Scientific Bulletin. Series F. Biotechnologies, Vol. XXX, No. 1, 2026
ISSN 2285-1364, CD-ROM ISSN 2285-5521, ISSN Online 2285-1372, ISSN-L 2285-1364

MICROBIAL BIOSURFACTANTS AS ANTIMICROBIAL AND THERAPEUTIC AGENTS: A MINI-REVIEW OF RECENT ADVANCES

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Abstract

Microbial biosurfactants are amphiphilic molecules produced by diverse microorganisms and are increasingly investigated as alternative antimicrobial agents in the context of increasing antimicrobial resistance (AMR). This mini-review summarizes current knowledge on the antimicrobial and antibiofilm activities of major biosurfactant classes, including rhamnolipids, lipopeptides, sophorolipids, and mannosylerythritol lipids (MELs), with emphasis on their mechanisms of action and structure-activity relationships.
Rhamnolipids and lipopeptides exhibit the highest antimicrobial potency, primarily through membrane disruption, whereas sophorolipids and MELs show reduced antimicrobial activity but improved biocompatibility. All classes act mainly through physico-chemical interactions with microbial membranes, resulting in membrane disruption and inhibition of biofilm formation. In addition, several studies report enhanced efficacy of conventional antibiotics in combination with biosurfactants against multidrug-resistant pathogens.
Despite these advantages, their clinical application remains limited by production costs, process variability, and regulatory constraints. Nevertheless, the use of renewable and agro-industrial waste substrates for biosurfactant production aligns with circular economy principles and improves their sustainability profile. Overall, microbial biosurfactants represent promising candidates for next-generation antimicrobial strategies, although further optimization and translational studies are required to support their practical implementation.

Key words*: microbial surfactants, antimicrobial activity, therapeutic applications.*

INTRODUCTION

Microbial biosurfactants are structurally and functionally diverse amphiphilic molecules produced by a wide range of microorganisms, including species belonging to the genera *Pseudomonas*, *Bacillus*, *Candida*, and *Moesziomyces*.
Their amphipathic nature enables strong interfacial activity and interaction with biological membranes, which supports their broad antimicrobial and antibiofilm properties.
Among the main biosurfactant classes, significant differences in antimicrobial potency and biomedical applicability have been reported.

Rhamnolipids, primarily produced by *Pseudomonas* spp., generally exhibit the strongest antibacterial activity, particularly against Gram-negative pathogens, due to their ability to insert into cell membranes, disrupt membrane integrity, and induce leakage of intracellular components (Soberón-Chávez et al., 2021). In comparative studies, rhamnolipids often exhibit lower minimum inhibitory concentrations (MICs) than sophorolipids against several Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus* and *Escherichia coli*, although activity is strongly dependent on molecular structure and biosurfactant form. In contrast, lipopeptides produced by *Bacillus* species, including

surfactin, iturin, and fengycin, demonstrate superior antifungal activity. Their mechanism involves pore formation and membrane permeabilization, with surfactin additionally affecting membrane-associated signaling processes, which contributes to both antimicrobial and antibiofilm effects (Ongena & Jacques, 2008). This makes lipopeptides particularly effective against fungal pathogens, such as *Candida albicans* and *Aspergillus* spp.

Yeast-derived glycolipids, including sophorolipids and mannosylerythritol lipids (MELs), generally exhibit lower direct antimicrobial potency compared to rhamnolipids and lipopeptides; however, they are characterized by significantly lower cytotoxicity and improved biocompatibility. Sophorolipids produced by *Candida* spp. display moderate antibacterial activity, mainly against Gram-positive bacteria, while MELs show promising antifungal and anti-inflammatory properties, which make them particularly suitable for dermal and cosmetic applications (Cho et al., 2022; Holguín-Salas et al., 2025).

Biosurfactants act mainly on microbial membranes through physico-chemical interactions, leading to increased membrane fluidity, permeability changes, and protein destabilization. This non-specific mode of action reduces selective pressure and the risk of resistance development compared to conventional antibiotics (Marchant & Banat, 2012; Luong et al., 2026).

Despite these properties, clinical translation remains limited. Major constraints include high production costs, and challenges in downstream purification. Recent advances in the metabolic and genetic engineering of *Pseudomonas* and *Bacillus* strains have led to improved production yields and modified congener profiles, indicating a promising route toward industrial scalability and functional optimization (Soberón-Chávez et al., 2021; Banat et al., 2021). Importantly, biosurfactants produced using renewable substrates and agro-industrial waste streams align with circular economy principles by enabling waste valorisation into high-value bioproducts. This dual functionality-biomedical relevance combined with environmental sustainability-highlights microbial biosurfactants as key candidates for the development of next-generation antimicrobial and eco-friendly technologies.

MATERIALS AND METHODS

A literature review was conducted using PubMed, ScienceDirect, and Web of Science databases to identify publications on microbial biosurfactants. The search was performed using keywords such as “microbial biosurfactant”, “rhamnolipid”, “lipopeptides”, “antimicrobial activity”, “sophorolipids”, or “biomedical applications”. Studies reporting *in vitro*, *in vivo*, or clinically relevant data on biosurfactant production and biological activity were considered. Representative biosurfactant-producing genera, including *Pseudomonas*, *Bacillus*, *Candida*, and *Moesziomyces*, were included. Selected papers were further evaluated based on their focus on antimicrobial mechanisms, antibiofilm properties, structure-activity relationships, and biomedical applications of microbial biosurfactants.

RESULTS AND DISCUSSIONS

Antimicrobial activity of biosurfactants

Microbial biosurfactants exhibit a broad antimicrobial spectrum against Gram-positive and Gram-negative bacteria, as well as pathogenic yeasts and filamentous fungi. Their antimicrobial activity is largely determined by the chemical structure of the biosurfactant, the producing microorganism, and environmental conditions such as pH, temperature, and ionic strength (Banat et al., 2010; Rodrigues et al., 2006). Structural properties, such as lipid chain length, degree of saturation, and glycosylation patterns, are key determinants of antimicrobial potency and selectivity, enabling selective activity against specific pathogens (Fracchia et al., 2015). The main characteristics, antimicrobial targets, mechanisms of action, advantages, and limitations of the major microbial biosurfactant classes are summarized in Table 1.

Table 1. Comparison of major biosurfactant classes

Biosurfactant type	Main producer organisms	Target pathogens	Main antimicrobial mechanism	Advantages	Limitations	References
Rhamnolipids	*Pseudomonas aeruginosa*, *Pseudomonas fluorescens*	*Staphylococcus aureus*, *Escherichia coli*	Membrane disruption and release of intracellular constituents	Antibacterial activity against Gram-positive and Gram-negative bacteria, antibiofilm properties	Potential cytotoxicity, production associated with pathogenic strains, high purification cost	Alyousif et al., 2023; Zhao et al., 2022; Wongsirichot et Winterburn, 2025
Lipopeptides (surfactin, iturin, fengycin)	*Bacillus subtilis*, *Bacillus licheniformis*	*Candida albicans*, *Aspergillus* spp., *Penicillium* spp., *Staphylococcus epidermidis*	Pore formation and membrane permeabilization	Strong antifungal activity, synergistic effects, potent antibiofilm action	Production variability, sensitivity to environmental conditions	Markelova et Chumak, 2025
Sophorolipids	*Candida bombicola*	*Staphylococcus aureus*, *Bacillus subtilis*, *Candida albicans*	Interaction with membrane lipids and alteration of membrane integrity	Low cytotoxicity, high biodegradability and good biocompatibility	Moderate antimicrobial potency compared with rhamnolipids and lipopeptides	Lourenço et al., 2024; Dengle-Pulate et al., 2014; Cho et al., 2022
Mannosylerythritol lipids (MELs)	*Moesziomyces* spp.	*Candida* spp., *S. aureus*	Membrane interaction and inhibition of microbial adhesion	Antifungal and antibacterial activity, low toxicity, moisturizing and skin-protective properties, favorable dermatological tolerance	Limited large-scale production data	Coelho et al., 2020; Ceresa et al., 2020; Holguín-Salas et al., 2025

Rhamnolipids, primarily produced by *Pseudomonas aeruginosa* and *Pseudomonas fluorescens*, have demonstrated antibacterial activity against clinically relevant pathogens, including *Staphylococcus aureus*, *Listeria monocytogenes*, *Bacillus cereus*, and *Escherichia coli* (Das et al., 2008; Sivasankar et al., 2010). Several *in vitro* studies have reported inhibition zones and low minimum inhibitory concentrations (MICs), highlighting the efficacy of rhamnolipids against both Gram-positive and Gram-negative bacteria. In addition to antibacterial effects, rhamnolipids exhibit antifungal activity against species such as *Fusarium solani* and *Penicillium funiculosum*, further expanding their biomedical relevance (Das et al., 2008).

Lipopeptides synthesized by *Bacillus* species, including surfactin, iturin, and fengycin, represent one of the most highly active classes of antimicrobial biosurfactants (Ongena & Jacques, 2008). These compounds display strong antibacterial activity against *Staphylococcus epidermidis*, *Listeria monocytogenes*, and *Salmonella enterica*, as well as pronounced antifungal effects against *Candida albicans*, *Aspergillus niger*, and *Fusarium oxysporum* (Sivasankar et al., 2010; Van Bogaert et al., 2009). Notably, lipopeptides often act synergistically, with mixed lipopeptide fractions exhibiting enhanced antimicrobial efficacy compared to individual components (Ongena & Jacques, 2008).

Sophorolipids, produced mainly by *Candida bombicola*, exhibit moderate antibacterial activity, particularly against Gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*, as well as antifungal effects against *Candida albicans* (Singh et al., 2004; Van Bogaert et al., 2009). Although their antimicrobial potency is generally lower than that of lipopeptides or rhamnolipids, sophorolipids are characterized by low cytotoxicity and excellent biodegradability, which are critical attributes for biomedical applications.

MELs synthesized by yeasts such as *Moesziomyces* and *Candida* species demonstrate antifungal activity against *Candida*

albicans and *Aspergillus fumigatus*, as well as antibacterial effects against Gram-positive bacteria (Singh et al., 2004; Van Bogaert et al., 2009).

Their unique molecular structure confers additional functional properties, including moisturizing and skin-protective effects, supporting their use in pharmaceutical and cosmetic formulations.

Antibiofilm and synergistic effects

Beyond their activity against various microorganisms, biosurfactants have demonstrated significant antibiofilm properties.

Biofilm-associated infections represent a significant challenge for eradication due to increased microbial resistance and protection from host immune responses. Several studies have shown that biosurfactants inhibit microbial adhesion to surfaces and disrupt established biofilms by altering surface hydrophobicity and interfering with extracellular polymeric substances (Rodrigues et al., 2006).

Several studies have shown that combining biosurfactants with enzymatic treatments or nanomaterials enhances biofilm disruption, providing innovative strategies to control persistent infections (Fracchia et al., 2015). Biosurfactants have also demonstrated potential in reducing biofilms on industrial surfaces, including food processing equipment and water systems, demonstrating their applicability beyond clinical contexts. Rhamnolipids and lipopeptides, in particular, have been shown to reduce biofilm formation by *Staphylococcus aureus* and *Escherichia coli* on medical-grade materials, highlighting their potential for application in medical device coatings (Das et al., 2008; Sivasankar et al., 2010). In addition, synergistic interactions between biosurfactants and conventional antimicrobial agents have been reported, leading to reduced antibiotic dosages and enhanced antimicrobial efficacy against multidrug-resistant (MDR) strains (Singh et al., 2004; Abdel-Mawgoud et al., 2014).

Recent studies suggest that microbial biosurfactants can enhance the efficacy of antibiotics (e.g., ciprofloxacin, vancomycin) against MDR pathogens by lowering minimum inhibitory concentrations (MICs) and disrupting resistance mechanisms, representing a promising combined approach for persistent infections (Dias-Souza et al., 2025). Such synergistic approaches may represent a promising strategy to extend the clinical utility of existing antibiotics.

Biomedical and therapeutic applications

The multifunctional properties of microbial biosurfactants have enabled their application across diverse biomedical fields.

In wound care, biosurfactant-based formulations have demonstrated both antimicrobial activity and the ability to promote tissue regeneration, contributing to improved healing outcomes (Sivasankar et al., 2010; Singh et al., 2004). Biosurfactant-coated surfaces have been explored for catheters, implants, and other medical devices to prevent microbial colonization and biofilm formation (Rodrigues et al., 2006).

Emerging research indicates that microbial biosurfactants can serve as functional components in advanced drug delivery systems, including biosurfactant-coated nanoparticles and stimuli-responsive hydrogels, improving drug stability, targeted release, and bioavailability of hydrophobic compounds (Bjerk et al., 2021; Rodrigues et al., 2006).

Recent studies further highlight the integration of biosurfactants into smart and stimuli-responsive biomaterials to enhance targeted antimicrobial performance and therapeutic efficiency (Wang et al., 2024).

Additionally, topical formulations containing sophorolipids and mannosylerythritol lipids (MELs) have demonstrated promising antifungal activity combined with favorable dermatological tolerance, supporting their application in medical and cosmetic formulations (Van Bogaert et al., 2011; Lourenço et al., 2024). Their combination with nanomaterials or polymeric carriers can further enhance antimicrobial efficacy and formulation stability, opening novel opportunities for advanced therapeutic and drug delivery systems (Abbot et al., 2022). From a sustainability perspective, the production of biosurfactants using renewable substrates, including agro-industrial waste and food industry by-products, aligns with circular economy principles and contributes to reduced environmental impact (Banat et al., 2010; Sivasankar et al., 2010). The

use of agro-industrial residues not only reduces production costs, but also minimizes environmental impact, promoting sustainable biotechnology practices. This aspect further enhances the attractiveness of biosurfactants as next-generation antimicrobial agents.

Limitations and future perspectives

While numerous studies highlight the biomedical potential of microbial biosurfactants, their translation from experimental models to practical applications remains challenging (Marchant & Banat, 2012). Despite promising laboratory-scale results, several obstacles limit their widespread use, including low production yields, high downstream processing costs, and variability in biosurfactant composition (Banat et al., 2014).

From an economic and technological perspective, biosurfactant production is not yet cost-competitive with conventional antimicrobial agents due to high costs associated with substrates, fermentation processes, and purification steps, which limits large-scale industrial adoption. Scaling up microbial biosurfactant production requires precise control of fermentation parameters, such as pH, temperature, and aeration, to ensure consistent yield, composition, and bioactivity.

Genetic and metabolic engineering of biosurfactant-producing strains offers promising strategies to enhance yields, optimize molecular structures, and tailor functional properties for specific biomedical applications (Soberon-Chavez et al., 2021; Banat et al., 2010; Abdel-Mawgoud et al., 2010). In addition, formulation stability and the absence of standardized regulatory frameworks further constrain their clinical translation. Future research should focus on optimizing fermentation processes, identifying novel high-yield producers, and exploring structure-activity relationships to enhance antimicrobial potency. Comprehensive preclinical and clinical studies will be essential to validate safety, efficacy, and long-term performance in biomedical applications (Fracchia et al., 2015).

CONCLUSIONS

Microbial biosurfactants, including rhamnolipids, lipopeptides, sophorolipids, and mannosylerythritol lipids, represent a versatile and sustainable class of bioactive compounds with significant antimicrobial and therapeutic potential. Their effectiveness against a broad range of pathogenic microorganisms, including MDR bacteria and fungi, combined with antibiofilm activity and favorable biocompatibility, highlights their relevance for biomedical applications.

Although challenges related to production scalability, formulation stability, and regulatory approval remain barriers, ongoing advances in microbial biotechnology and process optimization are expected to facilitate their transition from laboratory research to clinical and pharmaceutical use.

Furthermore, their production from renewable and agro-industrial waste substrates aligns with circular economy principles, offering environmentally friendly alternatives to synthetic surfactants.

Continued research into innovative formulations, combination therapies, and strain engineering will expand their application scope and reinforce their role as next-generation antimicrobial agents. In this context, microbial biosurfactants may play a key role in the development of future antimicrobial strategies that integrate efficacy, safety, and sustainability within an integrated biomedical framework.

ACKNOWLEDGEMENTS

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI-UEFISCDI, project number PN-III-P2-2.1-PED-2021-3528/731PED-2022 within PNCDI III. Additionally, this work was carried out with the support of the Culture Collection of Microorganisms of Industrial Importance CMII-ICCF-WFCC 232 (MIRRI-RO) of the National Institute for Chemical-Pharmaceutical Research and Development-ICCF Bucharest, Romania, part of Microbial Resource Research Infrastructure - European Research Infrastructure Consortium (MIRRI-ERIC).

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