, which has revealed drugs improved specificity liberate in the colon cancer treatment. EPSs serving as a substrate for microflora if the colon, is also used profitably in the conjugation of the drug in addition to matrix and coating agents (Vandamme *et al.,* 2002). It is reported that little exopolysaccharides that are selected are found to show activity like B-cell mitogen accompanying a capability to alter the splenocyte and macrophages functions (Kitazawa *et al.,* 2000). An exopolysaccharide obtained from L. *johnsonni* separated from mice intestinal tract displaying a wide range of reactions of immunity (Gorska-Fraczek *et al.,* 2013).

*Lactobacilli* and *Bifidobacteria* granted to be microorganisms that promote health having the potential capability to reduce microorganisms which are pathogenic and stimulate the system of host immunity dramatically (Mitsuoka, 1992). commonly, gastrointestinal tract microflora is consisting of around 1014 colony-forming unit/g of various species of both useful and pathogenic bacteria with a varied range of compositional

differentiation together with the gastrointestinal (Mitsuoka, 1992). Gastrointestinal microflora equilibrium significantly impacts the health of the host regarding the smooth moment of a bowl, nutrient absorption, and tympanites flatulence (Harutoshi, 2013).

A numeral of factors may show a detrimental effect on the equilibrium of this microflora, for instance, biotic or abiotic stress, consumption of antibiotics, the natural aging process, infection, food poisoning. on the other hand, to reduce this effect of detrimental and to enable the appropriate growth and biological actions of these useful microflorae, supply particular ingredients in consumable food may supply important improvements (Harutoshi, 2013). Additionally, group of fructans, levans, are used in cosmetic, pharma and food industries with specific prominence in as a feed and food additives in the food industry when utilized with prebiotics (Kang *et al.,* 2009). Dextrans and levans also reveal hypercholesterolemic impact (Kang *et al.,* 2009).

Also, alginates are used in the food industry as thickening agents (Remminghorst *et al.,* 2009). Also, xanthan has shown its dominant capacity is used as a thickener, stabilizer, emulsifier, or viscosity in the food industry (Becker and Vorholter, 2009). Exopolysaccharides of bacterial origin are recognized for their rheological versatile properties making them suitable members to be used in the food industry particularly in yogurts assortment with an elevated rate of purity (Tiekingand Ganzle, 2005). As reported before, fructose-oligosaccharides, low sugar, and low-calorie components having different food industry applications with a non-carcinogenic status (Yun, 1996). Also dependent on the properties of prebiotic of fructose-oligosaccharides and inulin, they are used in industry related to food (Rhee *et al.,* 2002). furthermore, fructans, fructose polymers are having an important part in plant cellular pressure tolerance via preserving the stabilization of membrane (Oliver *et al.,* 2001). Also, dextran is having the capability to defend the strain of producer during adverse conditions or starvation, for example, an acidic or alkaline state (Kim *et al.,* 2007).

Since exopolysaccharides and fructose-oligosaccharides having the capability of protection of bacteria by difficult conditions of stress, they may have practical application in the industry related to food to defend lactic acid bacteria which are health benefits in food products which are fermented and starter cultures storage (Tieking and Ganzle, 2005). Furthermore, a numeral of another vital function of bacterial exopolysaccharides which are reported newly (Liangand Wang, 2015). Different exopolysaccharides guard bacterias against bacteriophage attack, phagocytosis, predation, dehydration, and the antibiotics' adverse effect and toxic components (Roberts, 1996). Appropriate lactic acid bacteria exploitation may be a face able approach to creating versatile polymers of exopolysaccharides for their actual applications (Frengova *et al.,* 2002). Microbial EPSs show various biological activities that represent cholesterol-lowering impact, antiulcer, antitumor, and antimicrobial impact (Welman and Maddock, 2003). Lately, coconuts wastewater utilization is exploited in Thailand for the exopolysaccharide production by use of a productive strain L. *confuses* TISTR1498 limiting the wastewater supply of coconut as a waste to an enlarged quantity (Seesuriyachan *et al.,* 2011).

Tieking and Ganzle (2005) described the helpful significance of lactic acid bacteria-derived exopolysaccharides in bread and dough which may impact their technical characters in different aspects for instance of rheological properties, a property of water absorption, during the frozen state the stability, staling, and loaf volume. As well as, exopolysaccharide polymers are used successfully in a backing approach to advance the bread texture, flavor, metabolic traits, and shelf life (Tieking and Ganzle, 2005).

A descriptive survey of the pharmacological and industrial usefulness of bacterial exopolysaccharides is shown in fig. 5.

**Antimicrobial importance**

It is observed that a sulfated polysaccharides polymer group has revealed major functional and biological properties (Ghosh *et al.,* 2009). As such polysaccharides that are sulfated, being a macromolecules show reproduce figures of substitution of sulfate on glycosaminoglycans there in membranes of the cell, they are found to be strong antiviral agents. Usually, polysaccharides that are sulfated characterize a composite polymer shape of varying composition. Although the chemical structure and activity association of sulfated polysaccharide is not studied properly, a numeral of such macromolecule also in raw forms has revealed strong antiviral impact (Ghosh *et al.,* 2009).

Microbicides are biocidal substances or compounds that decrease the microbes infectivity, for example, viruses or bacteria. Usually, microbicides can be applied rectally or vaginally and defend the user from infections that are sexually transmitted and caused by fungi which are pathogenic, bacteria, or viruses. Electrolytes of high molecular weight, polyanions, have been considered to be the most effective microbicides. A structural-activity association study of sulfated polysaccharides has

complete these macromolecules' great efficacy as antiviral agents regarding their capability to be served as microbicides (Ghosh *et al.,* 2009).

Clinical trials suggest a rationalized approach of polysaccharides to be utilized in future generations as microbicides. Such approaches contain the synergistic or combinatorial effect of different drugs, particularly in the early viral infection inhibition steps. As sulfated polysaccharides derived from lactic acid bacteria confer the acceptable and safe status of strategies on rising microbicides which are next-generation and topical applications, using polysaccharides which are sulfated only or in a mixture can give ample better results on correcting diseases which are sexually transmitted regarding their antimicrobial or antiviral potency (Bollen *et al.,* 2008 and Kilmarx *et al.,* 2008).

A (PC-815) microbicide derived by combining the mixture formulation of nucleoside reverse transcriptase inhibitor MIV-150 and carrageenan, MIV-150 has established its efficiency as a microbicide of the upcoming generation (Malco*lm et al.,* 2005). On the other hand, these polysaccharide-based microbicide formulations' successful application has become a bloom and vital issue on such inhibitors for a proper delivery system of the vagina.

**Exopolysaccharides as antibacterial**

Exopolysaccharides, long-chain polysaccharides formed by LAB that are secreted into the growth medium during the metabolic process, have concerned new attention, chiefly because of their potential health-promoting functions. Interest has grown in exploiting the EPS-producing LAB for their possible biological activities. lately, numerous new LAB strains have has been found to have antibacterial activities only little studies have focused on the antibacterial impact of EPS created by LAB. The increasing occurrence of multidrug-resistant bacteria causing bacteremia, urinary tract infection, and oral infection constitutes a major health problem. (Mahdi *et al.,*2018; Mater *et al.,*2019)

In a study institute that EPS from *Lactobacillus Plantarum* R315 and *Bifidobacterium bifidum* WBIN03 exhibited major useful effects on gut microbiota, and the assay of agar diffusion have demonstrated that both EPS exhibits antimicrobial actions against pathogens which are tested for example *Shigella sonnei, Cronobacter sakazakii*, *Staphyloccocus aureus*, *Escherichia coli*, *Salmonella typhimurium*, *Bacillus cereus*, *Listeria monocytogenes*, *Candida albicans*, (Li *et al.,* 2014).

**Exopolysaccharides as antiviral drugs and target modes of action**

Lactic acid bacteria show the great potential of severe gastrointestinal disorders prevention in animals and human beings (Oh *et al.,* 2010; Kumar *et al.,* 2010; Mahdi *et al.,* 2018). Though the antiviral actions mode of lactic acid bacteria is not elucidated properly, they have revealed the major capability of inhibiting viral infections and/or replication either indirectly or directly caused by gastroenteric, influenza, new castle, herpes, murine and respiratory disease viruses (Lange-Starke *et al.,* 2014; Kassaa *et al.,* 2014). On the other hand, differentiation in the antiviral impact is demonstrated at the level of species depend on the biological properties and efficiency of the test strain. Usually, actions mode of lactic acid bacteria as antiviral components accompanied in four main parts which include i) hindrance of adsorption, ii) virus internalization in the cell, iii) antiviral substances creation, and iv) antiviral impact establishment through immunomodulation or cross-talk. A summary of feasible antiviral action modes of lactic acid bacteria is summarized in fig. 6.

Liu *et al.,* (2004) shown that polysaccharides can avoid infection of viruses through virus adsorption blockage onto the cells of the host by interaction either with host cells or with virus particles. The present study has established that strong verifications on polysaccharide molecule interaction and membrane of the cell should happen to fix the receptors' proper blocking resulting in the virus adsorption on the membrane of the cell (Liu *et al.,* 2004).

Amid the polysaccharides which are tested, sulfated polysaccharides are showing a strong ability to show antiviral effect (Oh *et al.,* 2010). Virus-cell adsorption inhibition onto the host cell is regarded to be the initial pace in the process of viral infection. It is found that sulfated polysaccharides inhibit the attachment of virus-cell and show antiviral impact in opposition to different varieties of viruses including human cytomegalovirus, influenza virus, hepatitis B virus, herpes simplex virus (Oh *et al.,* 2010). Thus, in the current antiviral research scenario, lactic acid bacteria and their resulting polysaccharides are regarded as possible members in antiviral therapy to treat or avoid infections of viruses in both animals and humans with remarkable efficiency and may have an important contribution in pharmaceutical and medical industries in future (Oh *et al.,* 2010).

An effective antiviral compound or substance having the capacity to avoid the cells from infections of viruses either directly by the virus particles inactivation or by interfering with the cycle of virus replication. On the contrary, any antiviral drugs intracellular activity should be interpreted by the exclusion of the possible capacity

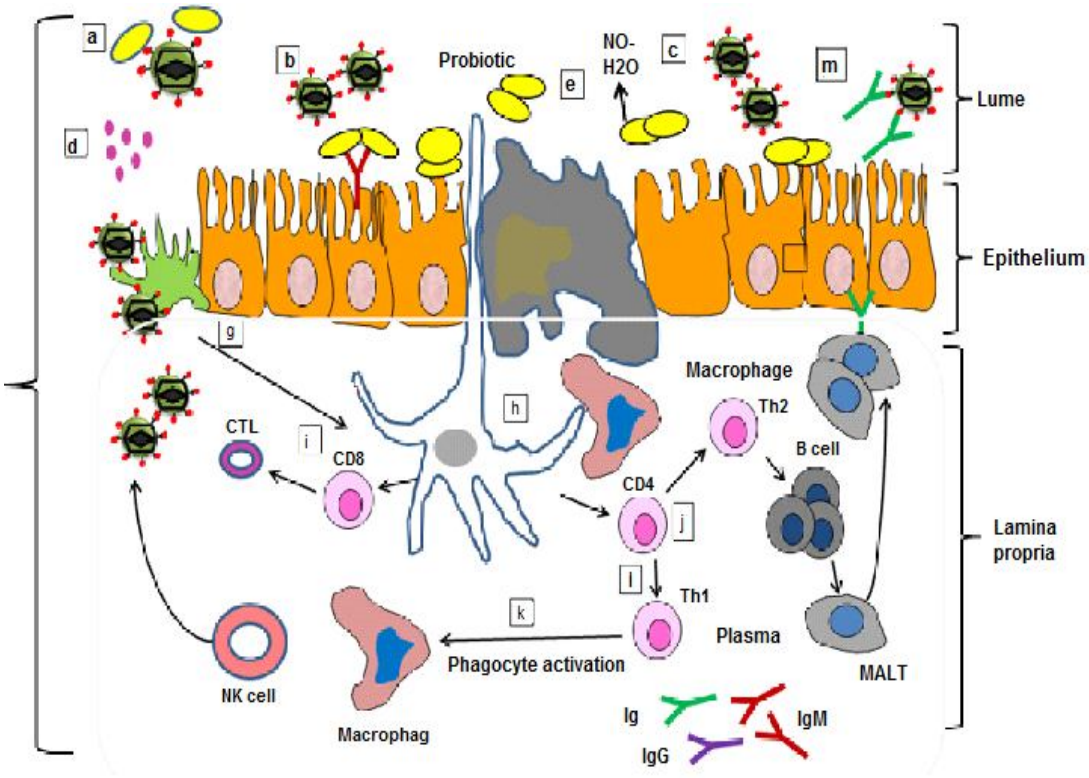


**Fig. 6:** Diagrammatic presentation of varied antiviral actions mode of probiotics involving virus inhibition by viral particles direct binding (a); viral attachment blockage by steric hindrance, cover receptor sites blockage in non-specific manner (b); mucosal regeneration induction thus attaching particles of virus and inhibits adhesion to epithelial cells leads to virus replication inhibition (c); antiviral compounds production (d); antiviral effect via dehydrogenase and nitric oxide production (e); normalization promotion of mucosal barrier and integrity enhancement of mucosal cells (f); modulation of immune response of epithelial cells, (g); modulation of immune response via macrophages (h); antiviral effect via activation of CD + and differentiation of T lymphocyte into cytotoxic T lymphocytes (i); antiviral effect by promotion of phagocyte through activation of Th1 (j); through proliferation induction of B cells (k); and viral or antiviral neutralization effect through antibodies secretion (l) (Lehtoranta, 2012).

of virus inactivation extracellularly. A microbial polysaccharide which is protein-bound showed the potent capability to decrease the viral titer of herpes simplex virus-2 and herpes simplex virus-1 viruses (Eo *et al.,* 2000).

Though no exact antiviral mode of action of polysaccharide which is protein-bound was specified, the notable antiviral activity opposing herpes simplex viruses may be credited to the following causes involving disintegration of the complete particles of herpes simplex virus, virus envelope solubilization, changes in the composition of chemicals, degradation of protein, or by covering the virus envelops vital proteins (Eo *et al.,* 2000). The present study exposed that polysaccharides that are protein bound may employ its incomplete antiviral action mode against herpes simplex virus-2 by glycoproteins binding of herpes simplex virus-2 to polysaccharide which is protein-bound which may intervene at the virus replications first state or any virions release. Also, the polysaccharides which are sulfated heparin and dextran sulfate demonstrate the striking antiviral activity by their virus particle interaction connection to the cells of the host (Bouhlal *et al.,* 2011). as well, other sulfated polysaccharides involving polysulphate, xylofuranan sulfate, pentosan, mannan sulphate, ribofuranan sulfate, and sulfated cyclodextrins are also found to display viral replication process inhibition for herpes simplex virus, human immune deficiency virus, human cytomegalovirus (Bouhlal *et al.,* 2011).

Exopolysaccharide polymers have revealed strong antiviral impacts, on the other hand, concerns are elevated on their acceptability because of their relatives being compounds of big molecular weight and having a phenomenon of blocking attachment of virus, none favorable pace in antiviral therapy, making them the uncertainty molecules which may be passed via the dissimilar body barriers even membrane of the cell (Bouhlal *et al.,*2011). Big molecules of a polymer may be hard to enter to certain expanse when to be used in topical supplication for curing of specific infections of

cutaneous herpes simplex virus-1, little polymers of oligosaccharides, for instance, dextran sulfate having the capacity to pass effortlessly from different barriers of the body. Also, these oligosaccharides show finer diffusion capability in blood if supplied in the experimental rats with oral heparin (Li *et al.,* 2011).

Present study definite that polymers of oligosaccharides, for instance, dextrans having sulfate group may serve as antiviral therapies natural alternatives leads to the perfect use of such inexpensive polysaccharides found largely in nature (Bouhlal *et al.,* 2011). But, other functional groups presence apart from sulfate may too having possibilities on the antiviral properties and efficiency of another type of polysaccharides. It is described that polysaccharides for example carrageenan hinder antiviral effect by viral protein production process inhibition just when it is existing at virus particle entries early stage (Bouhlal *et al.,* 2011). Also, although sulfated polysaccharides have revealed their capability to decrease the viral plaques number when used in raw appearance, the virions may be internalized even at a 10-times greater concentration of carrageenan, essential in blocking the viral replications early step. In comparison, lactic acid bacteria or lactic acid bacteria-derived polysaccharides demonstrate a varied range of biological properties. lately, *L. brevis* KB290, a lactic acid bacterium having known immunomodulatory characters revealed strong antiviral impact against influenza virus in experimental models of mice (Waki *et al.,* 2013).

The results have established that KB290 when orally administered alleviated influenza virus- showed clinical signs which may be produced by interferon-α-production long-lasting enhancement and the augmentation of production of influenza virus-specific immunoglobulin-A, suggests that KB290 may be having exopolysaccharide like constituents in charge for such antiviral impact (Waki *et al.,* 2013). Kawase *et al.,* (2010) demonstrated that a strain of *Lactobacilli* isolated from the intestinal tract of humans prevented infection of viruses sourced by an influenza virus. From a probiotic strain L. *bulgaricus* OLL1073R-1 an exopolysaccharide was isolated showed strong immunostimulatory impact (Makino *et al.,* 2006). Further, the impact of fermented yogurt with OLL1073R-1 on the decreased risk of respiratory infections was elderly visualized following companion studies (Nagai *et al.,* 2011). It is found that yogurt which is fermented have augmented the activity of NK cell in the subjects who were having a lower activity of NK cell, confirming that exopolysaccharide administration containing yogurt may have a prospective role to avoid the influenza virus infections since natural killer cells, lymphocytes of an innate immune system having a vital role in the early defense of host against various infections of viruses (Makino *et al.,*2010).

Before reported studies have fixed that primary generation antiviral drugs have shown fewer potency in the prevention of the viral infection of vagina generated by human immunodeficiency virus-1 transmitted virus. On the other hand, polysaccharides, as second-generation drugs only or in shared formulations with other drugs or polysaccharides have shown a wide range of spectrum of antivirals leads to provide a sustainable antiviral cure against the pathogenesis of vagina (Ghosh *et al.,* 2009).

Lactic acid bacteria and lactic acid bacteria-derived polysaccharide usually sulfated polysaccharides are having many advantages above varying categories of antibiotic and synthetic antiviral components having major side impacts. Such polysaccharides are having a relatively little cost of production, exerting antiviral efficiencies broad range, shows toxicities low range, shows viral drug resistance low range, and illustrate high lipophilicity, makes them the members of the promising discovery of antiviral drug in next future with widely acceptable and safe levels which demonstrate correct antiviral action modes.

**Exopolysaccharides as antifungal**

Exopolysaccharides fromLAB is found to demonstrate activity as antifungal., LAB's diûerent strains are screened out for identifying their prospective antifungal action. Among different LAB strains, *Lactobacillus fermentum* is marked having a potent antifungal property, particularly against *Candida glabrata* and *Candida albicans* (Masood *et al.,* 2011).

**Exopolysaccharides as antioxidant and antitumor**

Exopolysaccharides obtained from bacterial sources are reported for having activities as an antioxidant (Kong *et al*., 2010) and antitumor property (Leung *et al*., 2006). The microbial polysaccharides' main biotechnological advantages are a process of short fermentation and simply stable and formed emulsions. These polysaccharides generally have little side effects and cytotoxicity, making them immunotherapies good candidates as anti-oxidants and against cancer. Species of reactive oxygen are recognized to be elaborated in different biological processes results in the progression or development of numerous diseases. EPSs are found to take part in the removal of the free radicals, thereby working as strong anti-oxidants. Two important bioactivities showed by EPS from lactic acid bacteria are the anticancer and immunomodulatory impacts.

The potential wide spectrum bioactivity of this compounds class as adjuvants as anti-cancer agents are

spotted by the biological activities, for example, anti-angiogenic and apoptotic effects involving their impacts on the c-Fos, c-Myc and growth factor expression of vascular endothelium. EPS formed by Lactococcus lactis cremoris species KVS20 exhibiting bioactivity, for instance, mitogenicity of lymphocyte, cytostatic of macrophage, and cytokine (IL-1$\beta$ and IFN-$\gamma$) formation in macrophages. Antitumour action mechanism of polysaccharides consisting in the prompt of such immune system components, chiefly B- and T lymphocytes, induction of the release of interleukin by NK cells and macrophages. Polysaccharides are more often given parenterally, sometimes orally, when the peptide fragment presence allowed for such route. The administration method of such compounds, mostly resulting from their structure of chemicals, is not troublesome to patients, this is the undoubted benefit of such compounds (Ismail and Namboothiri, 2013).

## Conclusion

Many studies have fixed that lactic acid bacteria are having a strong capacity to create different varieties of chemically complex oligo- and polysaccharides. On the other hand, efficiency on a low quantity of creation by these *Lactobacilli* has restricted their application as additives of food-grade. Affected with these hurdles in the production of exopolysaccharide from lactic acid bacteria, studies for efficient fermentation on optimized parameters in mixture with metabolic and molecular engineering techniques can assist to realize the higher quantity of biosynthesis of exopolysaccharide by lactic acid bacteria. Also, detailed facts on the structural and chemical relativity relationship may assist to provide bacterial exopolysaccharides a newer way for their pragmatic applications in different advantageous fields to be used as promoters of natural health with a declared span of biological properties. Within a short time, the level of gene expression studies and molecular techniques may provide a new perception on better creation of bacterial exopolysaccharides under the controlled environment of chemicals leading to more versatile and functional exopolysaccharide creation.

Lactic acid bacteria which provides exopolysaccharides may be served as natural and potent microbial sources as effective starter cultures having expected chemical characteristics which can give sufficiently to increase newer approaches for the increased creation of different types of exopolysaccharides added with additional and new functional biological efficacy tracts (Bajpai *et al.,* 2016).

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