Recent Developments and Future Prospects of Fungal Sophorolipids

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Abstract

Sophorolipids (SPLs) are glycolipid biosurfactants and are amphiphilic molecules. Structurally SPLs consist of sugar sophorose head group (2-*O*-β-D-glucopyranosyl-D-glucopyranose) attached to a long chain of C18 or C16, hydroxyl fatty acid tail group by a glycosidic linkage between the anomeric C atom of the sugar and the hydroxyl group of the fatty acid. SPLs are synthesized by a variety of microorganisms as a mixture of related molecules with differences in the fatty acid part (chain length, saturation and position of hydroxylation) and the lactonization and acetylation pattern. SLPs are one of the most promising biosurfactants that belong to the glycolipid group and are synthesized extracellularly. SLPs are secreted as secondary metabolites in the stationary phase during nitrogen-limiting conditions. SLPs have been widely studied for their potential application in various fields and are more attractive for commercial purposes. In this chapter, we have discussed the various fermentation parameters essential for optimum production of SPLs and their applications in agriculture, cosmetics, nanotechnology, bioremediation, antimicrobial, anticancer, immunomodulation, drug delivery and others.

Keywords

Sophorolipids (SPLs) · Biosurfactant · Nanotechnology · Cosmetics · Agriculture

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19.1 Introduction

The global production of surfactants has reached around ten million tons per year to fulfil the demands for household and industrial applications (Van Bogaert et al. 2007). The petrochemical-based production has been remarkably replaced by the development of economical and sustainable methods through bioactivity (Ma et al. 2020). Surfactants are amphiphilic, surface active molecules containing both hydrophilic and hydrophobic moieties, and those of microbial origin from bacteria, yeasts and fungi that are known as biosurfactants. Biosurfactants are produced by renewable primary products or agro-industrial wastes having better prospects than chemical surfactants, which possess low-toxicity, biodegradable and environment-friendly characteristics and better adjustable biological activities (Makkar et al. 2011; Marchant and Banat 2012; Saharan et al. 2011; Vatsa et al. 2010). The demand for biosurfactants in the coming years will increase enormously due to their value in many industries including cosmetics, laundry detergents, textile, pharmaceutics, food and agriculture (Sekhon Randhawa and Rahman 2014). Biosurfactants possess unique chemical structures ensuring better interfacial properties which make them good emulsifying agents with a lower value of critical micellar concentration (CMC) as compared to synthetic surfactants, thus widening their applications (Jahan et al. 2020). Biosurfactants have come across long journeys since the first biosurfactant called "surfactin" which was purified and characterized by Arima (1968). Though many researchers have satisfactorily studied biosurfactants, some features are still left to be understood. At present, biosurfactants are replacing chemical surfactants as potential alternatives in many industries because of the environmental concerns of the latter (Banat et al. 2010; Marchant and Banat 2012).

Biosurfactants are categorized into low molecular weight (LMW) [e.g. glycolipids and lipopeptides] and high molecular weight (HMW) (e.g. polysaccharides, proteins and lipoproteins or lipopolysaccharides) (Banat et al. 2010; Ron and Rosenberg 2001; Rosenberg and Ron 1999). Biosurfactants have promising applications in agricultural, pharmaceutical, food, cosmetics, and detergent industries. So far, there are more than 250 patents granted for biodegradable molecules (Rahman and Gakpe 2008; Shete et al. 2006). Some studies reported that microbial biosurfactants are advantageous over plant-based biosurfactants due to their scale-up capacity, rapid production and versatile properties. Various plant-based biosurfactants like saponins and lecithins and soy proteins have significant emulsification properties but are costly at industrial scale and thus have other disputable factors such as solubility and hydrophobicity (Xu et al. 2011). Among different categories of biosurfactants (sophorolipids, rhamnolipids, trehalose lipids, cellobiose lipids, mannosylerythritol lipids, surfactin and emulsan) are glycolipid biosurfactants except for surfactin and emulsan. Glycolipid biosurfactants belong to the non-ionic class which are composed of a carbohydrate head and a lipid tail. Since glycolipid biosurfactants offer promising properties as compared to other traditional and chemical surfactants, the first generation of glycolipids was produced from renewable resources by chemical synthesis [e.g. alkyl polyglycosides (APGs)]; the second generation was achieved through the biotechnological procedure, and thus at

present, glycolipids are produced through fermentation, particularly rhamnolipids and sophorolipids (Van Bogaert et al. 2007). Sophorolipids are produced mainly from non-pathogenic yeasts; in contrast to rhamnolipids which are mainly obtained from the bacterial species *Pseudomonas aeruginosa*, sophorolipids make them more attractive for commercial purposes.

19.1.1 Sophorolipid-Producing Strains

A century back, Gorin et al. (1961) were the first to describe the extracellular glycolipid obtained from the yeast *Torulopsis magnolia*, and later the authors in 1968 corrected and identified the same species as *Torulopsis apicola* (Hajsig), which is currently known as *Candida apicola*.

The structure of the hydroxy-fatty acid sophoroside mixture was elucidated as a partially acetylated 2-*O*-β-D-glucopyranosyl-D-glucopyranose unit attached β-glycosidically to 17-L-hydroxyoctadecanoic or 17-L-hydroxy-Δ9-octadecenoic acid (Tulloch et al. 1962, 1968b). Also, Tulloch et al. (1968a) discovered a new sophorolipid from *Candida bogoriensis* (now known as *Rhodotorula bogoriensis*). The overall structure is similar to the sophorolipids of *Candida apicola* but differs in its hydroxy-fatty acid moiety: the sophorose unit is linked to 13-hydroxydocosanoic acid. A third sophorolipid-secreting yeast strain was identified by the same researchers as *Candida bombicola* (named initially as *Torulopsis bombicola*). The glycolipids and production characteristics of this species are nearly identical to those of *Candida apicola* (Spencer et al. 1970). Rosa and Lachance (1998) described the novel yeast species *Starmerella bombicola* and introduced it as the teleomorph of *Candida bombicola* based on the high 18S rDNA identity between both strains (more than 98%) and their ability to mate with each other to form ascospores. Chen et al. (2006a) also proved sophorolipid synthesis in a new strain of *Wickerhamiella domericqiae*. They observed more than six glycolipids and identified one of the three main products as 17-L-(-oxy)-octadecanoic acid 1,4″-lactone 6′,6″-diacetate, which is identical to the major component of the sophorolipids of *C. apicola* and *C. bombicola*. SPLs are produced not only by a single yeast species but also by other related microorganisms which belong to the *Wickerhamiella*, *Starmerella* and *Rhodotorula* species which is capable of producing similar kind of SPL molecules (Van Bogaert et al. 2011, 2007).

19.1.2 Sophorolipid Structure

SPLs are glycolipid biosurfactants and are amphiphilic molecules. They structurally consist of a sugar sophorose head group (2-*O*-β-D-glucopyranosyl-D-glucopyranose) attached to a long chain of C18 or C16, hydroxyl fatty acid tail group by a glycosidic linkage between the anomeric C atom of the sugar and the hydroxyl group of the fatty acid (Baccile et al. 2017). The head group, sophorose, is a disaccharide having a β-1,2 bond and acetylated on the 6′- and/or 6″-positions (Fig. 19.1). The acetylation

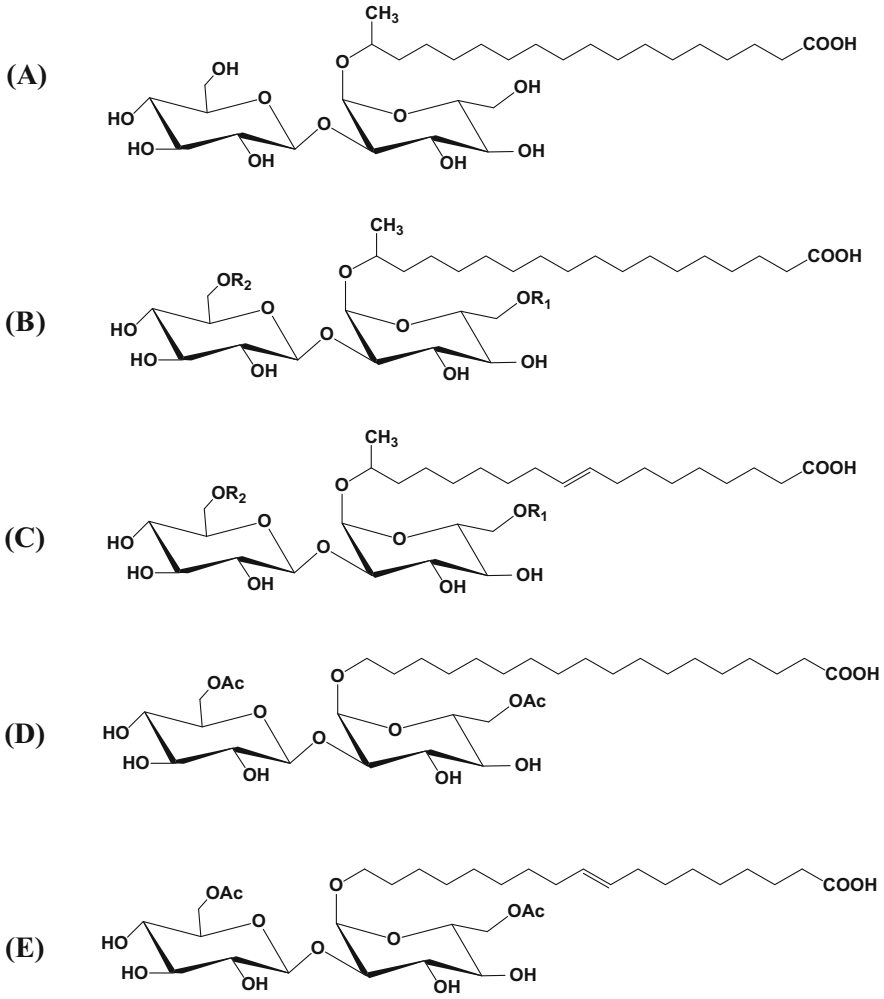

Fig. 19.1 Structures of sophorolipids: (**a**) Deacetylated sophorolipids, (**b**, **c**) major sophorolipids of *Starmerella bombicola* and (**d**, **e**) major sophorolipids of *Candida batistae*

is on the 6- and/or 6′-positions of sophorose residue. One terminal or subterminal hydroxylated fatty acid is β-glycosidically linked to the sophorose molecule. The hydroxy-fatty acid residue can have one or more unsaturated bonds (Fig. 19.1). The carboxylic group of fatty acids is either free (acidic or open form) or internally esterified (lactonic form) (Fig. 19.1). Sophorolipids can exist in the form of lactones both in monomeric and in dimeric forms (Nuñez et al. 2004). The carboxylic end of this fatty acid is either free (acidic or open form) or internally esterified at the 4″ or in some rare cases at the 6′- or 6″-position (lactonic form). The hydroxy-fatty acid itself counts in general 16 or 18 carbon atoms and can have one more unsaturated bond (Asmer et al. 1988; Davila et al. 1993). As such, the SPLs synthesized by

C. bombicola are a mixture of related molecules with differences in the fatty acid part (chain length, saturation and position of hydroxylation) and the lactonization and acetylation pattern. Asmer et al. (1988) were the first to shed light on this structural variation. However, differences in fatty acid length and hydroxylation patterns were not taken into account. Davila et al. (1993) separated the SPLs mixture by a gradient elution high-performance liquid chromatography (HPLC) method and used an evaporative light scattering for the detection of the individual SPLs. The group analysed the fatty acid chain and identified over 20 components.

19.2 Biosynthesis of Sophorolipids

Sophorolipids (SLPs) are one of the most promising biosurfactants that belong to the glycolipid group and synthesized extracellularly. SLPs are produced by the non-pathogenic yeast strain *Candida bombicola* as a mixture of different molecules. Generally found in two groups, acidic and lactonic, they hence show variation in physicochemical and biological properties (Daverey and Pakshirajan 2009). SLPs are secreted as secondary metabolites in the stationary phase during nitrogen-limiting conditions. Secretion can be induced in the presence of both lipophilic and hydrophilic carbon source, agitation-aeration, and growing the cells under stress condition (Desai and Banat 1997). The various factors are discussed below.

19.2.1 Carbon Source

The carbon source plays an important role in the production of SLPs. When both hydrophobic and hydrophilic carbon sources are applied to the medium, then SLPs production is optimal. SLPs biosynthesis is observed with two main inputs, glucose and fatty acids (FA), where the process begins with hydroxylation of FA. In the absence of a hydrophobic substrate, FA is formed by the de novo pathway from acetyl-CoA (Inoue and Ito 1982). Glucose is added to the synthesis pathway after the conversion of FA to hydroxy-FA. Glucose is further glycosidically converted to ω-1 hydroxyl group of FA by a specific transferase enzyme. A second glucose molecule is added to C2′ position of first glucose by transferase II (Esders and Light 1972). Acidic non-acetylated SLPs are obtained after this second glycosylation. The mixture of SLPs is obtained by further modifications caused by acetylation or lactonization of the sophorose unit. When either glucose or vegetable oil was used for the production of biosurfactant, a low yield was obtained by *Torulopsis*. An increased yield of SLPs was produced by the same organism when both the carbon sources were used in optimum quantity (Kim et al. 1997). Also, a higher yield of SLPs was obtained by *Candida bombicola* within 8 days by using sugar and oil as a carbon source (Casas et al. 1997).

19.2.2 Nitrogen Source

Nitrogen is the second most important component for the production of SL. Mainly when the yeast cell enters the stationary phase, SLP synthesis begins and is triggered in nitrogen starvation conditions (Davila et al. 1992). Normally, in fermentation processes, a higher C/N ratio that has lower nitrogen levels limits cell growth leading to the synthesis of secondary metabolites. It is assumed that *C. bombicola* prefers the same mechanism for the production of SLPs which is synthesized as extracellular storage material. Later, it was discovered that SLPs were not metabolized at a higher C/N ratio; indeed when added, carbon source is depleted (Garcia-Ochoa and Casas 1997). Hence, monitoring both the source is important for obtaining a high yield of SL. Initially, yeast extract and urea were used as a nitrogen source to increase SLP production by *Candida* and *Torulopsis*. The alternative for costly glucose and nitrogen source was first found by Solaiman and colleagues. They made the use of low-cost soy molasses with oleic acid for SLP production (Solaiman et al. 2007). Further using different yeast strains and by the combination of various fermentation parameters, Makoto et al. showed optimum SLP production by use of only sugarcane molasses and water as the most economic process (Takahashi et al. 2011).

19.3 Types of Biosurfactant Produced by Yeast/Fungi

Biosurfactants are amphiphilic molecules having a definite structure. The hydrophobic portion contains the hydrocarbon tail of long-chain fatty acid linked to hydrophilic moieties like alcohol, carbohydrate, amino acid or phosphate. Most biosurfactants are neutral or anionic, whereas few with amine groups are cationic. Synthetic surfactants are classified according to their polar group, but biosurfactants are categorized by chemical composition and microbial origin. Some of the most important types of biosurfactants are described in Table 19.1.

19.4 Advantages of Biosurfactants Over Normal Surfactants

Surfactants are widely used in almost every sector of industrial chemicals. The industrial demand of surfactants as well as household consumption is also growing faster accounting for larger production of surfactants to meet the increasing demand. Presently available commercial surfactants are synthesized mostly from petrochemicals (Farn 2008). Two major concerns related to the use of petrochemicals are an economic burden and an increase in environmental pollution. With the concern of global environment protection, there is a transformation in the use of chemical products according to environmental regulation, and demand for green alternative products has increased. The industries now propose the use of biological materials or methods in wide areas such as waste management, energy conservation, product modification and more. Thus advances in biological science have opened a way for the replacement of synthetic surfactant from petroleum

Table 19.1 Classes of biosurfactants and producing organisms

Biosurfactant			
Group	Class	Microorganism	References
Glycolipids	Rhamnolipids	*Pseudomonas aeruginosa*	Nitschke et al. (2011)
	Sophorolipids	*Candida*, *Torulopsis*	de Jesus Cortes-Sanchez et al. (2013)
	Trehalolipids	*Rhodococcus*, *Mycobacterium*, *Arthrobacter*	Lang and Philp (1998)
		F. fujikuroi	dos Reis et al. (2018)
Phospholipids and fatty acids		*Acinetobacter*	Gautam and Tyagi (2006)
		Candida sp. strain SY16	Kim et al. (2006)
		Candida antarctica	Kim et al. (2002)
Lipopeptides	Surfactin	*Bacillus* sp.	Fox and Bala (2000)
	Lichenysin	*Bacillus licheniformis*	Joshi et al. (2016)
Polymeric surfactant	Liposan	*Candida lipolytica*	Campos et al. (2013)
	Emulsan	*Acinetobacter calcoaceticus*	Gakpe et al. (2007)
		Candida lipolytica	Sarubbo et al. (2007)

feedstock to possible alternative biosurfactant (De et al. 2015). Being derived from natural products and organism sources, biosurfactants are eco-friendly. They possess various advantages over synthetic surfactants in terms of low-cost production, low toxicity, availability and sustainability. Also, they are considered a safe alternative for food, pharma and cosmetic industries (Bhadoriya et al. 2013). Biosurfactants have specific activity even at higher pH, temperature or other extreme conditions and are highly selective compared to synthetic surfactants. Few more advantages of biosurfactants are described below.

19.5 Availability of Raw Materials

In recent years, the disposal of industrial residues has been a major cause of pollution. The most efficient way of consuming this residual waste is by utilizing it as a substrate for the production of commercial compounds. These materials contain a large number of carbohydrates, oils and proteins which can serve as ideal raw material for the fermentation process. Biosurfactants are mostly produced extracellularly or as cell membrane part by various microorganisms. This bacteria, yeast or fungus uses sugars, oils, residues and waste materials as raw materials for their growth and synthesis of surfactant. Thus, biosurfactants can be produced from various oil refinery wastes, potato effluent, cassava waste, bagasse, etc. which are cheap and available in large quantities (Muthusamy et al. 2008).

19.6 Diversity

Surfactants produced by microorganisms are available in a wide range depending upon the environment and growth condition they are synthesized (Bodour et al. 2003). The different industrial processes demand a variety of surfactant to satisfy the commercial application. By changing the growth parameters and optimizing other fermentation conditions, different variants of surfactants can be generated from the same organism. This results in the formation of a surfactant mixture, and thus, even a small difference in structure can have a profound effect on its function (Symmank et al. 2002). This is of particular interest in the production of biosurfactant and is also economically favourable.

19.7 Selectivity and Specificity

Biomolecules are often found to be complex with specific functional groups. Microbial surfactants also possess particular functional moiety that shows specificity in action as compared to synthetic surfactants (Wick et al. 2002).

19.8 Low Toxicity

Biosurfactants are commonly considered as low toxic and cause no serious damage to the biotic ecosystem. Due to the low degree of toxicity, they are used in food, cosmetics and pharmaceutical industries. Biosurfactants do not have any harmful effects on the lung, heart, kidney or circulatory system. They hold lower chronic and acute toxicity compared to synthetic surfactants. It has been reported that synthetic anionic surfactant possesses ten times lower LC50 (lethal concentration) on test species compared to rhamnolipid. Flasz and colleagues perform an assay of toxicity and mutagenic properties of synthetic surfactant (Marlon) and biosurfactant derived from *Pseudomonas aeruginosa*. They found that synthetic surfactants showed higher toxicity and mutagenic effect (Flasz et al. 1998).

19.9 Biodegradability

Biodegradability of surfactants is the most important issue when evaluating environmental pollution (Berna et al. 2007). Biodegradation of surface-active agent occurs due to breaking down the molecule by a natural processor with the help of microorganisms. Biosurfactants can be easily degraded in nature by microorganisms into basic components. Microorganisms use BS as a carbon and energy source by transforming the hydrocarbon chain into CO_2, water and minerals (Garcia et al. 2006). However, there is very little literature available on the biodegradability of biosurfactants. However, it is shown recently that lipid biosurfactants are degraded under aerobic, sulphate-reducing, nitrate-reducing and fermentation conditions.

Also, biosurfactants surfactin, iturin and fengycin show degradation potential by soil microorganism as well as in liquid media, thus reducing the risk of environmental accumulation.

19.10 Applications

19.10.1 Antibacterial Activity

Sophorolipids (SLPs) have been widely studied for their potential antibacterial applications. Many researchers have used various methods for determining the antibacterial activity of sophorolipids which include serial dilution, microtitration and agar diffusion to determine the minimal inhibitory concentrations (MIC) or minimal lethal doses (50% lethal dose) of SLPs against various bacterial strains. In addition to SLPs acting as an antibacterial agent, they also act as anti-algal, antifungal, anticancer and antiviral agents. The antimicrobial activity of SLPs depends on its chemical structure and microbial cell wall structure.

Dengle-Pulate et al. (2014) produced SLPs by *Candida bombicola* with hydrophobic moiety derived from lauryl alcohol (SLPs-LA) having an effective antimicrobial activity against gram-negative bacteria, gram-positive bacteria and the pathogenic yeast. SLPs-LA shows a complete inhibition against gram-negative bacteria such as *Escherichia coli* and *Pseudomonas aeruginosa* along with gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis*. Gram-positive bacteria when treated with SLPs-LA results in the rupture of cells (lysis), while gram-negative bacteria showed shrinking of the cells rather than rupture.

Further, Gaur et al. (2019) isolated SLPs from the yeast strains *Candida albicans* SC5314 and *Candida glabrata* CBS138 which showed antibacterial properties against pathogenic bacteria and also generated reactive oxygen species in *Bacillus subtilis* and *Escherichia coli*. Some previous studies have reported that ROS generation results in the killing of pathogenic strains. SLPs exhibit bactericidal activities of antimicrobial agents which contribute to the generation of free hydroxyl radicals resulting in the killing of bacteria. The antibacterial properties of sophorolipids against pathogenic bacteria strongly suggest that they are likely to be used in food emulsions that protect against pathogenic bacteria.

Recent studies by Ceresa et al. (2020) showed that SLPs exhibit properties like anti-adhesive and antibiofilm, which can be exploited for the surface coating to prevent and treat infections in humans and animals. This study demonstrated the antimicrobial effect of sophorolipids on medical-grade silicone material surfaces using microbial strains: *Candida albicans*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*, respectively. Hence, SLPs help to reduce the cell attachment of microbial strain suggesting its effective role as coating agents on medical-grade silicone devices for the preventions of gram-positive bacteria and yeast infections.

19.10.2 Anticancer Activity

SLPs exhibit anticancer activity against many types of tumour cells and may have potential use in cancer treatment. Cell death is usually achieved by necrosis or apoptosis. Necrotic cell death is the process by which cells are destroyed resulting in lysis, while apoptosis involves programmed cell death through either intrinsic or extrinsic stimulation (Roelants et al. 2019).

The very first report of sophorolipids production by a new yeast strain of *Wickerhamiella domercqiae* showed anticancer effect and exhibited cytotoxic effects on different cancer cell lines, e.g., human liver cancer H7402, lung cancer A549, HL60 and K562. These results indicate a dose-dependent response on cell viability according to the drug concentration $\leq$62.5μg/ml (Chen et al. 2006b).

Further, Nawale et al. (2017) showed the apoptotic response of sophorolipids against HeLa cells through mitochondrial membrane depolymerization and by increasing the intracellular calcium levels which activate caspase-3, caspase-8 and caspase-9, playing essential roles in programmed cell death.

Besides this, Li et al. (2017) demonstrated SLPs to be effective against human cervical cancer cells. In that work, they synthesized SLPs by fermentation of *Stamerella bombicola* and reveal the anti-proliferative activity on HeLa and CaSki cells. The cytotoxic response of the SLPs molecule was proved to be influenced by the carbon chain length of sophorolipids. A direct correlation was observed between the length of the carbon chain and the cytotoxic response of SLPs. To increase the anticancer activity of SLPs, its structure can be modified with the enzymatic method. Thus, their work suggested a potential use of SLPs as anticancer medicine for cervical cancer treatment.

In this work, they have demonstrated SLPs to be effective against human pancreatic cancer cells. SLPs were synthesized by fermentation of *Candida bombicola* and showed the cytotoxic effect of the natural mixture or their derivatives (ethyl ester, methyl ester, ethyl ester monoacetate, ethyl ester diacetate, acidic sophorolipid, lactonic sophorolipid diacetate) against human pancreatic cancer cell lines by LDH release which often involves necrosis as a mechanism of action (Fu et al. 2008).

19.10.3 Antifungal activity

SLPs also exhibit antifungal activity against yeast including the various strain of *Candida*, *Pichia*, *Debaryomyces*, *Saccharomycopsis* and *Lodderomyces*.

Haque et al. (2019) demonstrated that the treatment of *Candida albicans* cells with SLPs increases the production of reactive oxygen species and upregulates the expression of SOD1 and CAT1, indicating high levels of oxidative stress and activation of stress response mechanism. Increased intracellular ROS level causes ER stress and the release of Ca^{2+} in the cytoplasm and changes in mitochondrial membrane potential (MMP). This study helps to know the mechanism of cell death initiation by glycolipids and indicated that further modification of these molecules

can lead to the development of a new therapeutic agent against fungal infection like *C. albicans*.

Sanada et al. (2014) reported the use of polyhexamethylene biguanide (PHMB) along with SLPs to prevent *Tinea pedis*. PHMB possesses antifungal activity and is used for disinfectant swimming pools, contact lenses and antimicrobial wound dressings. Non-woven textiles with PHMB are effective against *Trichophyton rubrum* and *Trichophyton mentagrophytes*. Non-woven textiles containing PHMB with SLPs increase PHMB access into the cuticle extensively reducing colony-forming units of *Trichophyton rubrum* and *Trichophyton mentagrophytes* suggesting that PHMB and SLPs are effective for *Tinea pedis* prevention.

19.10.4 Drug Delivery System

The use of biosurfactants as drug delivery agents offers attractive applications such as passive immunization, particularly where drug treatment options are limited.

Lactonic sophorolipid was formulated to develop solid lipid nanoparticle (SLPs) by the solvent injection method to encapsulate the antileprosy drug such as rifampicin and dapsone. For rifampicin, the EE (%) was 98.6 ± 0.2 and 98.8 ± 0.2, for SLN-3 and SLN-7 formulations, and for dapsone, it was 96.8 ± 0.2, and 96.9 ± 0.2, for SLN-3 and SLN-7 formulations, respectively. The kinetic model showed that the transport mechanism of rifampicin-releasing drugs is non-Fickian, and for dapsone, it is a Fickian-driven process. Due to easy preparation, biocompatibility, high entrapment efficiency, sustained release, increased bioavailability, etc., they have become a viable option for further research (Kanwar et al. 2018).

Darne et al. (2016) discussed the limiting factors for curcumin because of its low aqueous solubility, low retention time and poor bioavailability. SLPs were synthesized by non-pathogenic yeast such as *Candida bombicola* (ATCC 22214) and formulated curcumin-sophorolipids nano-conjugates (CurSL) to enhance the bioavailability. They have used gold salts, which act as potent-reducing and capping agents, resulting in synthesizing monodispersed, spherical gold nanoparticles (CurSL-GNPs) with sizes of 8–10 nm. Thus, Cur-SLPs-based nano-gold formulation was used as a good drug delivery carrier.

Another work done to enhance the bioavailability of the hydrophobic drug was studied (Yuan et al. 2019). In their study, they have fabricated the lutein-loaded zein nanoparticles with sophorolipid (ZSLNPs). These nanoparticles show good dispersibility and enhance water solubility of lutein with about 80 times higher than that of lutein alone.

19.10.5 Cosmetics

SLPs biosurfactants have been produced and commercially applied as an active ingredient in cosmetics products for body and skin applications.

Sophorolipids have antibacterial properties and are particularly active against gram-positive bacteria such as *Propionibacterium acnes* and *Corynebacterium xerosis*, the causal agents of acne and dandruff. Ashby et al. (2011) demonstrated different biopolymer matrices used to produce SLPs composite films with multiple antimicrobial effects against *P. acnes*. Pectin and alginate improve the transparency character of SLP composite films and also act as successful carriers of SLPs to *P. acnes*. SLPs in the lactone form have the best antimicrobial effect and work synergistically with all types of pectin or alginate biopolymers. It is a reproducible and eco-friendly measure against acne.

SLPs exhibited lower cytotoxicity than surfactin, which is a commercialized cosmetic ingredient (Hirata et al. 2009b).

19.10.6 Bioremediation

Bioremediation is a process that uses microorganisms to speed up the degradation of environmental contaminants. Biosurfactants produced by bacteria, fungi and yeast increase the surface area, solubility and bioavailability of hydrophobic water-insoluble substrates, stimulating the growth of oil-degrading microorganisms and improving their ability to utilize hydrocarbons.

The major problem facing today is the pollution of soils contaminated with poorly soluble polycyclic aromatic hydrocarbons (PAHs) like anthracene, fluorene, phenanthrene and pyrene. Phenanthrene is a model substrate for biodegradation research. SLPs increase the solubility and availability of phenanthrene stimulating the microbial biodegradation by *Sphingomonas yanoikuyae*. The maximum biodegradation achieved by *Sphingomonas yanoikuyae* is 1.3 mg/L h in the presence of SLPs compared to 0.8 mg/L h without SLPs. Two main problems can be solved by the use of surfactant—longer process time and residual pollutants (Schippers et al. 2000).

Oil pollution has caused a huge environmental problem for terrestrial and marine ecosystems. The components of petroleum have low aqueous solubility and strong binding and absorption in water and solid particles. The common method of remediation is based on the extraction of organic solvents or surfactants. SLPs improve the bioremediation of sites contaminated with hydrocarbons thereby increasing the bioavailability of microbial consortium for biodegradation. Adding SLPs to the site can improve the biodegradability of model compounds: 2-methylnaphthalene (95% degradation in 2 days), hexadecane (97%, 6 days) and pristane (85%, 6 days). SLPs show effective biodegradation of crude oil in soil (80% biodegradation of saturates and 72% aromatics hydrocarbon within in 8 weeks) (Kang et al. 2010).

19.10.7 Immunomodulatory Activity

Septic shock is a common cause of death in hospitals. In patients with sepsis caused by gram-negative bacteria, bacterial components including DNA, endotoxin and cell

wall lipopolysaccharide (LPS) are thought to be responsible for septic shock by inducing a cytokine cascade. Septic shock can lead to activation of the coagulation cascade and apoptosis, causing further organ damage and diffuse intravascular coagulation.

Hagler et al. (2007) demonstrated that SLPs decrease IgE production in U266 cells (IgE-producing myeloma cell line), by affecting the activity of plasma cells. This suggests that SLPs act as an anti-inflammatory agent and potential therapy in diseases with altered IgE regulation.

Sources of SPL	Application	Advantages	References
Candida bombicola	Antiviral and spermicidal activity	• It shows virucidal activity against HIV and sperm-immobilizing activity against human semen which is similar to nonoxynol-9 • Shows less cytotoxicity and higher activity	Shah et al. (2005)
Candida bombicola ATCC 22214	Bioremediation of lubricating oil-contaminated soils	• It increases the solubility, surface area and bioavailability of aqueous insoluble compounds • It also helps stimulate the growth of microorganisms that breakdown hydrocarbon and enhance their ability to use these hydrocarbons	Minucelli et al. (2017)
Candida bombicola ATCC 22214	Enhanced oil recovery	• Reduction of ST and IFT; it has a high %E24 for various hydrocarbons (including light and heavy crude oils) and also shows high stability under extreme conditions of salinity, pH and temperature	Elshafie et al. (2015)
Candida tropicalis	Bioremediation	• Good degrading agent of diesel oil • Higher emulsifying activity reduce surface tension	Chandran and Das (2012)
Candida kuoi NRRL Y-27208	Agriculture	• Natural surfactants/emulsifiers for post-emergence herbicides • SLPs can replace synthetic surfactants like polyethoxylated tallow amines (POEA)	Vaughn et al. (2014)
Candida bombicola	Cleaning agent	• Low cytotoxicity to human keratinocytes and fibroblasts • Biodegradable low-foaming surfactants with high detergency and hardness tolerance	Hirata et al. (2009a)
Torulopsis apicola and *Torulopsis bombicola*	Laundry detergent	• The detergent compositions show enhanced oily soil detergency in fabric washing	Flasz et al. (1998)

(continued)

Candida bombicola	Food	• Suitable for cleaning fruits, vegetables, skin and hair • This composition is sufficient to kill 100% of *E. coli*, *Salmonella typhi* and *Shigella dysenteriae* in 30 s	Data et al. (2001)
Chemically modified SLPs such as sophorolipid alkyl esters	Food	• Enhance the characteristics of prepared food products (bakery and oily emulsions)	Allingham (1971)
Candida species	Antibacterial activity	• Exhibited potential antibacterial activity towards pathogenic gram-negative and gram-positive bacteria	Archana et al. (2019)
Starmerella bombicola MTCC1910	Antifungal	• Inhibit *C. albicans* biofilm formation • It also shows inhibitory effect on hyphae formation	Haque et al. (2016)

19.11 Conclusions and Future Perspectives

Based on the origin, production and physicochemical properties of light-molecular-weight (LMW) and high-molecular-weight (HMW) microbial biosurfactants need to be explored and studied thoroughly to find their possible applications in nanotechnology. Most of the previous literature advocate the application of biosurfactant in synthesizing or stabilizing metal/metal oxide nanoparticles, but very recently (Bidyarani et al. 2020; Shinde et al. 2020), biosurfactants have been exploited for stabilizing protein nanoparticles for their application in drug delivery and agriculture. Due to their wide availability, low cost, biodegradability and environment-friendly nature, sophorolipids can be used in various industrial applications including food processing.

Sophorolipids are one of the most promising biosurfactants that belong to the glycolipid group and are synthesized extracellularly. These are produced mainly from non-pathogenic yeasts, in contrast to rhamnolipids which are mainly obtained from bacterial species *Pseudomonas aeruginosa*, making them more attractive for commercial purposes. Applications of sophorolipids have spiked over the last few decades, and their utilization has enhanced currently in the pursuit of natural ingredients. Various fermentation parameters essential for their optimal production and their various applications in agriculture, cosmetics, nanotechnology, bioremediation, antimicrobial, anticancer, immunomodulation, drug delivery, etc. have led to the replacement of synthetic surfactants.

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