Scientific Bulletin. Series F. Biotechnologies, Vol. XX, 2016
ISSN 2285-1364, CD-ROM ISSN 2285-5521, ISSN Online 2285-1372, ISSN-L 2285-1364

LEVAN - A MINI REVIEW

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Abstract

This review aimed to present a short summary of the biosynthesis, properties and industrial applications of levan, as a multiuse biopolymer. During the past years, a great number of bacterial polysaccharides have been discovered and nowadays, many studies about their molecular structure, biosynthesis and industrial development, or their functional properties establish correlations emphasizing their significant industrial value, especially as biomaterials. Levan and inulin are the main representative molecules, in the fructans group (as non-structural carbohydrates - fructose polymers). Levan is an extracellular polysaccharide (EPS), a biologically active polymer. It is a naturally occurring homopolymer of fructose, which can be found in plants and many microbial strains. Its main plant sources are: Agropyron cristatum, Dactylis glomerata, Poa secunda, Triticum aestivum, Cocksfoot and Pachysandra terminalis. As an EPS, levan is also produced, usually from sucrose-based substrates, by a variety of microorganisms: the most known microbial levan producers belong to the genera Zymomonas, Bacillus, Acetobacter, Aerobacter, Pseudomonas, Erwinia, Gluconobacter, Streptococcus and Corynebacterium. Many research works attribute levan a variety of potential applications in various fields, like: medical, chemical, pharmaceutical, cosmetics and food industries. General properties like film-forming ability, flexibility, renewability, biocompatibility, biodegradability and ecofriendliness, along with a number of remarkable physical, chemical and biomedical properties, made levan a superior biopolymer in many commercial sectors.

Key words*: biopolymers, levan, biosynthesis, properties, applications.*

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INTRODUCTION

During recent years, **polysaccharides** – natural polymers, offered a considerable promise as sustainable materials that embrace two highly important properties, biodegradability and biocompatibility (Poli et al, 2009; Chen et al, 2014).

Their natural origin is characterized by a wide variety of sources: bacterial, fungal, algal and plant (Donot et al, 2012).

This mini review proposes to present some general aspects regarding biosynthesis properties, and applications of levan polymers.

Exopolysaccharides (EPS) – polysaccharides exuded into the extracellular environment (e.g. homopolysaccharides like dextran or levan and heteropolysaccharides like xanthans or gellans) have received considerable research attention, due to both their environmental and human compatibility (Donot et al, 2012; Ates, 2015).

These polysaccharides (monomers of monosaccharides) as natural materials (highly stable and safe) derived from microbial sources have an outstanding potential for various industrial and medical applications, due largely to their susceptibility to biodegradation (comparative with synthetic polymers) (Liu et al, 2008; Rehm, 2010; Liang and Wang, 2015).

Microorganisms can synthesize a large number of polysaccharides that play important roles in biological functions such as adhesion, infection, immune response etc. Therefore, the carbon sources available in culture media are converted into a various range of polymers as materials with different properties, in many cases more advantageous than other gums (Ernandes and Cruz, 2011; Rehm, 2010; Öner, 2013).

During the last years, a great number of bacterial polysaccharides have been discovered and nowadays, many studies about their molecular structure, biosynthesis and industrial

development, or their functional properties, establish correlations emphasizing their significant industrial value, especially as biomaterials. These microbial polysaccharides, categorized as environmentally friendly materials, are called "the sleeping giant of biotechnology" (Freitaset al, 2011; Esawyet al, 2012).

In order to improve their properties (e.g. biocompatibility) or to enhance the productivity yield, new approaches that target the biological processes of EPS synthesis. Such studies involve many aspects (for example – related to fermentation process optimization by using renewable resources as cheaper substrates), the most important being the reduction of production costs (van Dyk et al, 2012).

Besides the EPS roles in nature, microbial polysaccharides have got several important industrial and medical applications. Due to their complex structures, biopolymers – superior to petrochemical – derived polymers, have various valuable properties in many sectors such as: pharmacology and medicine (drug delivery, anti-tumor, anti-mutant, anti-coagulant, antioxidant, immunostimulatory, antiviral and anti-inflammatory activities), cosmetology, textiles, adhesives, detergents, depollution – wastewater treatment (biofloculants, heavy metal removal agents, bioabsorbents), brewing and food production (additives – gelling, thickeners, emulsifying and stabilizing agents) (Poli et al, 2009; Rehm, 2010;Donot et al, 2012; van Dyk et al, 2012; Sarilmiser and Öner, 2014).

FRUCTANS

An important group of polysaccharides as non-structural carbohydrates (fructose polymers) can naturally occur in various microbial (bacteria, fungi) and plant species (monocots, dicots). Depending on their origin, fructans are characterized by β-(2,6) linkages (levan type) and β-(2,1) bonds (inulin type) (Kim et al, 2005; Banguela and Hernandez, 2006; Franken et al, 2013).

Levan and inulin are the main molecules, very representative for the fructans group, but also a third type of fructose polymers exists, namely fructo-oligosaccharides, FOS (short-chain sugar molecules) (Banguela and Hernandez, 2006; Linde et al, 2012).

A broad range of microorganisms, including Gram positive and Gram negative bacteria (*Pseudomonas, Bacillus subtilis, Xanthomonas, Streptococcus mutants, S. salivarius, Azotobacter chroococcum, Lactobacillus reuteri, Leuconostoc citreum, Zymomonas mobilis, Arthrobacter ureafaciens, Rothiadento cariosa*) and different fungal genera (*Fusarium, Aspergillus, Trichoderma, Aureobasidium, Penicillium, Phytophora*, *Pestaloptiosis, Myrotecium*) are currently known to synthesize fructans (Banguela and Hernandez, 2006; Gupta et al, 2011).

These homopolymers of fructose have various biological functions/roles in microorganisms such as: physical barrier forming, enhanced resistance against abiotic and biotic stress, improved nutrient assimilation, role in pathogenesis (Franken et al, 2013).

Fructosyltransferases, enzymes capable to catalyse trans-glycosylation and sucrose hydrolysis reactions, play a very important role in fructans biosynthesis. In addition, bacterial levansucrases (EC 2.4.1.10) and inulosucrases (EC 2.4.1.9) contribute to the sucrose conversion into high polymerization degrees (DP) fructans (e.g. levan polymers have a DP > 100, whereas inulin polymers range between 20 and 10000). Fungal fructans, fructo-oligosaccharides, predominantly have a DP of 3 to 10 (Banguela and Hernandez, 2006; Franken et al, 2013).

Fructose polymers are well known for their various applications in nutraceuticals, food and non-food industries (e.g. FOS are typical representatives of prebiotics with bifidogenic effect; inulin and levan are used in fructose syrups production; levan is used as an emulsifying or encapsulating agent, blood plasma volume extender etc.) (Abdel-Fatah et al, 2005; Banguela and Hernandez, 2006; Linde et al, 2012; Wang, 2015).

Due to their properties and beneficial roles for human and animals health, these molecules have been extensively used in different industry sectors and medicine.

LEVAN

Levan is an extracellular polysaccharide, a biologically active fructan polymer. It is a naturally occurring homopolymer of fructose, which can be found in plants and many microbial strains (Melo et al, 2007; Shih et al, 2010; Silbir et al, 2014; Sarilmiser et al, 2015).

It was firstly reported by Lipmann, in 1881 as a type of microbial fructan (similar with bacterial dextran) under the name of "levulan" (Gupta et al, 2011; Liang and Wang, 2015).

Levan, commonly reffered as polyfructose is made of repeating fructose sub-units which form a main chain with β-(2→6) fructofuranosidic bonds and occasionally with β-(2→1) branching. This backbone make levan a unique biopolymer, being at the same time one of the few natural polymers in which carbohydrate is found in the furanose form (Szwengiel et al, 2004; Gupta et al, 2011; Divya and Sugumaran, 2015; Liang and Wang, 2015; Srikanth et al, 2015).

STRUCTURE AND PROPERTIES

Over the years, the chemical structure and physical properties of levan were well studied and characterized.

Empirical formula: $(C_6O_{10}H_5)_n$(Han, 1989)

Structural formula: Fig. 1 (Han and Clarke, 1996).

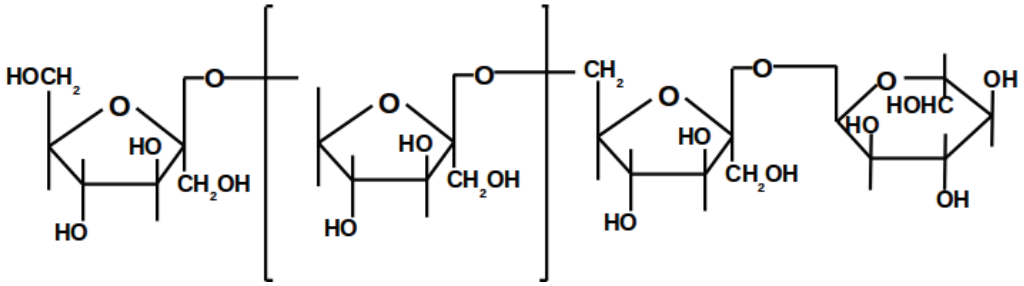

Fig. 1 Structural formula of levan (Han and Clarke, 1996)

The molecular weight of levan, its degree of polymerization and the branching of the repeating unit depend on the source. Levans from the plants are much smaller than those produced by microorganisms, usually with molecular weights between 2000 and 33000 Daltons (Da) (Esawy, 2012; Srikanth et al, 2015). On the other side, microbial levans generally have molecular weights up to several millions Da (10^5 to 10^8 Da; e.g. high molecular weight levans from *Bacillus polymyxa* – $2x10^7$ Da and *Z. mobilis* – 10^7 Da) (Chung et al, 1997; Freitas et al, 2011; Esawy et al, 2012; Report - CIR, 2012; Chen et al, 2014; Srikanth et al, 2015).

The main properties of levans are very similar to those of dextrans (Gupta et al, 2011). It is known that levan has some distinguished and interesting biochemical and biomedical properties and, in this context, they are shortly reviewed in Table 1 (Zhurina, 2009; Sarilmiser et al, 2015).

General properties like film-forming ability, flexibility, renewability, biocompatibility, biodegradability and ecofriendliness, along with a number of remarkable physical, chemical and biomedical properties, made levan a superior biopolymer in many commercial sectors and also, determined its classification in the most valuable and versatile polymers of the future (Srikanth et al, 2015; Adamberg et al, 2016).

BIOSYNTHESIS

Levan history begun in the years 1870-1881 with its discovery by Lipmann, followed in 1902 by Greig-Smith and Steel who reported levan produced by microorganisms isolated from a secretion of *Eucalyptus stuarina*. In the immediate following period (1870-1940), the research work in the field was focused on the biosynthesis, production and collection of levan, especially in Germany, England and France. Starting from 1930s, insights on the microbial levan production were brought to the researchers' attention and opened a new horizon for polymers applications, while in the USA a commercial market for polysaccharides started to develop (Gupta et al, 2011; Zhang et al, 2014; Srikanth et al, 2015).

Table 1. The main properties of levan

PHYSICO-CHEMICAL PROPERTIES		BIOMEDICAL PROPERTIES
Solubility (Manandhar et al, 2009; Zhurina, 2009; Belghith et al, 2011; Freitas et al, 2011; Gupta et al, 2011; Report - CIR, 2012; Sarilmiser and Öner, 2014;Silbir et al, 2014; Sarilmiser et al, 2015; Srikanth et al, 2015)	Water and oil soluble, due to its β-(2→6) linkage (high soluble in water at room temperature)	Not hydrolyzed by human digestive enzymes → bifidogenic effect (Belghithet al, 2011)
	Non-gelling in water	
	Insoluble in organic solvents like methanol, acetone, ethanol, n-propanol, methylethylketone, isopropanol, ethyl lactate, toluene (exception: dimethyl sulfoxide – DMSO); also, resistant to jet fuel and d-limonene	
Viscosity (Esawy et al, 2012; Report - CIR, 2012; Sarilmiser and Öner, 2014;Srikanth et al, 2015)	Low intrinsic viscosity (0,07 to 0,18 dL/g for levan with molecular weight between 16 to 24 million Da)	Antioxidant (Srikanth et al, 2015)
Particle size (Report - CIR, 2012)	Partially forms nanoparticle in water (224,3 nm) and in ethanol (251,8 nm)	Anti-inflammatory (Freitas et al, 2011; Srikanth et al, 2015)
Amorphous or microcrystalline (Gupta et al, 2011)		Anticarcinogenic (Abdel-Fatah et al, 2005; Freitas et al, 2011; Gupta et al, 2011; Srikanth et al, 2015)
Amphiphilic (Sezer et al, 2011)		Anti-AIDS (Srikanth et al, 2015)
Non-ionic (Report - CIR, 2012)		Antihyperlipidemic (Yussef et al, 2014), hypocholesterolemic (Abdel-Fatah et al, 2005)
Levorotatory (Gupta et al, 2011)		Antiviral effects (Esawy et al, 2011)
Self-assembling (Sarilmiser and Öner, 2014)		Non-toxic and ocular non-iritant (Sarilmiser and Öner, 2014; Srikanth et al, 2015)
Heat stable: melting point, 225°C (Manandhar et al, 2009; Zhurina, 2009)		Hyperglycaemic inhibitor (Srikanth et al, 2015)
Stability to heat acid and alkali media (Sarilmiser and Öner, 2014; Silbir et al, 2014)		
Glass transition temperature: 141°C (Manandhar et al, 2009)		
Tensile strength: "green" and strongly adhesive (easily removed with water) (Freitas et al, 2011; Sezer et al, 2011; Sarilmiser et al, 2015; Srikanth et al, 2015)		
Compatibility with salts and surfactants (Silbir et al, 2014)		

Levan is diversily distributed in plants and microorganisms.

Its main plant sources are: *Agropyron cristatum, Dactylis glomerata, Poa secunda* (levan is usually found in their stems and leaf sheats), *Triticum aestivum, Cocksfoot* and *Pachysandra terminalis* (Gupta et al, 2011; Silbir et al, 2014; Srikanth et al, 2015).

Levan is also produced as an exopolysaccharide, usually from sucrose-based substrates by a variety of microorganisms. There are some reports on microbial levan for which fructose, sugar cane syrup, glucose, molasses, glycerol or raffinose substrates were used (Jathore et al, 2012; Sarilmiser et al, 2015; Srikanth et al, 2015).

The main reaction involved in its biosynthesis is the transfructosylation and is carried out by an extracellular enzyme namely levan sucrase (sucrose 6-fructosyltransferase, EC 2.4.1.10) (Shih et al, 2010; Zhurina, 2009; Srikanth et al, 2015). Therefore, levansucrase (LSC) is considered to be key point of microbial levan production (Donot et al, 2012). The fructosyl-transferases were grouped into glycoside hydrolases 68 family (GH68) by CAZY (Carbohydrate-active enzymes) database(Alamäeet al, 2012) and besides transfructosylation (LSC catabolizes the sucrose and converts the fructose into levan) they are known to catalyse two more distinct reactions such as hydrolysis (of sucrose, when water is used as an acceptor) and polymerization (of fructose) (Inthanavong et al, 2013; Youssef et al, 2014; Goncalves et al, 2015). Studies on LSCs activities showed that they are involved in

phytopathogenesis (*Erwinia* and *Pseudomonas* strains), symbiosis (*Paenibacillus polymyxa*) and also in the survival of bacteria in soil (*Bacillus subtilis*) (Esawy et al, 2012). LSCs were also isolated from various strains like *Streptococcus* sp., *S. mutants, S. salivarius, Leuconostoc mesenteroides, Lactobacillus* sp., *L. johnsonii, L. gaserii, Acetobacter diazotrophicus, Gluconobacter oxydans, Bacillus amyloliquefaciens, B. natto, Pediococcus acidilactici, Aerobacter levanicum, Z. mobilis* (Zhurina, 2009; Youssef et al, 2014; Srikanth et al, 2015).

Many microorganisms, including Gram negative and Gram positive bacteria, yeasts and fungi are capable to produce levan. The main levan producers are: *Aspergillus sidawi* and *Aspergillus versicolor* (fungi) and *Zymomonas mobilis, Acetobacter xylinum, Gluconacetobacter diazotrophicus, Microbacterium laevaniformans, Bacillus subtilis, B.amyloliquefaciens, B. polymyxa, B.circulans, B.lentus, B.licheniformis, B.methylotrophicus, B.megaterium, Geobacillus stearothermophilus, Paenibacillus polymyxa, Pseudomonas syringae, Ps.syringae* pv. *glycinea, Ps.syringae* pv. *phaseolicola, Ps.fluorescens, Ps.prunicola, Lactobacillus sanfranciscensis, L.reuteri, Leuconostoc mesenteroides, Rahnella aquatilis, Erwinia amylovora, E.herbicola, Streptococcus salivarius, Seratia* sp., *S.laevanicum, Arthrobacter ureafaciens, A.acetigenum, Halomonas sp., H.smyrnensis, Aerobacter levanicum, A.aerogenes, Phytobacterium vitrosum, Xanthomona* ssp., *X.pruni, Actinomyces viscosus, Azotobacter* sp., *Mycobacterium* sp. (bacteria) (Han, 1989; Han and Clarke, 1996; Szwengiel et al, 2004; de Oliveira et al, 2007; Szwengiel et al, 2007; Bae et al, 2008; Zhurina, 2009; Ernandes et al, 2011; Gupta et al, 2011; Alamäe et al 2012;Donot et al, 2012; Jathore et al, 2012; Liu et al, 2012; Report CIR - 2012; Molinari and Boiardi, 2013; Sarilmiser andÖner, 2014; Silbir et al, 2014; Youssef et al, 2014; Zhang et al, 2014; Abou-Taleb et al, 2015; Divya and Sugumaran, 2015; Sarilmiser et al, 2015; Srikanth et al, 2015).

Therefore, the most known microbial levan producers belong to the genera: *Zymomonas, Bacillus, Acetobacter, Aerobacter, Pseudomonas, Erwinia, Gluconobacter, Streptococcus, Corynebacterium*.

APPLICATIONS

It is recognized that levan is a homopolysaccharide with multi-functional features and a wide range of potential industrial applications. In recent years, commercial interest for the levan production received considerable attention (Abdel-Fattah et al, 2005; Gupta et al, 2014; Ates, 2015; Sarilmiser et al, 2015).

Some recent studies proposed that this novel biopolymer together with pullulan, xanthan and curdlan will have a promising future in the polysaccharides industrial market. Many research works attribute levan a variety of potential applications in diverse fields like: medical, chemical, pharmaceutical, cosmetics and food industries (Adamberg et al, 2016).

In this context, some of the most relevant applications of levan will be overviewed below.

In **medical and pharmaceutical sectors**, levan finds many applications due to its biodegradability, biocompatibility and film-forming ability, especially. It can be used as a plasma substitute (e.g. levan with a molecular weight between 3000 and 100000 Da) (Barone and Medynets, 2007; Rairakhwada et al, 2007; Shih et al, 2010; Esawy et al, 2011; Sezer et al, 2011; van Dyk, 2012; Liu et al, 2012; Abou-Taleb et al, 2014; Santos et al, 2014; Sarilmiser and Öner, 2014; Silbir et al, 2014; Youssef et al, 2014; Zhang et al, 2014; Srikanth et al, 2015), prolongator of drug activity (Sarilmiser and Öner, 2014; Silbir et al, 2014; Zhang et al, 2014; Youssef et al, 2014; Sarilmiser et al, 2015), radioprotector, coating material in drug delivery systems (Sezer et al, 2011; Abou-Taleb et al, 2014), tablet binder (Abou-Taleb et a, 2014; Wang, 2015) or drug carrier of nano-scale size range for peptides and proteins (e.g. levan obtained from *Halomoas smyrnensis* AAD6^T) (Sezer et al, 2011; Ates, 2015), biofloculating agent (Sarilmiser and Öner, 2014; Sarilmiser et al, 2015), colour and flavour enhancer in the manufacturing of tablets and capsules (Srikanth et al, 2015), dietary supplement to common carp, *Cyprinuscarpio* juveniles (levan increases the total erythrocyte and haemoglobin content with immunostimulant and immunomodulatory effects on *C.*

carpio and *Labeorohita*; it offers protection against *Aeromonashydrophila* infection) (Rairakhwada et al, 2007; Gupta et al, 2014; Srikanth et al, 2015). Many studies reported levan's multiple beneficial effects on human and animal health. Therefore, levan is best known to have anti-tumour, antioxidant and anti-inflammatory effects.

As an anti-tumour agent, there are studies on levan's effects on the immunologic system, tumour suppression and enhancement of leukocyte anti-tumour activity (Abdel-Fatah et al, 2005), its ability to modify tumour cells permeability (Abou-Taleb et al, 2014) (increase cell permeability to cytotoxic agents) (Srikanth et al, 2015). Levans from *Z. mobilis* and *M. laevaniformans* are considered to be anti-tumour immune modulators in humans (Rairakhwada et al, 2007) and showing immune-modulatory effects on macrophage, B and T-cells (Srikanth et al, 2015); levan from *Z. mobilis* was studied against Sarcoma-180 cell and it was proven that its anti-tumour activity depends on its molecular weight (Moosavi-Nasab et al, 2010). Also, some studies on levan from *Aerobacter* sp. and *Microbacterium* sp. against stomach cancer demonstrated that it exhibits higher anti-proliferative activity against human gastric cancer cells (Srikanth et al, 2015). Levan's anti-tumour effect, obtained from *Z. mobilis, Rahnella aquatilis* and *Microbacterium laevaniformans*) has been shown against 8 different tumour cell lines (Esawy et al, 2011; Fattah et al, 2012).

Its role in alleviating oxidative stress and free radicals demonstrate levan's antioxidant potential (e.g. in high glucose condition in the pancreatic beta cells) (Dahech et al, 2011; Dahech et al, 2013; Sarilmiser and Öner, 2014; Srikanth et al, 2015).

Besides hypocholesterolemic (anti- hyperli-pidemic agent) (Zhang et al, 2014; Youssef et al, 2014; Sarilmiser et al, 2015; Srikanth et al, 2015); levan prevents hypercholesterolemic atherosclerosis (Abdel-Fattah et al, 2005; Shih et al, 2010; Sezer et al, 2011; BelghithBelghith, 2012; Esawy et al, 2012; Fattah et al, 2012; Liu et al, 2012; van Dyk et al, 2012; Dahech et al, 2013; Abou-Taleb, 2014; Santos et al, 2014; Sarilmiser and Öner, 2014; Silbir et al, 2014; Youssef et al, 2014), shows hypoglycaemic (Dahech et al, 2013; Srikanth et al, 2015) (antidiabetic agent) (Sarilmiser and Öner, 2014; Youssef et al, 2014) and anti-inflammatory effects (Sarilmiser and Öner, 2014, 2014; Srikanth et al, 2015). Levan is recognized for its bifidogenic effect. It can be used as a human or animal prebiotic, which can significantly modulate the colonic microbiota by stimulating the growth of lactic acid bacteria like *Bifido bacteria* and at the same time protecting the colon from carcinogens (Szwengiel et al, 2007; Gupta et al, 2011; Belghith et al, 2012; dos Santos et al, 2012; Esawy et al, 2012; van Dyk et al, 2012; Santos et al, 2014; Srikanth et al, 2015).

In other studies the levan's effects were demonstrated in the protection of liver and kidneys, pancreas and heart tissue from the damage in alloxan-induced diabetic rats and in enhancing enzymatic defensis (Dahech et al, 2011; Srikanth et al, 2015).

Furthermore, levan distinguished properties contribute in reducing risk factors for coronary artery disease (Belghith et al, 2012), prevention of infections and necrosis or in dermatological wounds healing (Srikanth et al, 2015). Also, it has a therapeutic role in dental caries (e.g. subcutaneous filling) (Fattah et al, 2012; Srikanth et al, 2015) and exhibits anti-clotting factor during the surgery of heart patients and also in the treatment of restenosis after angioplasty (Srikanth et al, 2015).

Esawy and colab.have mentioned the probable suitability of levan as a cheap and natural product in antiviral treatments (antiviral activity of levan was studied against respiratory virus HPA1, H5N1 and enteric virus, adenovirus type 40) (Esawy et al, 2011).

Levan sulphates, phosphates and acetates as levan derivatives can be used in the treatment of AIDS or as inhibitors for muscle proliferation (Barone, 2007; Abou-Talebet al, 2014; Divya and Sugumaran, 2015; Srikanth et al, 2015).

In **food industry**, levans can be used as industrial gums (e.g. substitute for gum Arabic) (Chung, 1997; Shih et al, 2010; Abou-Taleb et al, 2014), sweeteners (e.g. as a fructose source) (Baroneand Medynets, 2007; Shih et al, 2010; van Dyk et al, 2012; Abou-Taleb et al, 2014; Silbir et al, 2014; Dvya and Sugumaran, 2015), fat substitues (Santos et al, 2014), fillers (bulking agents) (Abou-Taleb et al, 2014),

emulsifiers and texture forming compounds (Barone and Medynets, 2007; Bae et al , 2008; Shih et al, 2010; Esawy et al, 2011; Liu et al, 2012; Jathore et al, 2012; van Dyk et al, 2012; Abou-Taleb et al, 2014; Santos et al, 2014; Youssef et al, 2014; Zhang et al, 2014; Silbir et al, 2014; Divya and Sugumaran, 2015; Sarilmiser et al, 2015), encapsulating agents and carriers for flavours (aromatic enhancers) (Shih et al, 2010; Esawy et al, 2011; Jathore et al, 2012; Liu, 2012; van Dyk et al, 2012; Abou-Taleb et al, 2014; Santos et al, 2014; Zhang et al, 2014; Divya and Sugumaran, 2015; Sarilmiser et al, 2015), food coating materials (e.g. bio-based plastics for packaging applications) (Barone and Medynets, 2007; Bae et al, 2008; Chen et al, 2014) and stabilizers or thickeners (Barone and Medynets, 2007; Bae et al, 2008; Shih et al, 2010; Esawy, 2011; Zhang, 2014; Jathore, 2012; Liu et al, 2012; van Dyk, 2012; Abou-Taleb, 2014; Santos, 2014; Youssef, 2014; Divya and Sugumaran, 2015; Sarilmiser, 2015).

As a formulation aid in **cosmetic** products (blending component), levan has been shown to exert excellent cell proliferation, skin-irritation-alleviating and skin moisturizing effects. Also, in hair care products, levan derivatives can be used (Shih et al, 2010; Gupta et al, 2011; Sezer et al, 2011; Fattah et al, 2012; Divya and Sugumaran, 2015; Srikanth et al, 2015).

Levan has also proven to be a promising biopolymer in **other industrial applications**. It can be used as a surface-finishing agent (Shih et al, 2010; van Dyk et al, 2012; Zhang et al, 2014), "green" adhesive (e.g. Montana Biotech SE Inc. produces 2 levan adhesives for indoor and external use) (Srikanth et al, 2015), surfactant for household use (Gupta et al, 2011; Esawy et al, 2012), or plugging agent (e.g. to plug pores of high permeability soils) (Ghaly et al, 2007). Another special uses of levan are in laser direct writing technologies (LDW) in order to obtain novel bioactive surfaces (Sarilmiser et al, 2015) and in the purification of biological materials through a PEG/levan two phase liquid system (Srikanth et al, 2015).

CONCLUSIONS

Due to an increased interest in discovering and developing biopolymers with innovative chemical structures, resulted from a continuous demand for natural products, biocompatible and biodegradable, this review proposed a summary analysis of levan biosynthesis, properties and potential applications in various industrial sectors.

FUTURE PROSPECTS

The increasing need for environmentally friendly products, in biomedical and pharmaceutical sectors or food and feed (e.g. aquaculture) has opened a new commercial market for bioproducts, among which levan made its way, succesfully. So far, the available information about levan's effects used as different bioactive agents in human and animal health is not complete. There is a need to extensively exploit its beneficial properties in biomedical sectors, especially in nanotechnology field (e.g. developing prophylactic medicines or preparation of novel nanocomposites – biopolymeric nanoscale drug carrier) or in aquaculture (as an immune stimulatory agent) (Gupta et al, 2011; Sezer et al, 2011; Srikanth et al, 2015).

ACKNOWLEDGEMENTS

This research work was carried out with the support of National Institute for Chemical-Pharmaceutical Research & Development, ICCF-Bucharest.

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BIOTECHNOLOGY IN VETERINARY MEDICINE