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(Review Article)

Current status and applications of biosurfactants

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Abstract

Surface active agents or surfactants are the compounds that lower the surface tension between two phases, like between two liquids, a gas and a liquid, or a liquid and a solid. Most of these compounds are chemically synthesized and potentially cause environmental and toxicity problems. To overcome these pitfalls the biosurfatants are used widely nowadays due to their unique properties like specificity, low toxicity and relative ease of preparation. They are derived from microorganisms, possessing both hydrophilic and hydrophobic ends. Due to their unique functional properties, they are used in several industries including organic chemicals, petroleum, petrochemicals, mining, metallurgy (mainly bioleaching), agrochemicals, fertilizers, foods, beverages, cosmetics, pharmaceuticals and many others. They can be used as emulsifiers as well as demulsifiers, wetting agents, foaming agents, spreading agents, functional food ingredients and detergents. In this review, we highlight the classification of biosurfactants, recent important relevant applications, and potential future applications for biosurfactants in pharmaceutical industries.

Keywords: Microbial surfactant; Emulsan; Surfactin; Application

1 Introduction

Surfactants are compounds that lower the surface tension between two liquids, between a gas and a liquid, or between a liquid and a solid. Surfactants may act as detergents, wetting agents, emulsifiers, foaming agents, or dispersants [1]. The *word surfactant* is a blend of surface-active agent, coined in 1950. Surfactants are amphiphilic molecules that have hydrophobic and hydrophilic parts. The hydrophobic portion is a nonpolar long chain of fatty acids, whereas the hydrophilic domain can be nonionic, positively or negatively charged, or amphoteric, frequently a carbohydrate, an amino acid, or a phosphate Surfactants can be classified according to the chemical structure that is according to polar position [2]. Due to the higher toxicity and degradability problems, the surfactants are replaced by the Biosurfactants.

Biosurfactants or Microbial surfactants are defined as structurally diverse heterogenous groups of surface-active molecules synthesized by microorganisms. They are capable of reducing surface and interfacial tension and have a wide range of industrial and environmental applications [3]. They are mainly classified by their chemical structure and their microbial origin [4]. In the first instance, biosurfactants attracted attention as hydrocarbon dissolving agents in the late 1960s as potential replacement for synthetic surfactants (carboxylates, sulfonates, and sulfate acid esters), especially in the food, pharmaceutical, and oil industries. Synthetic surfactants currently used are usually toxic and hardly degraded by microorganism, causing damage to the environment. These are the major reasons behind the publicizing of the biosurfactants [5].

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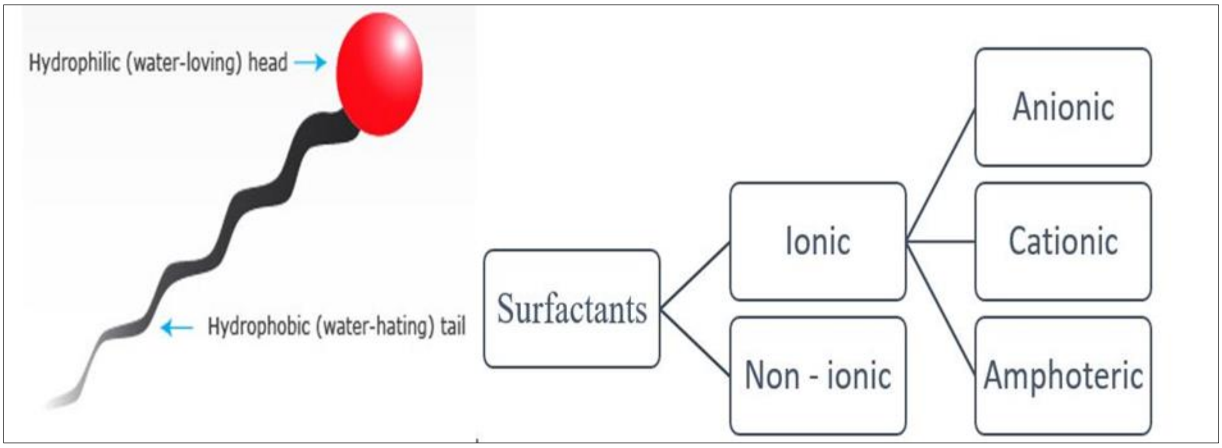

Figure 1 Structure of a surfactant and its classification

2 Features of biosurfactants

Biosurfactants have several advantages over chemical surfactants, including lower toxicity, higher biodegradability, effectiveness at extreme temperatures or pH values, biocompatibility, and digestibility [6]. They can be produced using agro industrial waste material. They can be economically produced and show better environmental compatibility [7]. The microorganisms that produce the biosurfactant can be modified by genetic engineering or biological and biochemical techniques [8].

3 Advantages and Disadvantages of Biosurfactants [9][10]

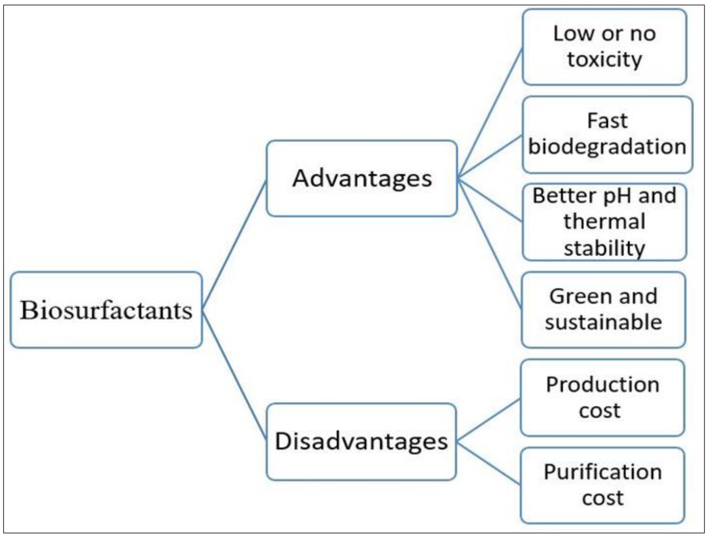

Figure 2 Advantages and Disadvantages of Biosurfactants

4 Classification of Biosurfactants

The classification of biosurfactants is based on

- Chemical composition,
- The microorganisms that produce it [11].

4.1 Classification of biosurfactant based on chemical composition and structure

Biosurfactants are made up of a hydrophilic moiety and a hydrophobic moiety. Hydrophilic moiety is comprising of an acid, peptide cations, or anions, mono-, di- or polysaccharides and Hydrophobic moieties comprising of an unsaturated or saturated hydrocarbon chains or fatty acids. These structures confer a wide range of properties, including the ability to lower the surface and interfacial tension of liquids and to form micelles and microemulsions between two different phases [12].Biosurfactants can be classified as,

- Low molecular weight biosurfactants
- High molecular weight biosurfactants

4.1.1 *Low molecular weight biosurfactants*

The low molecular weight biosurfactants are generally glycolipids or lipopeptides. The best investigated glycolipids are rhamnolipids, trehalolipids and sophorolipids which are disaccharides that are acylated with long-chain fatty acids or hydroxy fatty acids [13].Rhamnolipid, which is produced by *Pseudomonas aeruginosa* strains; composed of a backbone of two rhamnose moieties and two fatty acid residues. They are currently commercialised by JeneilBiosurfactant, USA, mainly as a fungicide for agricultural purposes or an additive to enhance bioremediation activities [14].In 1984, the first patent for the production of rhamnolipids was filed by Kaeppeli and Guerra-Santos and obtained the patent rights in 1986 for their work on *Pseudomonas aeruginosa* DSM 2659 [15].Trehalolipids are produced by a number of different microorganisms, such as *Mycobacterium* sp., *Nocardia* sp., and *Corynebacterium* sp. The most extensively studied compounds in this class are trehalosedimycolates produced by *Rhodococcuserythropolis*. Sophorolipids, on the other hand, are produced mainly by yeasts, such as *Candida bombicola* (also known as *Torulopsisbombicola*), *Centrolenepetrophilum, Candida apicola* and *Rhodotorulabogoriensis* [16]. Numerous lipopeptide antibiotics show potent surface-active properties. *Bacillus subtilis* produces a cyclic lipopeptide called surfactin, which has been reported to be the most active biosurfactant that has been discovered to date. The amphipathic nature of surfactin may contribute to some of its interesting biological properties, such as the formation of ion-conducting pores in membranes [17].Biosurfactants with low molecular mass are efficient in lowering surface and interfacial tensions [14].

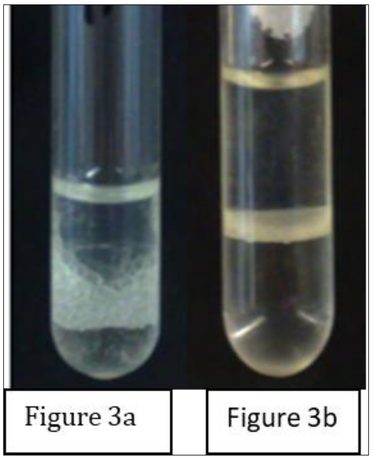

Figure 3 Stable emulsions produced by mixing a cell-free supernatant from a biosurfactant-producing yeast and hexadecane. The Fig 3a tube shows a clear emulsion characteristic of polymeric biosurfactants. The Fig 3b. tube shows a compact stable emulsion that is characteristic of low molecular weight biosurfactants

4.1.2 *High molecular weight biosurfactants*

High molecular weight biosurfactants are typically a complex mixture of macromolecules containing proteins, polysaccharides, and lipid residues. The most studied polymeric biosurfactant is emulsan, produced by *Acinetobactercalcoaceticus*were demonstrated to be effective in enhancing the solubility of polycyclic aromatic hydrocarbons (PAHs) [18].With the help of *A. calcoaceticus*, hazardous substances are converted into less or non-toxic forms, and it can be used to degrade and remove a wide range of organic and inorganic compounds [19].

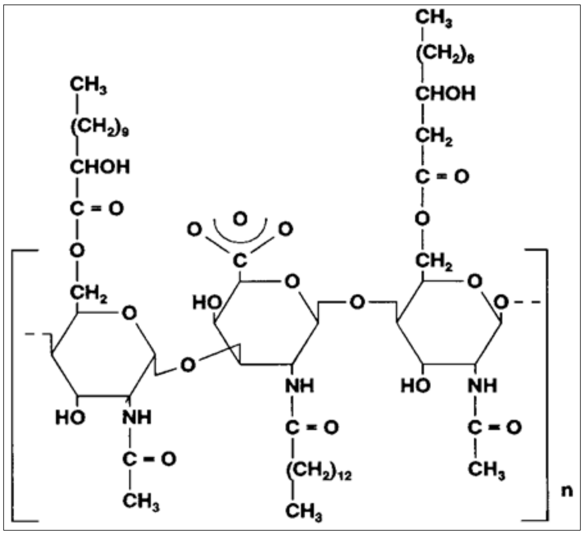

Figure 4 Structure of Emulsan

4.2 Classification of Biosurfactant based on the microorganisms that produce it

The Biosurfactants are mainly produced by Bacteria and Fungi and Yeasts.

4.2.1 Bacteria

The most reported genera of biosurfactant-producing bacteria include *Pseudomonas* sp., *Acinetobacter* sp., *Bacillus* sp., and *Rhodococcus* sp. *Pseudomonas* is the dominant genus involved in the biosurfactant production followed by other species.*Bacillus* sp. is mostly known for the production of Lipopeptides. Microorganisms that produce biosurfactants are isolated mainly from sites that are contaminated with petroleum hydrocarbons, contaminated soils, effluents, and wastewater sites. Thus, these have an ability to grow on substrates considered potentially noxious for other nonbiosurfactant-producing microorganisms [20].

Table 1 Biosurfactant-producing bacteria

Microorganism	Biosurfactant
Pseudomonas aeruginosa	Rhamnolipids
Pseudomonas fluorescens *Pseudomonas stutzeri* *Pseudomonas cepacia*	Ornithine lipids
Acinetobactercalcoaceticus	Lipopolysaccharides (Biodispersant)
Acinetobacterradioresistens	Heteropolysaccharide protein (Alasan)
Bacillus subtilis	Lipopeptides and lipoproteins (Surfactin)
Bacillus licheniformis	Lipopeptides (Lichenysin)
Tsukkamurella sp.	Di and Oligosaccharide lipids

4.2.2 Fungi and Yeasts

Candida sp. is the most commonly available fungal species for biosurfactant production comparing to other fungal species. Among the yeast species *Pseudozyma* sp. are most commonly reported for biosurfactant production. Yeasts can be preferred to bacteria as sources for biosurfactants because of their GRAS (generally regarded as safe) status, that is, they do not present risk of inducing toxicity or pathogenic reactions. Yeasts are also known for producing biosurfactants in higher concentrations than bacteria, which is an advantage for the development of production schemes [21]. On the other hand, when comparing bacteria and filamentous fungi to yeast, the latter has many advantages, including faster growth rate than filamentous fungi. *Yarrowialipolytica* was the first yeast used experimentally for the degradation of aliphatic hydrocarbon; this yeast also produces a highly efficient emulsifier [22].

Table 2 Biosurfactant-producing yeast

Microorganism	Biosurfactant
Candida bombicola *Candida apicola* *Candida rugosa* *Candida mucilaginosa*	Sophorolipid
Candida lipolytica	Carbohydrate-Protein (Liposan)
*Saccharomyces cerevisiae*2031	Mannoprotein

5 Applications

5.1 Biomedical applications

Mannosylerythritol lipid (MEL) produced by *Candida antartica*, rhamnolipids produced by *P. aeruginosa* and lipopeptides produced by *B. subtilis* and *B. licheniformis* have been shown to have antimicrobial activities [23].Biosurfactants, when purified, are a suitable alternative to synthetic medicines and antimicrobial agents and may be used as safe and effective therapeutic agents [24]. The biosurfactant isolated from *Candida parapsilosis* is conjugated with Graphene Quantum Dots (GQD) as a theranostic tool against cancer. This is an initial step to explore a novel bioconjugate for the diagnosis and therapy of cancer [25].Some of the biomedical applications of Biosurfactants are as follows:

Table 3 Biosurfactant-producing microorganisms and its biomedical applications

Microorganism	Biosurfactant Type	Activity/Application	Reference
Pseudomonas aeruginosa	Rhamnolipid	1. Antimicrobial activity against *Mycobacterium tuberculosis* 2. Anti-adhesive activity against several bacterial and yeast strains isolated from voice prostheses	[26][27]
Bacillus subtilis	Surfactin	1. Antimicrobial and antifungal activities 2. Inhibition of fibrin clot formation 3. Antitumor activity against Ehrlich's ascite carcinoma cells 4. Antiviral activity against HIV-1	[28][30]
Bacillus subtilis	Pumilacidin	1. Antiviral activity against herpes simplex virus 1 (HSV-1) 2. Inhibitory activity against H^+K^+ATPase and protection against gastric ulcers in vivo	[29]
Bacillus subtilis	Iturin	Antimicrobial activity and antifungal activity against profound mycosis	[30]
Bacillus licheniformis	Lichenysin	1. Antibacterial activity 2. Chelating properties that might explain the membrane disrupting effect of lipopeptides	[31]
Candida antartica	MEL	Antimicrobial, immunological and neurological properties	[32]

Streptococcus thermophiles	Glycolipid	Anti-adhesive activity against several bacterial and yeast strains isolated from voice prostheses	[33]
Rodococcuserythropolis	Treahalose lipid	Antiviral activity against HSV and influenza virus	[34]

5.2 Therapeutic applications

Biosurfactants have been delineated as suitable alternatives to synthetic medicines and antimicrobials and may be used as safe and effective therapeutic agents. Their feasible applications include gene transfection, as adjuvants for antigens, as inhibitors of fibrin clot formation, as activators of fibrin clot lysis, and also as an antiadhesive coatings for biomaterials, incorporated into probiotic preparations to fight urogenital tract infections, for pulmonary immunotherapy and have effects on cancer cells. The lipopeptidesurfactin was found to induce apoptosis in breast cancer cells and the glycolipids mannosylerythritol lipids (MELs) and succinoyltrehalose lipids (STLs) have been involved in growth arrest and apoptosis of tumor cells [35]. The novel uses of biosurfactants in nanotechnology are expanding day by day. A liposome vector containing β-sitosterolβ-D-glucosidebiosurfactant-complexed DNA was successfully used for herpes simplex virus thymidine kinase gene therapy [36].

The two important applications of Biosurfactant in therapeutic area are

- Biosurfactants as Antitumor agents
- Biosurfactants as Drug delivery agents

5.2.1 Biosurfactants as Antitumor agents

The biosurfactants have the ability to control a variety of mammalian cell functions and therefore they have the potential to act as antitumor agents interfering with some cancer progression processes. These molecules have been shown to participate in several intercellular molecular recognition steps such as signal transduction, cell differentiation, and cell immune response [37].

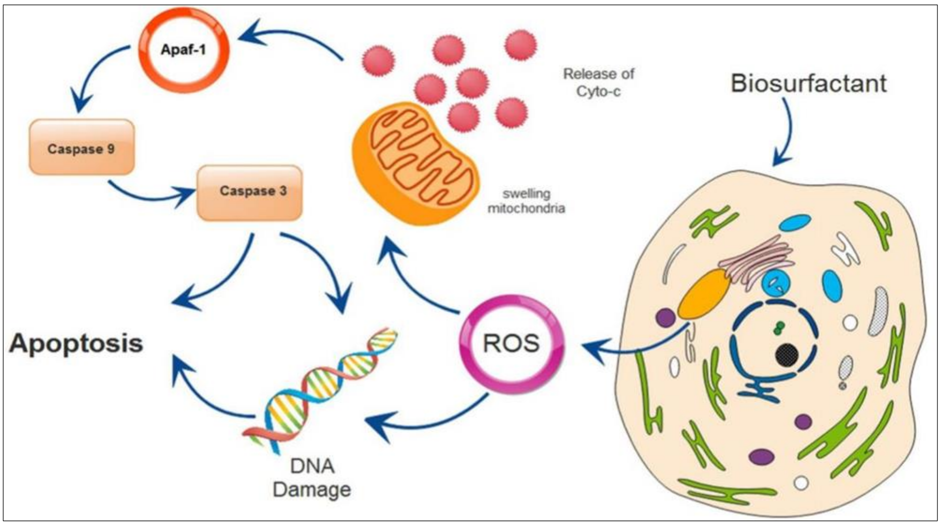

Figure 5 Mechanism involved in the antitumoral activity of surfactin (AIF- Apoptosis-Inducing Factor; Cyt c- Cytochrome c; ERK- Extracellular signal-Regulated protein Kinase; JNK- c-Jun N-Terminal Kinase; PI3K- Phosphoinositide 3-Kinase; ROS- Reactive Oxygen Species)

Glycolipids have been shown to be involved in growth arrest and apoptosis of mouse malignant melanoma B16 cells. The sophorolipid produced by *Wickerhamielladomercqiae* was shown to induce apoptosis in H7402 human liver cancer cells by blocking the cell cycle at G1 phase, activating caspase-3, and increasing Ca^{2+} concentration in the cytoplasm [38]. Lipopeptides, including surfactin, have potential antitumor activity against several cancer cell lines and they block cell proliferation by inducing proapoptotic activity and arresting the cell cycle as shown in figure 5 [39].

5.2.2 Biosurfactants as drug delivery agents

Rhamnolipids and Sophorolipids can be mixed with lecithins to prepare biocompatible microemulsions in which the phase behaviour is almost insensitive to changes in temperature and salt concentration, thus making them desirable for cosmetic and drug delivery applications. Rhamnolipid liposomes were patented as drug delivery systems, useful as microcapsules for drugs, proteins, nucleic acids, dyes and other compounds. These novel liposomes were described as safe and biologically decomposable, with suitable affinity for biological organisms, stable and with long service and shelf-life. Furthermore, rhamnolipids have been reported as safe adsorption enhancers for oral drugs. These microbial surfactants at low concentrations not only enhanced paracellular and transcellular transport pathways in Caco-2 (human colon adenocarcinoma) cells, but also inhibited P-gp activity. Surfactin was assembled by a solvent-emulsion method for the encapsulation of an anticancer drug doxorubicin.This is attributed to nanoparticles enhanced cellular uptake and cellular efflux reduction suggesting that surfactin based nanoparticles could be used as potential anticancer drug carriers for reversing MDR (Multi Drug Resistance) in cancer chemotherapy [40].

5.3 Pharmaceutical applications

Biosurfactants have prominent applications in Cosmetic industries. Biosurfactants have been exhibited to be compatible with the human skin and provide excellent skin surface moisturization. The MELs produced by *Candida* sp. have particular application in skin surface moisturization. The application of MELs in cosmetic products is associated to their potential to increase water retention in the stratum corneum and to repair damaged hair. Sophorolipids also have the potential to trigger beneficial events relating to damaged hair repair and skin protection [41]. Recently NIOT (National Institute of Ocean Technology) scientists developed a biosurfactant from a seabed sediment bacteria called brevibacterium as an emulsifying agent and an alternative to chemical surfactant for food, agricultural, industrial and pharmaceutical industries. Biosurfactants show some potential as antioxidant agents. MELs are versatile biosurfactants with antioxidant activity. MEL-C has highest antioxidant and protective effects in cells and suggests potential use as anti-aging skin care ingredients. Moreover biosurfactant obtained from *B. subtilis* RW-I showing antioxidant capacity to scavenge free radicals and suggesting potential use as alternative natural antioxidants.

6 Future outlook

When considering possible treatment opportunities for the COVID-19 pandemic, it is crucial to decide upon a mode of drug delivery which doesn't compromise the molecular nature of the product while also being able to deliver it successfully to the area of interest. With the SARS-CoV-2 predominantly impacting the respiratory system and upper gastrointestinal tract, a likely mode of delivery would be via aerosol or lozenge [42]. The micellar nature of biosurfactants result in them being the ideal candidates for either system of drug delivery, allowing them to form a stable liposome which will encase the drug, protecting it from damage which may otherwise cause dysfunction. The physicochemical characteristics of biosurfactants allow them to maintain their integrity while used in an aerosol; this would be the likely mode of drug delivery considering the main area of virulence to be within the lungs [43]. Recently, there is an increased attention of Biosurfactants as therapeutic agents, due to their immunosuppressive potential and as a novel treatment molecule in most of the immune diseases. There are ongoing researches relating to the biosurfactant as the drug delivery agents. Biosurfactants as Micro emulsifying drug delivery system and liposomal carrier for various therapeutic applications are currently under investigation [44]. The global Biosurfactants market was valued at 765.15 Million USD in 2020 and will grow with a CAGR of 7.64% from 2020 to 2027.

7 Conclusion

Until now the use of biosurfactants has been limited to a few specialized applications because biosurfactants have been economically uncompetitive. The biosurfactants market is driven by the increasing global industrial waste. The continuous increase in industrial waste worldwide drives the rise in the production of biosurfactants since they act as a source of raw materials for the manufacture of biosurfactants. Although biosurfactants have wide applications in therapeutic, biomedical and pharmaceutical fields further research is needed to develop production processes to increase yield and minimize the cost of purification when purification is a requirement for application.

Compliance with ethical standards

Disclosure of conflict of interest

There was no conflict of interest what so ever because all the authors that appeared on the manuscript contributed significantly in making this publication processes a success.

References

[1] Salager JL. Surfactants types and uses. FIRP booklet. 2002; 300.

[2] Kresheck GC. Surfactants. Water a comprehensive treatise. 1975; 95-167.

[3] Mukherjee AK, Das K. Microbial surfactants and their potential applications: an overview. AdvExp Med Biol. 2010; 672: 54-64.

[4] Banat IM, Franzetti A, Gandolfi I, et al. Microbial biosurfactants production, applications and future potential. ApplMicrobiolBiotechnol. 2010; 87(2): 427-44.

[5] Sáenz-Marta CI, de Lourdes Ballinas-Casarrubias M, Rivera-Chavira BE, Nevárez-Moorillón GV. Biosurfactants as useful tools in bioremediation. Advances in bioremediation of wastewater and polluted soil. 2015; 5.

[6] Kosaric N. Biosurfactants and their application for soil bioremediation. Food Technology and Biotechnology. 2001; 39(4): 295–304.

[7] Al-Araji L, Rahman RN, Basri M, Salleh AB. Microbial surfactant. Asia Pacific J MolecBiol and Biotechnol. 2007; 15(3): 99-105.

[8] Pacwa-Płociniczak M, Płaza GA, Piotrowska-Seget Z, Cameotra SS. Environmental applications of biosurfactants: recent advances.Int J Mol Sci. 2011; 12(1): 633-54.

[9] Tripathy DB, Mishra A. Sustainable biosurfactants. Sustainable Inorganic Chemistry. 2016; 21: 175.

[10] Magalhaes FF, Nunes JCF, Araújo MT, et al. Anti-Cancer Biosurfactants. InMicrobial Biosurfactants. 2021; 159-96.

[11] Mulligan CN. Environmental applications for biosurfactants. Environ pollut. 2005; 133(2): 183-98.

[12] Ron EZ, Rosenberg E. Natural roles of biosurfactants. Environ Microbiol. 2001; 3(4): 229-36.

[13] Muthusamy K, Gopalakrishnan S, Ravi TK, Sivachidambaram P. Biosurfactants: properties, commercial production and application. Current science. 2008; 94(6): 736-47.

[14] Thakur P, Saini NK, Thakur VK, et al. Rhamnolipid the Glycolipid Biosurfactant: Emerging trends and promising strategies in the field of biotechnology and biomedicine. Microb Cell Fact. 2021; 20(1): 1-5.

[15] Sekhon Randhawa KK, Rahman PKSM. Rhamnolipidbiosurfactants—past, present, and future scenario of global market. FrontMicrobiol. 2014; 5: 454.

[16] Sobrinho HB, Luna JM, Rufino RD, et al. Biosurfactants: classification, properties and environmental applications. Recent developments in biotechnology. 2013; 11(14): 1-29.

[17] Chen Y, Liu SA, Mou H, et al. Characterization of lipopeptidebiosurfactants produced by Bacillus licheniformis MB01 from marine sediments. Front Microbiol. 2017; 8: 871.

[18] Wong JW, Zhao Z, Zheng G. Biosurfactants from Acinetobactercalcoaceticus BU03 enhance the bioavailability and biodegradation of polycyclic aromatic hydrocarbons. InProceedings of the annual international conference on soils, sediments, water and energy. 2010; 15(1): 5.

[19] Mujumdar S, Joshi P, Karve N. Production, characterization, and applications of bioemulsifiers (BE) and biosurfactants (BS) produced by Acinetobacter spp.: a review. J Basic Microbiol. 2019; 59(3): 277-87.

[20] Rani M, Weadge JT, Jabaji S. Isolation and characterization of biosurfactant-producing bacteria from oil well batteries with antimicrobial activities against food-borne and plant pathogens. Front Microbiol. 2020; 27: 11-64.

[21] Campos-Takaki GM, Sarubbo LA, Albuquerque CD. Environmentally friendly biosurfactants produced by yeasts. AdvExp Med Biol. 2010; 672: 250-60.

[22] Accorsini FR, Mutton MJ, Lemos EG, Benincasa M. Biosurfactants production by yeasts using soybean oil and glycerol as low cost substrate. Braz J Microbiol. 2012; 43(1): 116-25.

[23] Rodrigues L, Banat IM, Teixeira J, Oliveira R. Biosurfactants: potential applications in medicine. J AntimicrobChemother. 2006; 57(4): 609-18.

[24] MdFakruddin. Biosurfactant: production and application. J Pet Environ Biotechnol. 2012; 3(4): 124.

[25] Bansal S, Singh J, Kumari U, et al. Development of biosurfactant-based graphene quantum dot conjugate as a novel and fluorescent theranostic tool for cancer. Int J Nanomedicine. 2019; 14: 809-818.

[26] El-Sheshtawy HS, Doheim MM. Selection of Pseudomonas aeruginosa for biosurfactant production and studies of its antimicrobial activity. Egyptian journal of petroleum. 2014; 23(1): 1-6.

[27] de Freitas Ferreira J, Vieira EA, Nitschke M. The antibacterial activity of rhamnolipidbiosurfactant is pH dependent. Food Res Int. 2019; 116: 737-44.

[28] Al-Wahaibi Y, Joshi S, Al-Bahry S, et al. Biosurfactant production by Bacillus subtilis B30 and its application in enhancing oil recovery.Colloids Surf B Biointerfaces. 2014; 114: 324-33.

[29] Mnif I, Ghribi D. Review lipopeptidesbiosurfactants: mean classes and new insights for industrial, biomedical, and environmental applications. Biopolymers. 2015; 104(3): 129-47.

[30] Nelson J, El-Gendy AO, Mansy MS, et al. The biosurfactantsiturin, lichenysin and surfactin, from vaginally isolated lactobacilli, prevent biofilm formation by pathogenic Candida. FEMS MicrobiolLett. 2020; 367(15): fnaa126.

[31] Saggese A, Culurciello R, Casillo A, et al. A marine isolate of Bacillus pumilus secretes a pumilacidin active against Staphylococcus aureus. Mar Drugs. 2018; 16(6): 180.

[32] Luna JM, Rufino RD, Sarubbo LA, et al. Evaluation antimicrobial and antiadhesive properties of the biosurfactantLunasan produced by Candida sphaerica UCP 0995. CurrMicrobiol. 2011; 62(5): 1527-34.

[33] Gudiña EJ, Fernandes EC, Teixeira JA, Rodrigues LR. Antimicrobial and anti-adhesive activities of cell-bound biosurfactant from Lactobacillus agilis CCUG31450. RSC Advances. 2015; 5(110): 90960-8.

[34] Roy A. Review on the biosurfactants: properties, types and its applications. J Fundam Renew Energy Appl. 2017; 8: 1-4.

[35] Gudina EJ, Rangarajan V, Sen R, Rodrigues LR. Potential therapeutic applications of biosurfactants. Trends Pharmacol Sci. Dec 2013; 34(12): 667-75.

[36] Eswari JS, Dhagat S, Mishra P. Biosurfactant assisted silver nanoparticle synthesis: A critical analysis of its drug design aspects. Advances in Natural Sciences: Nanoscience and Nanotechnology. 20 Nov 2018; 9(4):045007.

[37] Wu YS, Ngai SC, Goh BH, et al. Anticancer activities of surfactin and potential application of nanotechnology assisted surfactin delivery. Front Pharmacol. 26 Oct 2017;8: 761.

[38] Chen J, Song X, Zhang H, Qu Y. Production, structure elucidation and anticancer properties of sophorolipid from Wickerhamielladomercqiae. Enzyme and microbial technology. 3 Jul 2006;39(3):501-6.

[39] Rofeal M, Abd El-Malek F. Valorization of lipopeptidesbiosurfactants as anticancer agents. International Journal of Peptide Research and Therapeutics. Mar 2021; 27(1): 447-55.

[40] Rodrigues LR. Microbial surfactants: fundamentals and applicability in the formulation of nano-sized drug delivery vectors. J Colloid Interface Sci. 1 Jul 2015;449: 304-16.

[41] Campos JM, Montenegro Stamford TL, Sarubbo LA, et al. Microbial biosurfactants as additives for food industries. BiotechnolProg. Sep 2013; 29(5):1097-108.

[42] Smith ML, Gandolfi S, Coshall PM, Rahman PK. Biosurfactants: a Covid-19 perspective. Front Microbiol. 9 Jun 2020;11:1341.

[43] Vellingiri B, Jayaramayya K, Iyer M, et al. COVID-19: A promising cure for the global panic. Sci Total Environ. 10 Jul 2020; 725: 138277.

[44] Subramaniam MD, Venkatesan D, Iyer M, et al. Biosurfactants and anti-inflammatory activity: A potential new approach towards COVID-19. CurrOpin Environ SciHealth. Oct 2020;17: 72-81.