

Review

Microbial biosurfactant: A new frontier for sustainable agriculture and pharmaceutical industries

Ajay Kumar^{1#}, Sandeep Kumar Singh^{2#}, Chandra Kant³, Hariom Verma⁴, Dharmendra Kumar², Prem Pratap Singh², Arpan Modi¹, Samir Droby¹, Mahipal Singh Kesawat⁵, Hemasundar Alavilli⁶, Shashi Kant Bhatia⁷, Ganesh Dattatraya Saratale⁸, Rijuta Ganesh Saratale⁹, Sang-Min Chung¹⁰ and Manu Kumar^{10*}

1. Department of Postharvest Science, Agriculture research organization, Volcani center, 50250, Israel (ajaykumar_bhu@yahoo.com; arpanbiotek@gmail.com; samird@volcani.agri.gov.il)
 2. Centre of Advance Study in Botany, Banaras Hindu University, Varanasi, India (sandeepksingh015@gmail.com; dharambhu@gmail.com; prempratapsingh31@gmail.com)
 3. Department of Botany, Dharma Samaj College, Aligarh, 202001, India (ckantop@gmail.com)
 4. Department of Botany, B.R.D. Government Degree College Duddhi, Sonbhadra 231218, India (vermahariom87bhu@gmail.com)
 5. Faculty of Agriculture, Sri Sri University, Cuttack 754006, India (mahipal.s@srisriuniversity.edu.in)
 6. Department of Bioresources Engineering, Sejong University, Seoul 05006, Korea (alavilli.sundar@gmail.com)
 7. Department of Biological Engineering, College of Engineering, Konkuk University, Seoul 143701, Korea (shashibiotechpu@gmail.com)
 8. Department of Food Science and Biotechnology, Dongguk University, Seoul 10326, Korea (gdsaratale@gmail.com)
 9. Research Institute of Biotechnology and Medical Converged Science, Dongguk University-Seoul, Il-sandong-gu, Goyang-si, Seoul 10326, Korea (rijutaganesh@gmail.com)
 10. Department of Life Science, College of Life Science and Biotechnology, Dongguk University, Seoul 10326, Korea (smchung@dongguk.edu; manukumar007@gmail.com)
- * Correspondence: manukumar007@gmail.com; Tel.: +82-31-961-5157
 #First two authors share equal contribution

Abstract: In the current scenario of changing climatic conditions and the rising global population, there is an urgent need to explore novel, efficient, and economical natural products for the benefit of humankind. Biosurfactant is one of the latest explored microbial synthesized biomolecules that have been used in numerous fields, including agriculture, pharmaceuticals, cosmetics, food processing, and environment-cleaning industries as a source of raw material lubrication, wetting, foaming, making emulsions, and the stabilization of dispersions. The amphiphilic nature of biosurfactants showed a great advantage, distributing themselves into two immiscible surfaces by reducing interfacial surface tension and increasing the solubility of hydrophobic compounds. Furthermore, their eco-friendly nature, low or even no toxic nature, durability at higher temperatures, and withstanding a wide range of pH fluctuations making the microbial surfactants preferable compared to their chemical counterparts. Additionally, the biosurfactants can obviate the oxidation flow by eliciting the antioxidant property, antimicrobial, anticancer activity, and drug delivery system, further broadening their applicability in the food, pharmaceutical, and pharma industries. Nowadays, biosurfactant has been broadly utilized to improve the soil quality by improving the concentration of trace elements and mixed with pesticides or applied singly on the plant surfaces for plant disease management. In the present review, we summarize the latest aspect of microbial synthesized biosurfactant compounds, limiting factors of biosurfactant production, and their application in improving soil quality, plant disease management, and as antioxidant or antimicrobial compounds in the pharmaceutical industries.

Keywords: Biosurfactants; Critical micelle concentration (C.M.C.), Antioxidant; Microorganism; Soil quality; Plant disease management

1. Introduction

The rapid industrialization and rising global population excavate the challenges of food security and environmental management. Moreover, the changing climatic conditions such as rising temperature, irregular rainfall, biotic and abiotic stress factors adversely affect agricultural productivity. In addition, an eruption of new pests, pathogens, or plant diseases are some primary concerns for the agronomist, researchers, and scientific community. Indeed, a larger population of developed and developing countries rely on chemical pesticides or agrochemicals for pathogen control or plant disease management. Nevertheless, the undistributed and continuous use of agrochemicals results in the deposition of toxic chemical residue in the food, low nutrient quality, and the emergence of pesticide resistance pathogens.

Additionally, the deposition of agrochemicals adversely affects the texture, nutrient quality, or the native microflora of the soil and also leads to environmental challenges via polluting soil and water ecosystems [1]. However, to mitigate these challenges, since the last two decades, microbes and their products have been frequently utilized to enhance agricultural productivity and crop yield or mitigate toxic and hazardous environmental contaminants. Moreover, the ubiquitous nature of microbes, easy cultivation methods, cost-effectiveness, low or even no toxic effect on the surrounding environment makes it most preferable in the various fields for sustainable growth and production.

Biosurfactants are one of the latest explored microbial produced/synthesized biomolecules frequently utilized in the various agricultural, waste management, or pharma industries as raw material, lubricating, wetting, foaming, etc. emulsion making or for the stabilization of dispersions [2, 3]. The term biosurfactant has been referred to as the surface-acting agents that can improve surface-surface interactions through forming micelles produced by the natural source of origin, such as plants, microbes, and animals [4,5]. In addition, biosurfactants have been used during the applications to reduce the interfacial surface tension between solution and the surface, or air/ water or oil/water interfaces [6]. In other aspects, the addition of surfactants into an oil/water or water/air system cause reduction in the surface tension up to a point at which surfactants form structures like micelles, vesicles, and bilayers; usually, this critical point is known as critical micelle concentration (C.M.C.) (Figure 1).

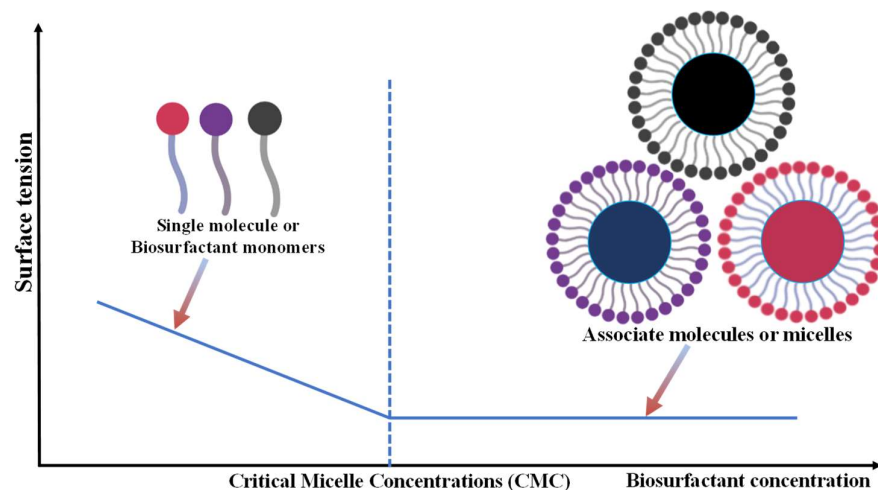


Figure 1. Critical micelle concentration (CMC) and micelle formation of biosurfactant monomers.

However, in a combined mixture or after the addition of surfactant in the water and oil mixture, the surfactant resides at the water-oil interface and forms emulsions, which confer excellent emulsifying, foaming, and dispersing capacities. This makes surfactants

one of the most versatile chemicals for industrial processes [7]. The commonly used surfactant is of chemical origin, but their toxic nature, low degradation rate, and high persistence power limit their frequent use in the food, cosmetics, and pharmaceutical industries [8]. The surfactant of microbial origin has several advantages over the synthetic or chemical surfactant: higher temperature tolerance, stability in pH variation, high salinity tolerance, higher degradation rate, less toxicity, and better selectivity [9,10].

The biosurfactants are usually composed of amphipathic molecules having both hydrophilic and hydrophobic constituents. The hydrophilic compound generally consists of either positive, negative, or amphoteric charged ions, whereas the hydrophobic ends are made up of a long chain of fatty acids [11]. Irrespective of chemical counterparts, biosurfactants are generally classified based on molecular weight (low or high), critical micelle concentration (C.M.C.), microorganism produced, and their mode of action. Glycolipids, phospholipids, and lipopeptides are the most commonly reported low molecular weight; however, high molecular weight biosurfactants are comprised of polysaccharides, lipopolysaccharides, and a complex mixture of biopolymers. The detailed classification and their common examples are illustrated in table 1 and Figure 2.

Table 1. Biosurfactant classification and their common examples.

Types of Biosurfactants		Common examples
Low molecular mass	Glycolipids	Rhamnolipids
		Sophorolipids
		Trehalose lipids
	Phospholipids	Phospholipids
		Corinomiocolic acid
		Fatty acids
	Lipopeptides	Surfactin
		Wisconsin
		Gramicidin
		Subtilisin
Peptide lipid		
High molecular mass	Polymeric	Lichenysin
		Liposan
		Emulsan
		Biodispersion
		Mannan-lipid protein
		Carbohydrate lipid-protein
	Particulate	Vesicles

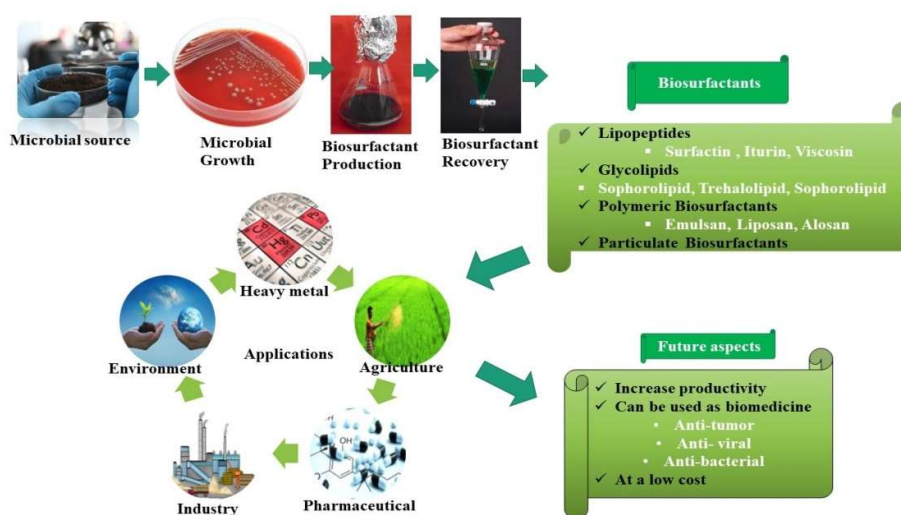


Figure 2. Schematic representation of biosurfactants production utilizing microbial resources and their potential applications.

The low molecular weight microbial synthesized biosurfactants have excellent capability of reducing surface tension; however, high molecular weight is associated with making stable emulsion [7, 12,13]. The eco-friendly and multifunctional attributes of biosurfactants are considered the surfactant of the next generation and are frequently utilized in various industries worldwide. According to a published report, the market size of Biosurfactant is expected to increase with 0.8% of the compound annual growth rate (CAGR) in the forecast period of 2020 to 2025. It will be expected to reach about USD 1446.5 million by 2025 from the USD 1403.1 million reported in 2019 (Global Biosurfactant Market 2020 by Manufacturers, Regions, Type, and Application, Forecast to 2025).

For sustainable agricultural practices, biosurfactants have been used to improve soil quality by degrading toxic and hazardous contaminants or making trace elements available in the soil and frequently utilized as antagonistic molecules against the pest/pathogens or plant diseases. Surfactants produced by microbial strain possess antimicrobial properties, which effectively inhibit pathogen growth. In several cases, it protects the plant from pathogen infection *via* stimulating the plant immune system [14]. Furthermore, utilization of biosurfactants showed additional benefit in the plant through enhancing growth promotion. Additionally, the native microflora of the soil or plant system uses these biosurfactant molecules as a source of energy for regulating plants' physiological parameters and maintaining the plant system's health and quality.

Moreover, nowadays, in pharmaceutical industries, biosurfactant molecules are broadly used as antioxidants, anti-microbial, anti-cancerous agents, or as raw materials, emulsifying or dispersing agents. Thus, the application of biosurfactants in treating human ailments is cost-effective and safe from toxic side effects. In the present review, we summarize the latest aspect of biosurfactant synthesis from microbial sources, limiting factors of biosurfactant production. In addition, it also discussed the potential application of biosurfactants in sustainable agriculture, specifically their role in improving soil quality or plant pathogen management and pharmaceutical industries as an antioxidant or anti-microbial molecule.

2. Microorganism and biosurfactants

Currently, numerous microbial strains of bacteria, fungi, and yeast have been reported for the efficient production of biosurfactants. However, the quality and quantity of biosurfactants depend on several factors, including the type of microorganism, media

supplements, nature of the substrate, and different intrinsic and extrinsic factors at the time of microbial culture growth [15, 16]. The selection of microbial strain is the primary step of biosurfactant production. However, biosurfactant synthesis in the microbial strain is carried out either intracellularly or extracellularly during the exponential or stationary phase of growth, when the nutrient conditions are limiting [17]. The nature of biosurfactants also depends upon microorganisms' source and isolation strategies; for instance, a strain isolated from a contaminated site is considered a suitable choice for the degradation of that particular contaminant. The probable reason for this concept is that the isolated microorganism can use that contaminant as a source of energy or substrate, where other microorganisms or non-surfactant-producing microorganisms cannot survive [18].

Furthermore, biosurfactants play a physiologic role in increasing the bioavailability of hydrophobic molecules involved in cellular signaling or differentiation processes and facilitate the consumption of carbon sources present in the soil [19]. Indeed, the physiological aspect of biosurfactant production in the contaminated site is not clearly understood but considered for enhancing the nutrient uptake from the hydrophobic substrate, biofilm formation, and cellular motility by reducing the surface tension at the phase boundary [7]. The development of rapid and reliable methods for the isolation and screening of microbial strains and further evaluation of role in emulsification, reducing interfacial or surface tension are critical factors during the exploration of biosurfactant molecules [20]. In early 1941, Bushnell and Hass [21] reported biosurfactants produced by the bacterial strain *Corynebacterium simplex* and *Pseudomonas* grown in the minimal media containing kerosene, mineral oil, or paraffin [22]. Then, numerous microbial strains, including bacteria, fungi, and yeast, have been reported for efficient biosurfactant production. Details of microbial strains and their synthesized biosurfactants are illustrated in Tables 2A, B, C.

Table 2. A. Different types of biosurfactants produced from bacterial strains.

Bacterial strains	Biosurfactants	Properties	Isolation source	References
<i>Pontibacter korlensis</i> strain SBK-47	Pontifactin	Surface-active, antimicrobial, and anti-biofilm activities	Coastal waters of Karaikal, Puducherry, India	[23]
<i>Bacillus licheniformis</i>	Lipopeptides	Heat resistance and capacity to emulsify oils used in cosmetics	Deception Island (Antarctica)	[24]
<i>Paracoccus</i> sp. MJ9	Rhamnolipid	Enhance solubility of hydrophobic compounds	Jiaozhou Bay in Qingdao, Shandong Province	[25]
<i>Pseudomonas aeruginosa</i> UCP0992	Rhamnolipids	High emulsifying activities against different oils, capacity to remove hydrophobic contaminants and did not show toxicity	Centre of Research in Environmental Sciences, Catholic University of Pernambuco, Brazil	[26]
<i>Pseudomonas aeruginosa</i> PA1	Rhamnolipid	Capacity to use as carbon sources	Oil production wastewater in the Northeast of Brazil	[27]
<i>Pseudomonas desmolyticum</i> NCIM 2112	Rhamnolipid	Degradation of textile dye	National Center for Industrial Microorganisms (NCIM), Pune, India	[28]
<i>Serratia marcescens</i> SS-1	Serrawettins	Produces lipopeptide surfactants, having capability to reduce surface-tension	Taiwan	[29]
<i>Bacillus subtilis</i>	Cyclic lipopeptides	A significant reduction in the activities of acetylcholinesterase, α -carboxylesterase, and acid phosphatases	Namakkal and Tirunelveli district, Tamil Nadu, India	[30]

<i>Bacillus subtilis</i>	Pumilacidin	Antiviral activity against Herpes simplex virus 1 (HSV-1)	Tree trunk near lake Yamanaka, Japan	[31]
<i>Pseudomonas aeruginosa</i> S5	Glycolipid	Removal of polycyclic aromatic hydrocarbons	Supelco (Bellefonte, PA, USA)	[32]
<i>Pseudomonas protegens</i> F6	Orfamide A	Insecticidal against <i>Myzus persicae</i>	Soil from previously reported diesel oil-contaminated site	[33]
<i>Pseudomonas aeruginosa</i> DS9	Rhamnolipid	Antifungal agents against <i>F. sacchari</i> in pokkah boeng Disease	Lakota oil-field of Sivsagar district, Assam, India	[34]
<i>Pseudomonas fluorescens</i> BD5	Pseudofactin II	Anti-adhesive activity and disinfectant	Freshwater from the Arctic Archipelago of Svalbard	[35]
<i>Bacillus</i> sp. BS3	Lipopeptide	Anticancer activity and antiviral properties	Solar salt works in Tamilnadu, India	[36]
<i>Pseudomonas aeruginosa</i>	Rhamnolipid	Enhanced oil recovery through anaerobic production of Rhamnolipid	Daqing oilfield-produced water	[37]
<i>Bacillus subtilis</i> A21	Lipopeptide	Removal of petroleum hydrocarbons, heavy metals	Adityapur Industrial Area, Jharkhand	[38]
<i>Rhodotorula bogoriensis</i>	Sophorolipid	Antimicrobial property against <i>Propionibacterium acnes</i>	American Type Culture Collection	[39]

Table 2. B. Different types of biosurfactants produced from fungal strains.

Fungi	Biosurfactants	Properties	Isolation source	References
<i>Candida utilis</i>	Emulsifiers	Emulsifiers	Culture collection from the Department of Antibiotics of the Universidade Federal de, Pernambuco, Brazil	[40]
<i>Candida lipolytica</i> UCP 0988	Lipopeptide	Not toxicity against different vegetable seed	Culture collection of Nucleus of Research in Environmental Sciences, Catholic University of Pernambuco, Recife-PE, Brazil	[41]
<i>Penicillium chrysogenum</i> SNP5	Lipopeptide	Role in pharmaceuticals as well as in petroleum and oil industry	Soil contaminated grease waste	[42]
<i>Cunninghamella echinulata</i>	Complex Carbohydrate/protein/lipid	Reduce and increase the viscosity of hydrophobic substrates and their molecules	Caatinga soil of Pernambuco, Northeast of Brazil	[43]
<i>Candida Antarctica</i>	Mixtures of 4 mannosylerythritol lipids	Produced the lipids from different vegetable oils	Centraalbureau voor Schimmel cultures, the Netherlands	[44]
<i>Microsphaeropsis</i> sp.	Eremophilane derivative	Antimicrobial properties	Waters around the Caribbean Island of Dominica	[45]
<i>Yarrowia lipolytica</i> NCIM 3589	Bioemulsifier	Increased the hydrophobicity of the cells during the growth phase	Seawater near Mumbai, India	[46]

<i>Yarrowia lipolytica</i> IMUFRJ50682	Carbohydrate protein complex	Capable of stabilizing oil-in- water emulsions	Guanabara Bay in Rio de Janeiro	[47]
<i>Ustilago maydis</i>	Cellobiose lipids	Secreted cellobiose lipid having antifungal activity	-	[48]
<i>Torulopsis bombicola</i>	Sophorose lipid	Sophorose lipid fermentation	American Type Culture Collection	[49]
<i>Aspergillus ustus</i>	Glycolipoprote	Antimicrobial activity	Peninsular coast of India	[50]
<i>Candida bombicola</i> ATCC 22214	Sophorolipid	Used in low-end consumer products and household application	American Type Culture Collection	[51]
<i>Ustilago maydis</i> FBD12	Glycolipids	Antimicrobial activity	American Type Culture Collection	[52]

Table 2. C. Different types of biosurfactants produced from yeast strains.

Yeast	Biosurfactants	Properties	Isolation source	References
<i>Starmerella bombicola</i>	Sophorolipids	Cytotoxic effect on MDA-MB- 321 breast cancer cell line	Fungal Biodiversity Centre	[53]
<i>Torulopsis Petrophilum</i> ATCC 20225	Glycolipids	Protein emulsifier	American Type Culture Collection	[54]
<i>Kluyveromyces marxianus</i> FII 510700	Mannanoprotein	Source of emulsifier in the food industry	Culture Collection of the University of New South Wales, UNSW	[55]
<i>Pseudozyma aphids</i> , DSM 70725 and DSM 14930	Mannosylerythrit ol lipids	Foam formation	Deutsche Stammsammlung von Mikroorganismen und Zellkulturen (DSMZ), Braunschweig, Germany	[56]
<i>Pseudozyma tsukubaensis</i>	Glycolipid	Producing diastereomer MEL- B from vegetable oils	Leaves of <i>Perilla frutescens</i> on Ibaraki in Japan	[57]
<i>Saccharomyces cerevisiae</i> URM 6670	Glycolipid	Antioxidant activity and cytotoxic potential	Culture Collection of the Department of Antibiotics of the Federal University of Pernambuco (Brazil)	[58]
<i>Trichosporon asahii</i>	Sophorolipid	Efficient degrader of diesel oil, higher hydrophobicity, emulsification activity, surface tension reduction	petroleum hydrocarbon contaminated soil in India	[59]
<i>Meyerozyma guilliermondii</i> YK32	Sophorolipid	Emulsification properties	Soil samples collected from hydrocarbon-polluted locations of Hisar, Haryana	[60]
<i>Rhodotorula babjevae</i> YS3	Sophorolipid	Antimicrobial activity	Agricultural field in Assam, Northeast India	[61]

<i>Pichia caribbica</i>	Xylolipid	Reduced the surface tension of distilled water	Microbial type culture collection, India	[62]
<i>Candida ishiwadae</i> Y12	Monoacylglycerols: Glycolipid	Exhibited high surfactant activities	Plant material in Thailand	[63]

3. Factor affecting biosurfactant production

Traditionally, most biosurfactants producing bacterial strains are isolated from the petroleum/ oil contaminated soil or fermented food, but nowadays, microbial isolates are screened from various sources. The production of biosurfactants started with the growth, identification, and characterization of microbial strain. The growth conditions of the cultures should be maintained according to the sample sites. However, the methodology, substrate, and purification process should be cost-effective for biosurfactant production at a commercial or industrial scale. According to a published report, 10-30 % of the total cost accounted for raw materials during biosurfactant production [64], while up to 60% of the total cost has been spent on the downstream or purification processes [64, 65]. The media components of the microorganism play an essential role in biosurfactant production and significantly impact the production cost. Carbon (C) and nitrogen (N) source in the media is an essential requirement for microbial growth [66]. The type, amount, and ratio of carbon and nitrogen in the media directly affect microbial growth and biosurfactant production in both laboratories and large-scale industrial fermenters [67]. In most studies, glucose, sucrose, and glycerol are being used as carbon and yeast extract, NaNO₃, urea, soya broth has been used as a nitrogen source in the media [68,69]. For instance, an abundance of carbon sources and limiting nitrogen conditions are preferred for optimum biosurfactant production. For example, the ratio of C: N≈20 has been found most favorable for *Pseudomonas* sp. [70]. In a study, Onwosi and Odibo [71] evaluated the role of carbon and nitrogen source on the rhamnolipid produced by the strain *Pseudomonas nitroreductase* and found glucose (carbon source), and sodium nitrate (nitrogen source) was the most preferred source, in which able to recovered 5.28 and 4.38 g l⁻¹ of rhamnolipid respectively.

Furthermore, the highest yield of 5.46 g l⁻¹ was observed when the ratio of C: N (glucose/sodium nitrate) was 22. Thus, the selection of media sources has a significant impact on biosurfactant production. A detailed survey on the utilization of carbon and nitrogen sources and their implications for biosurfactant recovery has been described in Table 3A, B.

Table 3. A. The common substrate used in biosurfactant production and their yields.

Substrate	Conc. (g l ⁻¹)	Microorganisms	Yield (g l ⁻¹)	References
Glucose	40	<i>P. aeruginosa</i>	0.3	[72]
	40	<i>B. subtilis</i>	3.6	[73]
	40	<i>B.subtilis</i>	0.72	[74]
	30	<i>B. pumilus</i>	0.72	[75]
	20	<i>P. aeruginosa</i>	3.88	[76]
	10	<i>B.subtilis</i>	0.16	[77]
	-	<i>Pseudomonas</i> sp.	0.35	[78]
Sucrose	20	<i>P. putida</i>	1.30	[79]
Glucose and fructose	16.55	<i>B. subtilis</i>	0.93	[80]
Glucose+ Yeast extract	1:3	<i>Bacillus</i> sp.	2.56	[81]
Glycerol+ yeast extract	30:5	<i>P. aeruginosa</i>	2.7	[82]
Yeast extract	1	<i>P.taiwanensis</i>	1.12	[83]
Yeast extract	2	<i>Bacillus</i> sp.	2.5	[84]
NaNO ₃	0.2 M	<i>P. aeruginosa</i>	2.73	[85]

NaNO ₃	5	<i>B. subtilis</i>	1.12	[86]
Peptone	4	<i>Serratia marcescens</i>	1.2	[87]
NH ₄ NO ₃	1	<i>P. fluorescens</i>	2	[88]

The production cost of biosurfactants largely depends upon the media source, primarily carbon and nitrogen sources. Therefore, in recent past, a range of new and novel resources such as residual waste products of the food industry, frying oil, distillery, molasses, vegetable, and plant-derived oil, has been trailed in the media as a carbon and nitrogen source as single or along with the stabilized resource. The utilization of these products can cut or reduce the cost of biosurfactant production [89, 90]. The use of vegetable oil and hydrocarbon-based substrates appear as economical and profitable substrates for large-scale biosurfactant production, especially from *Pseudomonas*, *Bacillus*, and *Candida* sp. [91].

There are numerous reports available in biosurfactant production using different nutritional sources and limiting environmental factors. For example, Agarwal and Sharma [92] utilized different C sources such as glycerol, molasses, rice water, cheese whey, potato peels, and glucose to evaluate their impact on biosurfactant production. They observed similar biosurfactant activity, using molasses and glycerol sources, and biosurfactant produced using glucose source. In addition, utilization of NH₄Cl, NH₄NO₃, and NaNO₃ as a nitrogen source yielded good results. Similarly, Al-Bahry et al. [93] recovered 2.29 ± 0.38 gl⁻¹ of biosurfactant, using date molasses as a carbon source from the strain *Bacillus subtilis* B20, which had the capability to reduce surface tension and interfacial tension from 60 to 25 mN m⁻¹ and 27 to 5.02 mN m⁻¹, respectively. In addition, biosurfactants showed stability against a wide range of temperatures, pH variations, and range of salt concentrations. Hentati et al. [94] reported 50 mg l⁻¹ of biosurfactant production by the strain *Bacillus stratosphericus* FLU5 using residual frying oil as a carbon source. At this concentration, the surface tension of the water was reduced from 72 to 28 mN m⁻¹. Similarly, Souza et al. [95] reported biosurfactant production by the strain *Wickerhamomyces anomalus* CCMA. Under optimized culture conditions, various amount of biosurfactant has been recovered from the yeast strain using different energy resources like yeast extract (4.64 gL⁻¹), ammonium sulfate (4.22 gl⁻¹), glucose (1.39 gL⁻¹) and olive oil (10 gL⁻¹). However, the highest yield of biosurfactant was recovered from the 24 h old culture. Additionally, the biosurfactant remained stable even at a higher temperature of 121 °C, 300gl⁻¹ of NaCl concentrations, and 6 -12 pH ranges.

Table 3. B. The common alternative substrate and their impact on biosurfactant yield.

Microorganism	Alternative media source	Yield and properties	References
<i>Bacillus subtilis</i> B20	Date molasses	The product yield of 2.29 ± 0.38 gl ⁻¹ reduced surface tension and interfacial tension from 60 to 25 mN m ⁻¹ to 27 and 5.02 mN m ⁻¹ , respectively.	[96]
<i>Bacillus subtilis</i> PC	Sugar cane vinasse	Able to reduce surface tension 32 mN m ⁻¹ and the E24 to 51.10 %.	[97]
<i>Bacillus subtilis</i>	Corn steep liquor	Biosurfactant yields 1.3 g l ⁻¹ ; the different yields increased (up to 4.1, 4.4, and 3.5 g/l for iron, manganese, and magnesium, respectively supplements). However, at the optimum concentration, these three metals' yield increased up to 4.8 g l ⁻¹ .	[98]
<i>Bacillus subtilis</i> MTCC 2423	Rice mill polishing residue	Surfactin yield 4.17 g kg ⁻¹ residue	[99]
<i>Bacillus licheniformis</i> AL1.1	Molasses	Lichenysin yield of 3.2 g l ⁻¹	[100]

<i>Bacillus pseudomycoides</i>	Soybean oil waste	C.M.C. of lipopeptide 56 mg l ⁻¹ and able to reduce the surface tension of water from 71.6 mN m ⁻¹ to 30.2 mN m ⁻¹	[101]
<i>Bacillus subtilis</i> DSM 3256	Two-phase olive mill waste	Surfactin yields 0.068 g g ⁻¹ , and the surface tension of the culture medium is reduced to 30.1 ± 0.9 mN m ⁻¹ .	[102]
<i>Bacillus subtilis</i>	Rapeseed cake	Surfactin analogues	[103]
<i>Bacillus amyloliquefaciens</i>	Distillers' grains	Surfactin yield 1.04 g l ⁻¹	[104]
<i>Wickerhamomyces anomalus</i> CCMA 0358	The optimized culture medium contained yeast extract (4.64 g/L), ammonium sulfate (4.22 g/L), glucose (1.39 g/L), and olive oil (10 g/L).	Biosurfactant reduced the surface tension from 49.0 mN m ⁻¹ to 31.4 mN m ⁻¹ and 29.3 mN m ⁻¹ in flask and bioreactor, respectively. In both the cases, highest biosurfactant production was achieved after 24 h of growth. In addition, the biosurfactant showed stability up to 121 °C, 300 g L ⁻¹ of NaCl, and 6-12 range of pH.	[105]
<i>Bacillus stratospheric</i>	Residual frying oil,	The C.M.C. of the purified lipopeptides was 50 mg l ⁻¹ and reduced surface tension of water from 72 to 28 mN m ⁻¹ . Additionally stable against a broad range of pH, temperature, and salinity.	[106]
<i>Halomonas venusta</i> PHKT	Glycerol	Surfactin, Pumilacidin, and Bios-PHKT have a critical micelle concentration (C.M.C.) of 125 mg L ⁻¹ and showed a high steadiness against a broad spectrum of salinity (0–120 g L ⁻¹ NaCl), temperature (4–121 °C) and pH (2–12).	[107]
<i>Rhodotorula</i> sp.	Olive oil mills	Potent biosurfactant producer with E24 = 69% and a significant reduction in S.T. from 72 to 35 mN m ⁻¹ . In addition, shown stability over a wide range of pH (2–12), temperature (4–100 °C), and (1–10%) salinity	[108]
<i>Volvariella volvacea</i>	Edible paddy straw mushroom	Biosurfactant effectively showed a reduction in the surface tension, emulsification index, and oil spreading activity as 35.15 dyne/cm, 80%, and 11 cm, respectively.	[109]

Besides nutrient sources, the production of biosurfactants depends upon several factors such as incubation time, incubation temperature, pH of growth culture, and the speed of rotation rate of shaking incubator, which directly affects microbial growth and biosurfactant production. In a study, Achim et al. [110] evaluated the biosurfactant production potential of *Azotobacter chroococcum* under controlled nutritional and environmental conditions. The highest 68% of surface tension and emulsification index (EC24) was observed at pH 7. Sunflower oil and heavy oil 150 had shown the best response among different carbon sources and accounted for 76.6% and 74.1% of E.C. 24, respectively. However, higher EC24 was recorded after supplementing yeast extract (83.3%) and (NH₄)₂SO₄ (80%) among different nitrogen sources. The optimum recovery of biosurfactant was achieved from 4 days old culture incubated at 30°C, at the shaking incubator at 150 rpm.

Similarly, Joaad and Hassan [111] evaluated the biosurfactant potential of yeast strain *Candida guilliermondii* using the VITTEK2 compact system under controlled environmental and nutritional conditions. The maximum EC24 was 70 % observed at pH 4 and 75% at 30 °C. However, sesame oil and heavy oil 150 were shown the best response

as a carbon source, yeast extract, and NaNO_3 as a nitrogen source. Additionally, the shaking incubator at 150 rpm recorded higher emulsifier production on the 7th day of culture growth.

4. Biosurfactant applications in improving soil quality

The growth and productivity of the crop ecosystem rely on the availability and presence of an optimum concentration of micro or macronutrients in the soil. Trace elements present in the soil directly influence the physiological processes of the plant. Indeed, deficiency or excess availability of these elements led to various diseases and poor quality of plant growth. The ongoing changing climatic condition, rising global temperature, variation in soil pH, increase in salinity, or deposition of environmental contaminants adversely affect the efficacy of trace elements in the soil, resulting in poor availability to the plants, which ultimately results in lower crop production and poor quality of foods [112].

The addition of biosurfactants in the soil significantly enhances the availability of micronutrients in the mineral deficient soil through various processes. The addition of surfactant makes a complex with the metal ion, which, through biochemical processes like oxidation-reduction, adsorption, and desorption, increases their bioavailability or concentration in the soil [113]. In detail, an anionic charge of surfactant binds with the cationic charge of the metal and forms a complex, through this way, acts as a sequestering agent and performs desorption of soil [114]. Although in contaminated water, the flushing of water through soil can remove metal surfactant complex from the soil because of strong electrostatic interaction between the opposite charge ion of the metal and surfactant, resulting in metal mobilization in the water [115,116]. The application of biosurfactants can also help mitigate the challenges of soil alkalinity, which are considered one of the paramount factors of micronutrient deficiency in the soil. The addition of biosurfactants makes the metal-biosurfactant complex available by removing or unbinding the metal from the soil complex [117]. During this interaction, the bond strength of metal-biosurfactant is much higher than the metal-soil interaction, which further desorbed metal-biosurfactant from the soil matrix to soil solution due to lowering of interfacial tension, resulting in the availability of trace elements to the plant roots [115, 118]. The addition of surfactant reduces the interfacial tension between the metal and soil, forms micelles, and transfers them to the root zone interface.

The use of biosurfactants in the agricultural field to improve or enhance the availability of micronutrients to the soil is the new approach and is nowadays broadly practiced in different parts of the world [115]. The amphipathic nature of biosurfactants can reduce the interfacial tension between two immiscible liquids and enhance the solubility of organic and inorganic components [119, 120]. In the agricultural process, different biosurfactants are reported to decrease the interfacial surface tension between the solid surfaces and the trace metal cations, resulting, increased solubility and mobility of trace elements [121] (Figure 3).

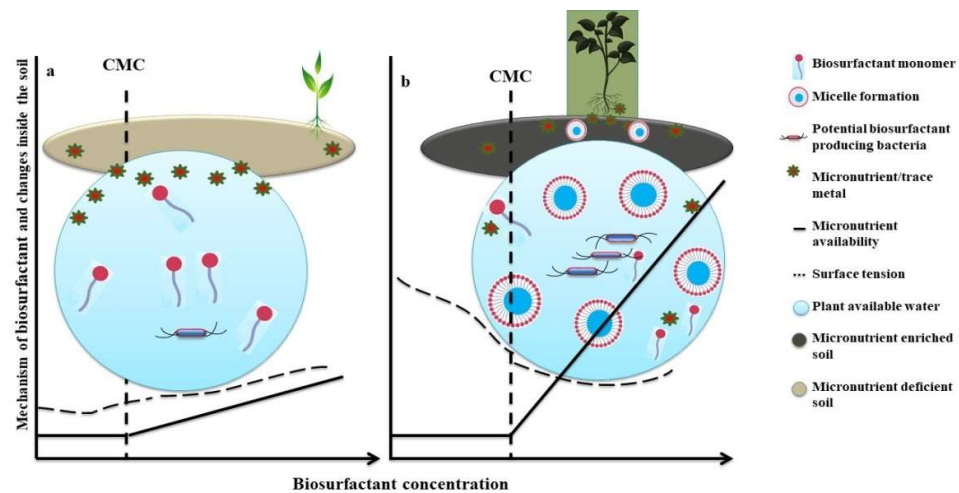


Figure 3. Impact of micronutrient deficiency on plant growth and soil quality on a micronutrient-deficient soil. **(a)** Mechanisms of biosurfactant application enhancing micronutrient availability in micronutrient-deficient soil to the plant, soil quality, and related water quality through increasing nutrient solubility at a fixed concentration of biosurfactant molecule. **(b)** CMC at which there is a sudden increase in metal solubility in the system. Figures are adapted and modified from Mulligan (13) and Singh et al. (114).

For instance, Sheng et al. [122] reported the strain *Bacillus* sp. J119 has biosurfactant capability, which significantly enhances the uptake of trace elements and promotes the growth potential of canola maize, sudangrass, and tomato. Further, Stacey et al. [123] reported the formation and plant uptake of lipophilic metal-rhamnolipid complexes that facilitate the Cu, Mn, and Zn uptake and movement in *Brassica napus* and *Triticum durum* roots.

In addition, the application of biosurfactant, as it is of microbial origin, significantly modulates plant growth via synthesizing phytohormones and induces resistance. Therefore, the efficiency and availability of the micronutrient in the soil to the plants might be increased, either due to bioaugmentation of biosurfactant-producing bacteria [124]. The application of biosurfactants also influences the native microflora of the plants or soil, directly or indirectly responsible for growth promotion, mitigating biotic and abiotic stresses, and removing contaminants from the soil or plant roots. In a study, Liao et al. [125] used the pot experiment with maize to examine the effect of biosurfactant (rhamnolipid and lecithin) and chemical surfactant (Tween 80). After application in the crude oil contaminated soil could not significantly affect the maize biomass, rhamnolipid and lecithin application enhanced the microbial population, resulting in increased petroleum hydrocarbons from the contaminated soil. March-Mikołajczyk et al. [126] reported about the Glycolipid produced by endophytic bacterial strain *Bacillus pumilus* 2A, which after application significantly improves the growth of bean, radish, and beetroot. Chopra et al. [127] evaluated different rhizobacterial strains of Tea, in which one of the strains *Pseudomonas aeruginosa* RTE4, produced di-rhamnolipid biosurfactant and showed multiple growth-promoting traits as well as fungicidal activity. Similarly, Alsohim et al. [128] reported the viscosin produced by *Pseudomonas fluorescens* S.B.W. 25 that helps in spreading motility, which facilitates the colonization efficacy of microbial strain and showed growth promotion potential.

5. Biosurfactant application in plant disease management

Plant disease causes a significant reduction in agricultural commodities during pre- or post-harvest conditions and is considered a severe threat to food security for the rising global population. It has been estimated that approximately 30 % of the total agricultural

production is destroyed due to various plant diseases and pathogen attacks either during pre- or post-harvest storage conditions [129]. However, to manage phytopathogen and plant diseases, farmers most often rely on chemical pesticides. Nevertheless, the undistributed and continuous use of chemical pesticides during crop production led to various adverse consequences like poor food quality, soil and water pollution, pest resistance, effect on natural microbiota, and severe health issues to consumers. Moreover, various microbial biocontrol agents, including bacteria, fungi, yeast, have been frequently utilized to manage plant diseases. They showed effective response against phytopathogen growth, fruit quality maintenance, or storage life enhancement.

Agrochemicals are preferred more frequently than other crop protection or plant disease management resources because of easy availability and quick response. Nevertheless, traditional formulation and low dispersion capacity on the target site, either the plant surface or the pathogen, led to lower efficacy and environmental pollution. According to the report, it has been estimated that only about 0.1% of the total applied pesticides reach the target organisms and the remaining bulk contaminates the surrounding [130, 131].

In common practice, a pesticide is either sprayed directly on the plant and surfaces or sometimes dipped into the pesticides solutions. Still, drift does not reach the target site and shows poor efficacy against disease management [132]. However, nowadays, to improve the effectiveness of pesticides applications, the delivery mechanism has been upgraded via adding surfactants, nano-based formulations, and improved spraying technology [133, 134]. In general, during pesticide application, surfactants have been being used as an additive or adjuvants and mixed with pesticides that help in dispersion, emulsification, better spreading, or increase the contact area with the plant surface that enable the better reach of pesticides to the target pest or target organism [135] (Figure 4).

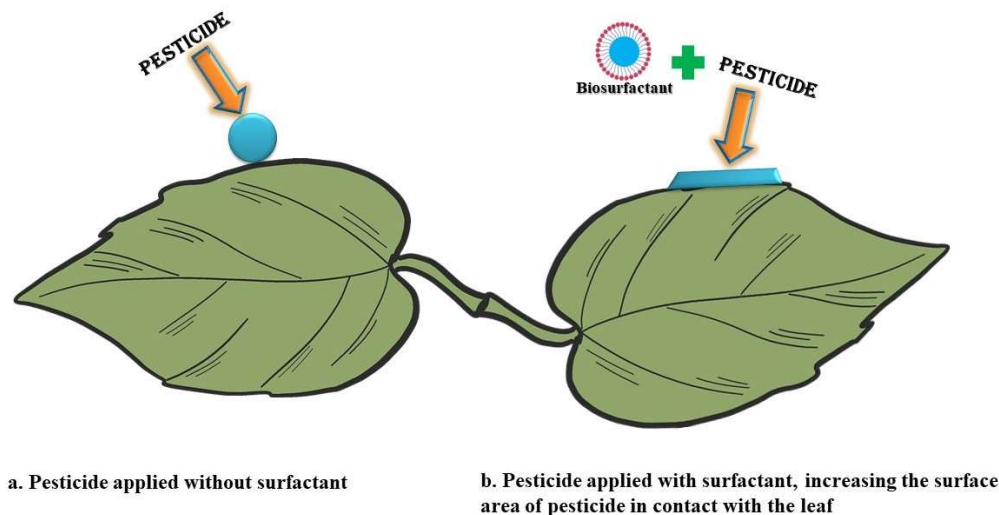


Figure 4. Depiction of the effect of surfactant on leaf surfaces. (a) Pesticide applied without surfactant; (b) pesticide applied with a surfactant, increasing the surface area of pesticide in contact with the leaf, Figure adapted from *Jibrin et al. (138)*.

However, after mixing and applying biosurfactants with pesticides, care should be taken because surfactant application may harm the non-target phytobiome and plant physiological process [136]. Moreover, the enhanced permeability of pesticides may lead to increased residue levels in plant tissue and fruits [137]. Therefore, selection and the concentration of surfactants are prime factors that need to be considered for better disease management strategies.

Currently, a range of chemically synthesized surfactants such as Triton X-100, Cohere, Agral 90, Silwet L-77, Tween 20 are the some most common synthetic surfactant, has been available in the market used for plant disease management and displayed improve insecticidal potential during in *vitro* and in *vivo* applications [138, 139]. However, due to its chemical and toxic nature, it avoided direct application on the plant surface. Unlike synthetic surfactants that are usually used as adjuvants, most biosurfactants have been directly applied on the plant surface for disease management [140, 141] and nowadays, continuously new biosurfactant producing microorganism has been screened and explored for the optimum recovery and application as antagonistic agents against a range of pest and plant pathogens. The utilization of microbial antagonistic bacteria, fungi, and yeast strains to manage plant disease or growth of phytopathogen during pre- or post-harvest management has been well elucidated [142, 143]. Indeed, the addition of biosurfactants modulates the action mechanism such as antibiosis, induced systemic resistance, competition, parasitism of biocontrol agents [139].

Pseudomonas and *Bacillus* are the most common bacterial genera used for biosurfactant production. There are numerous reports available that showed their potency in biosurfactant production and their implication in successful phytopathogen management [138]. Varnier et al. [144] reported about Rhamnolipid produced by the *Pseudomonas aeruginosa*, which enhanced the immune response of grapevine against the *Botrytis cinerea* after application. In addition, the application of surfactant inhibits the spore germination and mycelium growth of the pathogen. Kruijt et al. [145] reported the surfactant produced by *Pseudomonas putida*, which after application, impede the growth of pathogen *Phytophthora capsici* in cucumber through zoospores lysis. Nielsen and Sorensen [146] reported that the surfactant cyclic lipopeptide produced by *Pseudomonas fluorescens* having antifungal properties. Pernell et al. [147] evaluated the combined application of phenazines and rhamnolipid surfactant produced by *Pseudomonas aeruginosa* PNA1 strain. The application of both the metabolites showed a synergistic effect against the pathogen *Pythium splendens* of bean and *Pythium myriotylum* of cocoyam. In addition, substantial vacuolization and disintegration of *Pythium* hyphae were observed during microscopic analysis. Similarly, D'aes et al. [148] reported that phenazine and cyclic lipopeptide produced strain *Pseudomonas* CMR12a that showed effective biocontrol potential against the *Rhizoctonia* root rot on the bean. Velho et al. [149] reported about the lipopeptide surfactant produced by the *Bacillus*, having strong antagonistic activity against the pathogen *Aspergillus* sp., *Fusarium* sp., and *Biopolaris sorokiniana*.

Similarly, in another study, Akladios et al. [150] evaluated the biosurfactant produced by strain *Bacillus licheniformis*, which after application significantly controls the pathogen *Rhizoctonia solani*, the causal agent of root rot in faba beans. Hussain et al. [151] reported biosurfactant produced by *Bacillus subtilis*, having bio-nematicidal activities against the pathogen *Meloidogyne incognita* causal agent of Root gall. Shalini et al. [152] reported glycolipid surfactant produced by the *Acinetobacter* sp., which showed antagonistic activity against *Xanthomonas oryzae* P.V. Oryzae XAV24. Haddad et al. [153] reported surfactin biosurfactant produced by *Brevibacillus brevis* having antibacterial and antifungal properties. Similarly, the endophytic strain *Burkholderia* sp. produced Glycolipid. The biosurfactant showed broad-spectrum antibacterial activity against pathogen *Pseudomonas aeruginosa*, *E. coli*, *Salmonella paratyphi* [154]. A detailed survey of biosurfactants used in plant disease management has been described in table 4.

Table 4. The common biosurfactant used in plant disease management.

Microorganism	Biosurfactant	Properties	Reference
<i>Pseudomonas</i> sp. EP-3	Rhamnolipid	Insecticidal activity	[155]
<i>Pseudomonasaeruginosa</i> PAO1	Rhamnolipid	Biofilm formation	[156]
<i>Pseudomonas aeruginosa</i>	Rhamnolipids	Control of <i>Phytophthora cryptogea</i>	[157]
<i>Pseudomonas aeruginosa</i>	Rhamnolipids	Resistance to <i>Botrytis cinerea</i> in grapevine	[158]

<i>Pseudomonas putida</i>	Biosurfactants	Zoospores of the oomycete pathogen <i>Phytophthora capsici</i>	[159]
<i>Pseudomonas koreensis</i>	Biosurfactant	Late blight on potato	[160]
<i>Acinetobacter</i> sp. ACMS25	<u>Glycolipid</u>	Biocontrol of <i>Xanthomonas oryzae</i>	[161]
<i>Burkholderia</i> sp. WYAT7	Glycolipid	Antibacterial and ant- biofilm potentials	[162]
<i>Bacillus licheniformis</i>	Biosurfactant	Biocontrol of <i>Rhizoctonia solani</i> causing root rot in faba bean	[163]
<i>Pseudomonas</i> CMR12a	Lipopeptides	Biological control of <i>Rhizoctonia</i> root rot on bean	[164]
<i>Brevibacillus brevis</i>	Lipopeptides	Antibacterial and Antifungal properties	[165]
<i>Bacillus</i> sp.	Lipopeptides	Growth inhibition of <i>Fusarium</i> spp., <i>Aspergillus</i> spp., and <i>Biopolaris sorokiniana</i>	[166]
<i>Bacillus subtilis</i> R14	Lipopeptide	Antimicrobial activity	[167]
<i>Bacillus subtilis</i>	Lipopeptides Iturin A, fengycin, and surfactin	<i>Colletotrichum gloeosporioides</i> , the causative agent for anthracnose on papaya leaves	[168]

The application of surfactants acts differently during pathogen management. For example, Edosa et al. [169] reported the action mechanism of some biosurfactants in insect pest management. The biosurfactant acts upon the cell wall of the pest and causes significant damage due to dehydration. In a study, Yun et al. [170] reported surfactin produced by *Bacillus amyloliquefaciens*, which affects the aphid cuticle after application, resulting in dehydration from the cuticle membrane, leading to dehydration to death. Similarly, Khedher et al. [171] observed vacuolization, necrosis, and basement membrane disintegration in the larval midgut of *Spodoptera littoralis* after histopathological examination biosurfactant treatment. These reported biosurfactants and their application in plant disease management showed an excellent alternative to chemical pesticides, which are currently utilized in different parts of the world. However, the additional benefit of using microbial surfactant is the enhancement in plant growth and the providing nutrient source and favorable conditions for the native microflora that are essential for the plants to mitigate them from various biotic and abiotic stresses and for the degradation of toxic and hazardous environmental contaminants.

6. Biosurfactant application in pharmaceutical industries

6.1. Antioxidant properties of Biosurfactants

Nowadays, microbial surfactants have been used in the food and pharmaceutical industries as antioxidant agents. The antioxidants are the compounds need to neutralize the free radicals generated in the body during various physiological processes. The highly reactive nature of free radicals led to severe damage known as oxidative stress or oxidative damage [172]. The microbial origin source of biosurfactants can alter the physico-chemical properties of surfaces. Thus, they can obviate the binding of other bacterial adhesions on the surface [173].

Similarly, they can also block the oxidative chain reaction flow by rendering the antioxidant activities [173]. Considering the biosurfactant characteristics like low toxicity, biodegradable, antimicrobial, and antioxidant properties, they gained significant industrial attention and became a preference over the usage of synthetic antioxidants [174]. To overcome the toxic effects of synthetic surfactants and subside their side effects upon consumption, it is a prerequisite for finding natural and non-toxic bio-based products with potential antioxidant products [175]. Natural biosurfactants are one such natural product that are also reportedly capable of blocking the oxidative chain reaction flow by rendering

the antioxidant activities. Hence, they also can effectively impede the elevation of reactive oxygen species (ROS) and reactive nitrogen species (RNS); hence could be highly useful for therapeutic purposes against cancer and the cure of diseases related to heart and neurodegenerative diseases [176]. Likewise, they were also highly instrumental in manufacturing the probiotic, bio preservative, and food ingredients [177].

Recently, several research groups explored various biosurfactants bestowed with excellent potential antioxidant properties from diverse sources. In addition to their potential antioxidant activity, some of the biosurfactants also displayed antimicrobial and antiproliferative activities [178,179,180]. In the line of findings, biosurfactant MB15 isolated from a non-pathogenic marine bacteria *Marinobacter litoralis* [179], found to have no cytotoxic effect but had a potent antioxidant and antimicrobial activity. Another report by Giri *et al.* assessed the antioxidant, antibiotic, and anti-adhesive properties of the biosurfactant compounds isolated from *Bacillus subtilis* VSG4 and *Bacillus licheniformis* VS16. Their study revealed that the *Bacillus subtilis* VSG4 displayed better antioxidant activity than *Bacillus licheniformis* VS16 [181]. Meghna *et al.* also characterized a biosurfactant BS-LBL from *Lactobacillus casei*, and their experiment enlightened the efficient antioxidant, antimicrobial and antiproliferative properties upon testing [180]. Likewise, Ohadi *et al.* [182] examined a biosurfactant obtained from *Acinetobacter junii*. They confirmed that the lipopeptide biosurfactant (LBS) from *A. junii* bestowed high antioxidant capacity with excellent wound healing ability in the mouse. Similar findings were also reported by other studies [178,183,184]. Collectively, the utilization and application of biosurfactants with antioxidant, antimicrobial, and antiproliferative substances will be a great addition to the products to safeguard consumer health benefits.

Few more reports have also consolidated the potent antioxidant and antimicrobial activities of biosurfactants lately. For example, Mouafao *et al.* identified and characterized a biosurfactant from *Lactobacillus casei* subsp. *casei* TM1B also confers efficient antioxidant and broad-spectrum antimicrobial activities conveyed with good emulsification and surface activities [185]. In the line of findings, another report described the isolation and characterization of biosurfactants from *Halomonas elongata*, *Halobacillus karajiensis*, and *Alkalibacillus almallahensis* from high saline soil (Fariq and Yasmin, 2020). The biosurfactant MB588 from *Halobacillus karajiensis* showed comparable antioxidant capacity as a positive control among all the isolates. It also showed higher antimicrobial activity together suggests, the bacteria from extreme halophilic soils can also be helpful for the isolation of novel biosurfactants [186].

Similarly, another study by Abdollahi *et al.* compared two biosurfactants derived from two autochthonous strains for their antioxidant ability. Their study revealed that *Bacillus amyloliquefaciens* NS6 derived surfactin natured biosurfactant displayed more robust antioxidant capacity than *Pseudomonas aeruginosa* MN1 derived rhamnolipid structured biosurfactant. However, they found that the rhamnolipid treated surfaces displayed higher anti-adhesive and anti-biofilm activities than surfactin treated surfaces [173]. More examples of biosurfactants that possess antioxidant and antimicrobial activities [187,188] were listed in Table 5.

Table 5. Antioxidant properties of Biosurfactants.

Source	Chemical nature of biosurfactant	Antioxidant activity assessment	Antioxidant	Anti bacterial	Antiproliferative	Reference
<i>Lactobacillus casei</i> subsp. <i>casei</i> TM1B	Rhamnolipid-like biosurfactant	DPPH (1-diphenyl-2-picrylhydrazyl) assay, ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) assay	yes	yes	not tested	185

<i>Pseudomonas aeruginosa</i> MN1	Rhamnolipid	FRAP and DPPH assay	yes	yes	not tested	173
<i>Bacillus amyloliquefaciens</i> NS6	Surfactin	Ferric reducing antioxidant power (FRAP) and DPPH assay	yes	yes	not tested	173
<i>Marinobacter litoralis</i> MB15	Rhamnolipid	DPPH assay	yes	yes	yes	179
<i>Halomonas elongata</i> , <i>Halobacillus karajensis</i> and <i>Alkalibacillus almallahensis</i>	Glycolipid	DPPH assay	yes	yes	not tested	186
<i>Bacillus subtilis</i> VSG4	Lipopeptide	DPPH assay	yes	yes	not tested	181
<i>Bacillus licheniformis</i> VS16	Phospholipopeptide	DPPH assay	yes	yes	not tested	181
<i>Lactobacillus casei</i> (BS-LBI)	Not mentioned	DPPH assay	yes	yes	yes	180
<i>Acinetobacter junii</i> B6	Lipopeptide	DPPH and FRAP assay	yes	yes	not tested	182
<i>Bifidobacterium bifidum</i> WBINO3 and <i>Lactobacillus plantarum</i> R315	Exo polysaccharides	DPPH assay and superoxide and hydroxy radical estimation	yes	yes	not tested	188
<i>Bacillus methylotrophicus</i> DCS1	Lipopeptide	DPPH assay	yes	yes	not tested	187
<i>Pseudozyma hubeiensis</i>	Mannosylerythritol lipids	DPPH assay	yes	not tested	yes	183
<i>Bacillus subtilis</i> SPB1	Lipopeptide	DPPH assay	yes	not tested	yes	184
<i>Bacillus cereus</i> MMIC	Lipopeptide	DPPH assay	yes	yes	yes	178

Few studies have explored the efficacy of natural biosurfactants, which originated from a cost-effective substrate and compared their total antioxidant capacity (TAC) with a synthetic surfactant. Amaro da Silva et al. assed the TAC of a biosurfactant isolated from a low-cost substrate by *Candida bombicola* URM 3718 and compared it with a commonly used synthetic surfactant called Guar gum for its emulsification and total antioxidant capacity. Their study revealed that the biosurfactant predominantly displayed better antioxidant and emulsification ability than guar gum [174]. Other studies with different objectives also approved the need for biosurfactants to overcome the shortcomings of synthetic surfactants [189]. In summary, considering the numerous promising attributes of biosurfactants and their strong potential to elicit antioxidant activity on the detrimental reactive oxygen species and free oxygen radicals (H_2O_2 , O_2^- , OH^* and 1O_2) from diverse sources. Under their origin, the biosurfactants are also conferred antimicrobial activity and offer attractive opportunities to replace synthetic surfactants in the pharmaceutical,

probiotic, and cosmetic industries. Thus, there is an urgent need for comprehensive characterization of each type of biosurfactant to be established to harness the best benefits and efficient application process.

6.2. Antimicrobial Properties of biosurfactants

Multidrug resistance (MDR) is an emerging challenge for the growing world, especially in developing countries. However, in the recent past, antibiotic resistance opens the door to search for alternative antimicrobial medicine to treat human ailments [191]. In this context, biosurfactant properties as of bacteriostatic, bactericidal, and biofilm disruption, adjuvant with antibiotics, make them ideal for an antimicrobial agent [192]. Numerous reports are available that showed the effectiveness of biosurfactants against different pathogens. For example, Foschi and others [193] reported antimicrobial effects against *Neisseria gonorrhoeae*. Similarly, Morais and others [194] observed against *Candida albicans*, Dusane and others [195] reported biofilm degradative behavior of rhamnolipid surfactant against *Bacillus pumilus*.

However, biosurfactants produced by microbial strain act differentially during pathogen inhibition. For instance, Rhamnolipids possess activity through permeabilizing effect, which leads to disruption of the bacterial cell plasma membrane. The amphipathic nature of rhamnolipids binds with the charges of the bacterial cell membrane and changes their hydrophobicity. This prevents biofilm formation and makes the pathogen highly susceptible to the antimicrobial agent [196]. Several studies have suggested that rhamnolipids may act more effectively against Gram-positive bacteria than Gram-negative bacteria due to the absence of an outer membrane. The presence of the outer layer may exclude biosurfactant molecules [197]. However, the lipopolysaccharides biosurfactants attribute antimicrobial property via penetrating or damaging the lipid, constituting negatively charged cell membranes. The charge imbalance led to pore formation in the cell membrane lipids that were ultimately causing damage or death of pathogens, especially of Gram-negative bacteria [198].

In recent years, the biosurfactants such as lipopolysaccharides and glycolipids produced by microbial strains are used directly or indirectly as anticancer agents. Biosurfactants' structural diversity and physio-chemical nature showed a broad-spectrum application during the chemotherapy or drug delivery formulations. Currently, various reports show the effectiveness of glycolipids and lipopolysaccharides in controlling the proliferation of cancer cells and disrupting cell membranes through apoptosis pathways [199]. Zhao and others [200] reported the antitumor activity of lipopolysaccharides, composed of peptides and fatty acid chains. Dey and others [201] reported that Iturin synthesized by *Bacillus* strains inhibits the proliferation of MDA-MB-231 cancer cells.

7. Future Directions and Concluding Remarks

Biosurfactant is considered as a multifunctional Biomolecules of the 21st Century, due to their broad application ranging from daily life to industrial purposes. Currently, numerous microbial strains have been identified and screened for biosurfactant ability, and each day some novel biosurfactant molecules have been identified and recovered. However, the biosurfactant's fragile nature, lower stability, and high production cost appear as a critical barrier for frequent use in the industries. In the recent past, to reduce the production cost, various alternative sources of carbon or nitrogen, which are the essential requirements for microbial growth, have been utilized, and up to a certain extent, researchers have become successful. Nevertheless, the lower yield of biosurfactants, using alternative sources is still a limiting factor. Therefore, there is a need for extensive study of factors including biosynthesis pattern, growth, environmental conditions, and media composition for the large-scale production of biosurfactant molecules for the industrial uses and economic standpoint.

Currently, rapid industrialization and anthropogenic behavior led to the deposition of toxic and hazardous contaminants in the soil, affecting environmental conditions and limiting agricultural production. Nowadays, biosurfactants have been broadly utilized to degrade the toxic, hazardous, hydrophobic environmental contaminants and improve the soil quality by maintaining trace elements concentration. The most commonly used surfactants are of chemical origin, and their uses in the agricultural fields can lead to food toxicity and also adversely affect the natural microflora. However, the microbial origin surfactants have no such impact or even accelerate the growth of plants and microflora, which are required to degrade environmental contaminants. The selection of biosurfactants according to soil contaminants can enhance the soil quality better and in less time. For the sustainable growth of the rising global population, management of pre-and post-harvest losses of agricultural products is an immediate need. Currently, surfactants are mainly used as adjuvants or sometimes directly to the plant surface for phytopathogen management. However, there is still a need to explore the director adjuvants' use of biosurfactants and their impact on the natural phytomicrobiome, residual level in fruits, and their impact on the physiological aspect of plants.

Moreover, there is also a need for extensive investigation of biosurfactant molecules to explore novel antimicrobial agents, antioxidant molecules, and antiproliferative agents. This not only is cost-effective but also protects the body from its toxic side effects. The current ongoing research on cancer therapy and drug delivery using biosurfactants molecules needs extensive exercise. However, such advancement in technologies and resource materials, the high production cost, and low yield of biosurfactants is still a challenging task that needs to be overcome.

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