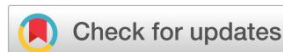
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Review Article

Glycolipid Biosurfactants as Multifunctional Ingredients in Leave-On Skin Care Formulations: Properties, Performance, and Clean Beauty Applications

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Abstract

Objective(s): To characterize the structural chemistry, physicochemical properties, skin bioactivities, formulation aspects, sustainability, therapeutic applications, commercialization, and regulatory aspects of sophorolipids, rhamnolipids, and mannosylerythritol lipids as biosurfactants with focus on their potential in leave-on cosmetic and topical pharmaceutical formulations, as well as highlight research and development gaps.

Data sources: Peer-reviewed scientific publications, patents, and market reports, as well as regulatory guidelines from the EU (Regulation (EC) No 1223/2009, and related Commission implementing acts), the US (FDA; Modernization of Cosmetics Regulation Act), and other regions.

Study selection: All reports, patents, and publications addressing any aspect of the structure-property-performance-benefit relations of sophorolipids, rhamnolipids, and mannosylerythritol lipids as biosurfactants for cosmetic and/or pharmaceutical applications were included. A preference was given to primary studies reporting experimentally obtained data over reviews and other secondary sources.

Summary of contents: The present review discusses the differences in the amphiphilic structure of sophorolipids, rhamnolipids, and mannosylerythritol lipids and their impact on the performance in leave-on and rinse-off formulations. The moisturizing, anti-inflammatory, and antimicrobial activities of glycolipids, as well as their emulsifying properties and versatility in formulation design, were also described. The commercial status of glycolipid biosurfactants, analytical techniques for physicochemical characterization, and regulatory aspects of their use in cosmetics and topical pharmaceutical formulations were briefly outlined and discussed in relation to sustainability.

Conclusion: Sophorolipids, rhamnolipids, and mannosylerythritol lipids are promising biosurfactants with a variety of beneficial properties for leave-on topical formulations and drug delivery; however, their clinical applications still require further validation, and their cost-effectiveness needs to be proved.

Keywords: Glycolipid biosurfactants; sophorolipids; rhamnolipids; mannosylerythritol lipids; leave-on cosmetics; topical drug delivery; skin barrier function.

1. Introduction

Surfactants are one of the most important ingredients used in the cosmetic industry. They are widely used in leave-on skin care products such as creams and lotions. Surfactants act as emulsifiers, solubilizers, and texture modifiers. Because they stay on the skin for a long time, it is necessary for them to have high functional performance, high skin compatibility, and long-term formulation stability.¹

Most of the surfactants used in cosmetics are petrochemical in nature. Common examples include polyethylene glycol based emulsifiers, sulphated fatty alcohols such as sodium lauryl sulphate (SLS) and silicone based emulsifiers such as dimethicone copolyols. These synthetic surfactants have good formulation stability, low cost and good functional performance but also carry several disadvantages like skin irritation,

barrier disruption at high concentrations or long term exposure² along with poor aquatic biodegradability which raises environmental concerns.³ Due to which, consumer preferences have shifted towards products which are labelled as clean, green, bio-based or sustainable.

To produce biosurfactants, microorganisms metabolize renewable carbon sources to make these low-molecular-weight, amphiphilic compounds. Their distinct molecular structure, which consists of a hydrophilic saccharide head group covalently bonded to one or more hydrophobic fatty acid chains, gives them a variety of additional biological activities that are especially relevant to leave-on skincare, as well as surface-active characteristics similar to those of synthetic surfactants.⁴

Three classes of glycolipid biosurfactants have been most extensively studied for cosmetic applications:

sophorolipids (SLs), produced primarily by the non-pathogenic yeast, *Starmerella bombicola*; rhamnolipids (RLs), produced mainly by *Pseudomonas* and *Burkholderia* species; and mannosylerythritol lipids (MELs), produced by *Moesziomyces* (including species formerly classified as *Pseudozyma*) and *Ustilago* species. Each class varies distinctly by structure, physicochemical profiles and biological activity that gives them particular advantages for different leave on formulation products.¹

Although there is an increasing amount of study on glycolipid biosurfactants in rinse-off cosmetic products like shampoos and face cleansers, their application in leave-on formulations has gotten very little attention. The surfactant in rinse-off solutions only comes into contact with the skin for a short time before being washed away, thus while irritation potential is important but it is not as important as in leave-on situations. However, any leftover surfactant in leave-on products constantly interacts with skin lipids, proteins, and local bacteria, therefore biological compatibility and long-term functional performance are crucial factors.⁵

Therefore, the current review's objectives are to: (i) analyze the structural chemistry and physicochemical characteristics of the main classes of glycolipid biosurfactants in the context of leave-on formulation requirements; (ii) review the reported skin bioactive properties, such as moisturization, barrier support, anti-inflammatory, and antimicrobial activities; (iii) assess important formulation factors, such as stability, compatibility, and rheological behavior; (iv) talk about commercial developments and regulatory frameworks governing their use in cosmetics; and (v) identify knowledge gaps and future research directions that will enable their wider adoption in next-generation leave-on skincare products.

2. Structural Chemistry and Physicochemical Properties Relevant to Leave-On Applications

Due to their structural features, sophorolipids, rhamnolipids and MELs are better suited as biosurfactants for leave-on cosmetics such as creams and serums, rather than for rinse-off preparations such as detergents and shampoos. The molecular structure makes them mild on the skin and help them adhere to the skin, and prolong hydration.

Rhamnolipids are surface-active biosurfactants due to an anionic carboxylate group. They are composed of one or two L-rhamnose saccharides linked via glycosidic linkage to one or two C8-C10 β -hydroxy fatty acids.⁶ They have relatively low surface tension (28-30 mN/m), low critical micelle concentration (10-200 mg/L). They are moisturizing, have anti-adhesive characteristics and also showcase antibacterial activity.⁷ Such features make rhamnolipids a suitable contender for leave-on topical preparations as the activity of a surfactant would still be present after application to the skin, unlike rinse-off preparations where most of the active material gets eliminated by water during washing.

Sophorolipids are a complex mixture of acidic and lactonic biosurfactants in which sophorose is coupled to

a hydroxy-fatty acid via glycosidic linkages, with the sugar moiety subject to variable acetylation. Their chemical structure imparts physicochemical properties to these biosurfactants that depend on the specific combination of substituents, but their general features are moderate surface tension (35-40 mN/m), low CMC (approximately equal to that of rhamnolipids) and decreased foaming compared to rhamnolipids. The qualities of sophorolipids are even more valuable for leave-on preparations than rhamnolipids because they do not have the capacity to foam, one of the unwanted properties of leave-on surfactants. Hence, the difference in foaming capabilities between sophorolipids and rhamnolipids is more significant for leave-on cosmetics applications than for rinse-off.⁸

MELs consist of a hydrophilic sugar core of 4-O- β -D-mannopyranosyl-D-erythritol, with the C2' and C3' positions substituted by hydrophobic fatty acid chains and acetylated at the C4' and C6' positions.⁹ MELs can spontaneously form monolayers and liquid crystals on the surface of the skin, and penetrate the damaged skin layer to reconstruct it from the inside. The moisturizing action is similar to that of ceramide, since both MEL-A and MEL-B have the ability to almost completely restore the viability of SDS-treated skin cells and increase the hydration of the stratum corneum while decreasing the transepidermal water loss (TEWL).¹⁰ These properties are even more valuable for leave-on cosmetics than for rinse-off preparations, since for leave-on products it is necessary to rebuild the lipid barrier to extend the hydration after application.

3. Skin Bioactive and Moisturising Performance

A defining feature that distinguishes glycolipid biosurfactants from conventional synthetic surfactants is their innate biological activity. These compounds have surface-active properties, and they also interact with microbes and skin cells in ways that can provide significant dermatological advantages. These activities are of central importance in leave-on formulations, where the ingredients remain on the skin for extended period following each application. These ingredients have the time to interact with the skin and are reviewed below under the categories of moisturization and barrier function, anti-inflammatory activity, and antimicrobial properties.¹

3.1 Moisturization and Skin Barrier Support

The barrier of the stratum corneum is maintained by a tightly arranged lamellar lipid matrix. It is mostly made up of ceramides, free fatty acids, and cholesterol, that occupies the intercellular spaces between terminally differentiated corneocytes.¹¹ Disruption of this matrix causes an escalation in transepidermal water loss (TEWL), a decrease in stratum corneum moisture, and clinical signs of dry, sensitive, or damaged skin.¹² Ingredients in cosmetics that strengthen this barrier through the addition of lipid components, stimulating the skin's endogenous synthesis, or the regulation of keratinocyte differentiation are thus of considerable commercial and scientific significance.¹¹

Among glycolipid biosurfactants, MELs have demonstrated the most persuasive and mechanistically supported evidence of moisturizing and barrier-supporting activity. In vitro studies using human keratinocyte cultures subjected to sodium dodecyl sulphate (SDS)-induced damage have shown that MEL treatment promotes cell viability, stimulates differentiation markers, and enhances the expression of filaggrin and involucrin - crucial structural proteins for proper cornification and barrier formation.¹³ In vivo assessments on human forearm skin have confirmed that the topical application of MEL-B significantly increases stratum corneum hydration, as quantified by corneometry, and reduces TEWL, as measured by an evaporimetric tewameter, relative to untreated skin.¹⁰

Sophorolipids have also been reported to exhibit favorable skin-compatibility profiles in keratinocyte models, with effects dependent on structural congener and concentration. Acidic sophorolipids in particular show low cytotoxicity toward keratinocytes at non-inhibitory concentrations, in contrast to synthetic surfactants such as SLES, supporting their potential as a gentler, bioactive alternative for leave-on formulations, though direct evidence of ceramide biosynthesis stimulation by sophorolipids has not yet been established in the literature and represents an open area for future research.¹

Evidence on the moisturizing potential of rhamnolipids was mostly indirect and came from industry statements and general tolerance assessment rather than from clinical trials.¹ Rhamnolipids were reported in the literature to have moisturizing properties.⁷ Detailed descriptions of the efficacy of rhamnolipids can be found in the patent literature as well. Indeed, rhamnolipid esters were found to be "a smooth, silky-soft skin feel directly after shaving is retained for significantly longer than following application of non-inventive formulations" and "the skin is less severely degreased."¹⁴ This is also indirect evidence as it comes from the patent office not clinical studies. Moreover, there are no double-blind, placebo-controlled trials published in the peer-reviewed literature that compare the moisturizing efficacy of rhamnolipids to other moisturizing ingredients.¹ This is an important consideration as it would be necessary to prove with clinical trials that rhamnolipids are indeed efficacious moisturizers for leave-on preparations.

3.2 Anti-Inflammatory Activity

Skin inflammation is a key contributor to numerous dermatological conditions such as atopic dermatitis, acne, rosacea, and contact dermatitis.¹⁵ Cosmetic products are progressively designed to address mild skin inflammation, especially in relation to post-treatment care, sensitive skin solutions, and anti-aging products, where chronic subclinical inflammation, referred to as 'inflammaging,' leads to barrier degradation and photoaging.¹⁶ Biosurfactant ingredients with demonstrable anti-inflammatory properties therefore offer significant formulation advantages in these categories.¹⁷

Sophorolipids are amongst the most thoroughly studied glycolipid class with regard to their anti-inflammatory mechanism of action. When tested on LPS-stimulated RAW 264.7 macrophages, sophorolipid (SL) was found to attenuate the NF- κ B signalling cascade, which is a key pathway in the regulation of inflammatory response. Downstream effectors of this pathway, including pro-inflammatory cytokines TNF- α and IL-6 were also found to be significantly decreased following SL treatment, along with the levels of NO and ROS produced via the inhibition of iNOS and COX-2 expression. The latter effect is likely to result in the decreased production of prostaglandins, although it was not directly measured in this study. Moreover, treatment with SL resulted in decreased intracellular Ca²⁺ levels, which are known to play an important role in the development of inflammation. The immunomodulatory effect of sophorolipids has been linked to their capacity to reduce the irritation potential of the cleaning-product formulations in which they are used. Thus, it can be hypothesised that similar effects may be exerted by sophorolipids when used in leave-on preparations to ameliorate the potential irritation caused by other surfactants, although this application has not been directly tested in clinical trials.¹⁷

Rhamnolipids have been shown to inhibit the production of pro-inflammatory cytokines in certain in vitro systems at concentrations below their cytotoxic threshold; conversely, di-rhamnolipids have been shown to decrease inflammatory response and increase anti-inflammatory cytokine production at non-inhibitory concentrations.¹⁸ However, it is also important to note that rhamnolipids exhibit pro-inflammatory properties at higher concentrations, as they have been shown to activate immune cells and induce pro-inflammatory cytokine TNF- α secretion from human mononuclear cells as well as increase oxidative response when pre-incubated with monocytes.⁷ This duality of action may well be related to rhamnolipids' reported contribution as virulence factors to *Pseudomonas aeruginosa* pathogenicity, which participate in disruption of epithelial barrier function and impairment of macrophage-mediated phagocytosis.¹⁹ Thus, for leave-on preparations containing rhamnolipids, careful dose optimization is paramount, due to this concentration-dependent bifunctionality. However, conclusive proof of efficacy in humans is yet to be obtained. MELs have been shown to possess anti-inflammatory activity in preliminary studies namely, downregulation of secretion of multiple inflammatory mediators (TNF- α , leukotriene C4) from antigen-reactivated mast cells.²⁰

3.3 Antimicrobial and Antifungal Activity

The skin microbiome is increasingly acknowledged as an essential element of skin health. Cosmetic formulations are expected not only to maintain microbial diversity while selectively inhibiting pathogenic species without affecting beneficial populations.²¹ Conventional preservative systems in leave-on products, including methylisothiazolinone (MI), parabens, and phenoxyethanol, are under increasing regulatory pressure due to their tendency to cause allergies and

emerging resistance concerns.²² Glycolipid biosurfactants display selective antimicrobial activity against a range of skin-relevant pathogens and hence present a potentially profound solution to this challenge.⁷

Rhamnolipids demonstrated antimicrobial activity against Gram-positive and Gram-negative bacteria, although the effect was dependent on the concentration.²³ The antimicrobial mechanism of action was shown to involve membrane disruption and increased cellular permeability.²⁴ Rhamnolipids were effective against MRSA and *Candida albicans* when delivered in combination with essential oils as an emulsifier.²⁵ Although *S. aureus* is a common finding in patients with atopic dermatitis, *Malassezia* and not *Candida albicans* is the yeast associated with seborrheic dermatitis.²⁶ However, the literature does not provide sufficient evidence that rhamnolipids are selective for pathogens over normal human cells. Rhamnolipid micelles were found to disrupt human lung epithelial cells and red blood cells in addition to bacteria. However, the tested nano-formulation was less cytotoxic to the skin compared to conventional alcohol preparations.²⁷

Sophorolipids exhibit primarily antifungal activity, showing effectiveness against *Candida*, *Aspergillus*, and *Trichophyton* species at concentrations that are well tolerated by human keratinocytes in vitro.^{1,28,29}

Their mechanism similarly disrupts membranes, aided by the insertion of their hydrophobic lactone ring structure into fungal lipid bilayers. MELs have demonstrated efficacy against *Candida albicans* and *Escherichia coli* in minimum inhibitory concentration (MIC) assays with MEL-A exhibiting the highest antimicrobial effectiveness among the studied variants.³⁰ Antibiofilm activity has been recorded across all three categories, relevant to leave-on formulations applied to impaired skin where biofilm-producing bacteria such as *S. aureus* and *P. aeruginosa* could establish their colonies. The capability of glycolipid biosurfactants to serve as emulsifiers, moisturizers, and antimicrobial agents in one ingredient presents a significant advantage for cosmetic formulators.³¹

4. Formulation Considerations for Leave-On Products

4.1 Emulsification Ability and Droplet Stabilization

Rhamnolipid biosurfactants are generally more hydrophilic, while sophorolipids are generally hydrophobic, and their combination demonstrates outstanding emulsifying properties. Rhamnolipids can emulsify a wide range of hydrocarbons, aromatic hydrocarbons, and vegetable oils; their emulsifying properties depend on pH, with maximum emulsification (71.4%) being achieved for kerosene at pH 8, comparable to the commercial surfactant SDS. By contrast, sophorolipids are not efficient enough emulsifiers on their own. When used to make emulsions with medium-chain triglyceride oil, they initially formed large (about 1000 nm) unstable droplets. However, a 3:1 mixture of sophorolipids and soybean lecithin was shown to produce nano-emulsions (below 400 nm) that were

stable across a wide temperature (40-90 °C) and pH range (pH 3-9). Thus, the mixture of sophorolipids and lecithin can be a good emulsifier with excellent stability characteristics.

Marine rhamnolipids can also be used as emulsifiers since their emulsifying ability and surface activity were comparable to SDS at neutral and alkaline pH and higher than commercial sucrose esters. However, their efficiency was lower at acidic pH and high temperatures (90 °C). The emulsifying properties of rhamnolipids have also been studied for the ability to stabilize crude oil and tetradecane emulsions in seawater with modified silica nanoparticles. The emulsions obtained had smaller droplets than those obtained with SDS and were stable, which makes these biosurfactants promising as dispersants during an oil spill. Thus, both rhamnolipids and sophorolipids can be used as emulsifiers, with the rhamnolipids demonstrating better performance overall, with their efficiency dependent on pH. Sophorolipids are best used in a mixture with other emulsifiers such as lecithin or silica nanoparticles to achieve good results.³²

4.2 Rheology and Texture

Rhamnolipid solutions exhibit significant non-Newtonian properties. The solutions of rhamnolipids show strong shear thinning under steady shear flow and extensional hardening under extensional flow. Zero shear and extensional viscosities of rhamnolipid solutions are higher than those of solutions of the synthetic cationic surfactant CTAB, and the shear and extensional relaxation times also tend to be higher.³³

Besides, rhamnolipids increase the viscosity of the commonly used surfactant systems, such as SLES/CAPB, due to the formation of wormlike micelles, which entangle with one another and thereby strengthening the solution.³⁴

Sophorolipids differ from rhamnolipids in terms of their microstructural behavior. For instance, researchers apply the DLS microrheology technique to study the aggregation structure and dynamics of a surfactant on a microscopic scale related to personal-care and home-care products. They find that the mixture of acidic/lactonic sophorolipids shows unexpected weak rheological response to pH variations, although the sophorolipids in the mixture generally possess a carboxyl group that is normally sensitive to pH.³⁴

Moreover, the two biosurfactants differ in dilatational rheology at interfaces, which determines the foam and emulsion properties. The lowest dilatational interfacial elasticity was found for the sophorolipid/SDS mixture among the tested glycolipids and the reference surfactant system. The rhamnolipid fractions varied greatly: the interfacial elasticity (56.9 mN/m) and viscosity (6.2 mN·s/m) of one of the purified rhamnolipid fractions (R1) was the highest among all the surfactants tested, which also exceeded the commercial rhamnolipid mixture.³⁵

Thus, it can be concluded that rhamnolipids generally demonstrate more pronounced viscoelastic effects both in solution and at the interface, while sophorolipids are

relatively low in interfacial elasticity and viscosity and less sensitive to pH.

4.3 Compatibility with Cosmetic Co-Ingredients

There are differences in the compatibility of sophorolipids, MELs and rhamnolipids with other cosmetic ingredients such as emulsifiers, thickening agents, electrolytes, UV screens and preservatives, as found in studies.

Regarding rhamnolipids, a patented rhamnolipid formulation platform was found to be compatible with typical co-emulsifiers, oils, thickeners and stabilizers as well as burdening substances for emulsions such as UV filters and active antimicrobial and cosmetic ingredients, while the non-inventive comparative emulsifying agents had unacceptable viscosity and storage stability.³⁶ In contrast, in another study that evaluated the rheology and stability of sulfate-free rhamnolipid formulations, it was found that inorganic salts were ineffective as a thickener for rhamnolipids, while polymer thickeners such as Carbopol (R) Aqua SF-1 and Carbopol (R) 940 were appropriate for shampoo and moisturizer formulations, respectively. Thus, it can be concluded that rhamnolipids require specific thickeners rather than being compatible with all types of rheology modifiers.³⁷

Mixed surfactants have also shown favourable compatibility. For instance, lecithin/sophorolipid/rhamnolipid microemulsions in isopropyl myristate were found to be relatively stable under temperature and electrolyte concentration changes, desirable characteristics for cosmetic and drug delivery applications. In addition, rhamnolipid-surfactin nanoemulsions for cosmetic use were found to be highly resistant to pH changes, centrifugation, heating and salt addition.⁶

MELs are suitable as emulsifiers, dispersants and detergent components together with other chemicals in cosmetic and pharmaceutical formulations due to their low critical aggregation concentration and hydrophilicity. In general, *in vitro* studies have shown that rhamnolipids, sophorolipids, MELs and surfactin are compatible with human skin, allowing their combined use with other active substances in cosmetic formulations. Sophorolipids and rhamnolipids together are multifunctional cosmetic ingredients that are compatible with conventional personal care product ingredients.

4.4 Stability and Shelf Life

Long-term stability under storage and application conditions for sophorolipids, MELs, and rhamnolipids is significantly different, and recent studies have begun to examine the common assumption that all of these surfactants exhibit uniform stability.

Rhamnolipids were previously reported to exhibit tolerance to a wide range of pH levels (4–10) and temperatures (4–100 °C). Rhamnolipid-stabilized nanoemulsions have already proven stability against heating (30–90 °C), salting (below 100 mM NaCl), and pH changes (5–9) with no droplet aggregation or creaming even after 14 days at room temperature.³⁸ However, a

further study revealed that the concentration of rhamnolipid in aqueous solution decreased significantly at pH levels above 11, and the longer and at higher temperatures, the sample was held, the lower the concentration. This was explained by degradation of the glycosidic and ester bonds linking rhamnose to the fatty-acid chain, yielding lower-molecular-weight congeners, hydroxy fatty acids, free rhamnose, methylfurfural, and organic acids.

Sophorolipids also have stability issues due to the lactonic bond, which can be cleaved in alkaline conditions, resulting in the conversion of sophorolipids into hydroxy fatty acid isomers. For instance, one industrial storage-stability study exposed sophorolipid-containing formulations with residual oleic acid substrate to multi-week treatments at 4 °C, 20 °C, and 40 °C to assess formulation stability.³⁸

Meanwhile, both rhamnolipids and sophorolipids were reported to function as stabilizers of other biomolecules, for example, by preventing proteases from denaturation in surfactant mixtures at pH 8. As for MELs, review level literature suggests that they are stable under changes in most environmental conditions, but the available information comparing their stability to rhamnolipids and sophorolipids is very limited.³⁹

5. Beauty, Sustainability, and Consumer Positioning

The clean beauty movement, broadly defined as the preference for cosmetic products formulated without ingredients perceived as harmful, synthetic, or environmentally damaging, has emerged as a significant influence in the worldwide personal care industry.⁴⁰ Market analysis consistently reveals that an increasing segment of consumers deliberately pursues products that are devoid of petrochemical surfactants, synthetic preservatives, parabens, sulfates, and silicones, and that are manufactured through ecologically sustainable methods. Glycolipid biosurfactants inherently correspond with these consumer inclinations on multiple levels.⁴¹

From the standpoint of feedstock sustainability, glycolipid biosurfactants are synthesized through microbial fermentation utilizing renewable carbon substrates, such as sugars (glucose, sucrose), fatty acids sourced from vegetable oils (soybean, rapeseed, sunflower), and agricultural food waste streams like molasses, whey permeate, and discarded frying oils.⁴² The utilization of waste substrates not only lowers production expenses but also supports circular economy principles by valorising low-value by-products. Life cycle assessment (LCA) studies comparing sophorolipid production with synthetic surfactant manufacture have suggested potential environmental advantages in some cases, though the evidence base remains limited and results vary across studies.^{43,44}

For cosmetic brands, glycolipid biosurfactants open the door to highly appealing product label claims like bio-based, naturally derived, biodegradable, and microbiome-friendly. These terms strongly attract eco-conscious consumers, and their approval by natural

standards like COSMOS and NATRUE makes them easy to commercialize.⁴⁵ However, brands must note that regulations in many regions require strict proof for "natural" claims. Formulators must provide specific paperwork regarding the ingredient's origin, how it was processed, and its exact natural carbon content before displaying these claims.

6. Therapeutic Potential of Bio-glycolipids in Topical Drug Delivery

Besides being used as valuable ingredients in cosmetics, bio-glycolipids may also be used as excipients in topical drug delivery systems. Since they are amphiphilic molecules, glycolipids may form micelles, vesicles, and nanoemulsions, which may help deliver poorly soluble drugs into the skin.⁴⁶ Topical creams, gels, and ointments suitable for the treatment of various skin conditions may utilize these lipid-based delivery vehicles. Moreover, since glycolipids are generally biocompatible, biodegradable, and only mildly toxic, they can be used in place of conventional surfactants in topical pharmaceutical formulations to produce topically applied medication with fewer adverse reactions. Another advantage of using glycolipids in topical drug delivery is that certain types of glycolipids, such as sophorolipids, rhamnolipids, and mannosylerythritol lipids, may exhibit antimicrobial, anti-inflammatory, and anti-biofilm properties.⁴⁷

Therefore, glycolipids may be used in pharmaceutical formulations as penetration enhancers, surfactants, and bioactive compounds. It was shown that these biocompatible and biodegradable molecules disrupt bacterial cell membranes and prevent biofilm formation. Thus, sophorolipids, rhamnolipids, and mannosylerythritol lipids can be used in topical antibiotic creams and ointments to treat infected wounds, burns, and acne. Additionally, they could be used in pharmaceutical formulations meant for wound healing and reducing the risk of microbial infections.⁴⁸

7. Commercial Developments and Analytical Characterization

7.1 Commercial Availability and Industry Adoption

The production rates and costs differ substantially across all three classes of glycolipids, reflecting differing levels of industrial adoption.

Sophorolipids are the most advanced in terms of commercialization. The global sophorolipids market is estimated to be valued at around \$540 million in 2025 and projected to reach around \$844 million by 2034.⁴⁹ Godrej Industries announced in 2025 that it has expanded the production capacity of the Renewa™ biosurfactant platform to include sophorolipids and further diversified the application areas from personal care to textiles and coatings, animal health and nutrition, and food.⁵⁰ Similarly, Evonik offers REWOFORM® SL ONE as its sophorolipid of choice and, the company presented REWOFORM® RL 100, a rhamnolipid based fermentation-surface active agent designed for cleaning applications, thus expanding its range of biosurfactants.⁵¹

In turn, rhamnolipids are the earliest to reach mainstream adoption. The overall sophorolipid-and-rhamnolipid market size was valued at around \$335 million in 2023 market analysis and is projected to reach \$542 million by 2030,⁵² whereas in 2025, the rhamnolipid market value hit \$1.22 billion,⁵³ with an expected increase in the forecast period. Notable events in 2020 and 2021 include the opening of Evonik's Slovakian production site to meet the demand from its Unilever partnership and the acquisition of the NatSurFact rhamnolipid business from Logos Technologies by Stepan Company, with the 2020 acquisition closing later in the year.^{54,55}

7.2 Analytical Characterization Methods

Analytical methods for the characterization of sophorolipids, MELs and rhamnolipids are based on a common toolbox, ranging from low resolution methods for screening to high resolution methods for structural determination respectively. They are often used in combination for confirmation.

Low-resolution screening tools are thin-layer chromatography (TLC) and colorimetric assays, while high-resolution mass spectrometry and NMR spectroscopy provide detailed molecular mass and structural information on rhamnolipids, sophorolipids, trehalose lipids and MELs.⁵⁷ For sophorolipids specifically, HPLC coupled with evaporative light-scattering detection (HPLC-ELSD) has been correlated with HPLC-ESI-MS/MS, allowing TLC-scraped bands to be identified via established retention-factor correlations and mass-fragmentation patterns. In one such study, this approach enabled identification of longer-chain C24:0 acetylated sophorolipid variants for the first time, in addition to the more common C16–C18 forms.⁵⁸

For rhamnolipids, a combination of TLC, Fourier-transform infrared spectroscopy (FTIR), and proton NMR (¹H-NMR) has been used to confirm biosurfactant identity, with TLC separation typically performed on silica gel plates using a chloroform:methanol:aqueous acetic acid solvent system.⁵⁹

MELs have been structurally confirmed using FTIR to identify functional groups, liquid chromatography-mass spectrometry (LC/MS) for molecular composition, and both ¹H- and ¹³C-NMR for detailed structural assignment, alongside separate measurements of surface tension, critical micelle concentration, foaming, and emulsification, which together characterize functional performance.⁶⁰

8. Regulatory Framework

The application of glycolipid biosurfactants as ingredients in cosmetic leave-on products is governed by the regulations for cosmetics and their ingredients established in each market. For instance, in the European Union, cosmetics are subject to Regulation (EC) No 1223/2009, which stipulates that all ingredients should be listed in the EU Cosmetic Ingredient Database (CosIng), a Cosmetic Product Safety Report (CPSR) should be drawn up by a qualified safety assessor, and a

Product Information File (PIF) should be prepared and regularly updated by the responsible person, in which the Cosmetic Safety Assessment as well as the technical specifications of the substance or mixture, its formulation, process conditions, and product safety justification are included.⁶²

For biosurfactant ingredients, Section 3 of the European Commission's Guidelines on Annex I to Regulation (EC) No 1223/2009 (2013/674/EU) requires that the Cosmetic Product Safety Report document the physico-chemical properties of each substance and mixture used in a formulation including molecular weight, chemical identification, and purity for evaluation by the qualified safety assessor.⁶⁴ This is especially important for glycolipid biosurfactants due to their structural complexity and the heterogeneous nature of fermentation-derived products. Consequently, downstream processing is needed to remove impurities such as residual proteins, unconsumed substrates (e.g., unreacted triacylglycerols and free fatty acids), and other cellular materials remaining from the fermentation broth.⁶⁵ To ensure consumer protection and regulatory compliance, manufacturers must ensure batch-to-batch consistency in the chemical composition of each biosurfactant lot, and confirm that the finished substance is adequately purified, a requirement that is broadly analogous to established quality-control practices for other fermentation-derived biologics, in which residual host-cell proteins, process-related contaminants, and solvent residues must be characterized and controlled during purification.⁶⁶

In the United States, the FDA supervises the manufacture and sale of cosmetics and recently updated the regulation called the Federal Food, Drug, and Cosmetic Act (FD&C Act), which was substantially amended by Modernization of Cosmetics Regulation Act (MoCRA, 2022). \ MoCRA requires registering facilities and products with the FDA and reporting any adverse events.⁶⁷ In the US, the FDA does not approve ingredients; however, they should be safe for their intended use. Ingredients are subject to the INCI (International Nomenclature of Cosmetic Ingredients) naming system, which currently includes several glycolipid biosurfactants (for example, Sophorolipids and Rhamnolipids). This classification helps to determine what substances can be included in the final product and helps the FDA review the application.⁶⁸

The way to get your glycolipid biosurfactant ingredients on the global market is complicated, but it is achievable. The task becomes much easier if the produced substance has been previously tested and proven safe for cosmetic use, and there are sufficient research papers about it.

9. Challenges and Future Research Directions

Despite the growing industrial interest, each of these biosurfactants has its own challenges to wide application and further development, as well as some common limitations in production economics.¹ A significant limitation in terms of production for all three glycolipids is their high production cost compared to traditional chemical surfactants, although industrial-scale

production of sophorolipids has already overcome this obstacle. The low yield is particularly problematic for rhamnolipids, while its application is limited by pathogenicity of *Pseudomonas aeruginosa* to cause disease, and the use of rhamnolipid is hampered by the presence of impurities and a mixture of congeners, the properties of which are not always known.⁶⁹

For MELs, achieving industrial-scale MEL production remains limited by the underdeveloped state of fungal cell engineering technology, while the high cost of production is due to low fermentation yields and an unprofitable downstream process. In addition, the productivity of MELs is significantly lower than that of rhamnolipids and sophorolipids.⁷⁰

At the same time, the current state of sophorolipid production is promising, as the capacity of one of the manufacturers reached more than 1000 tons per year. Industrial production of rhamnolipids and sophorolipids has also begun, and research priorities include finding strains that yield high levels of surfactant, using alternative non-pathogenic hosts for their production, and determining the optimal conditions for fermentation. Thus, the prospects for research into all three types of biosurfactants are vast, targeting the current limitations in their use in cosmetics and detergents, as well as other industries.

Conclusion

The reviewed literature highlights the special nature of sophorolipids, rhamnolipids, and MELs, which are beneficial for leave-on cosmetic formulations, as they have specific advantages and disadvantages with varying degrees of scientific validation. MELs were the most effective skin repairing and moisturizing molecules with confirmed tolerability benefits. Sophorolipids exhibited the most anti-inflammatory and antifungal activity with favourable tolerability. Rhamnolipids, in turn, were confirmed to exhibit antibacterial properties, emulsifying ability, and, interestingly, their effectiveness depends on the concentration, while low doses have a beneficial effect on the skin, high doses are cytotoxic and cause inflammation. This is possibly due to the pathogenic potential of their bacterial producer, *Pseudomonas aeruginosa*. Thus, in general, the claims regarding the moisturizing and selective properties of these biosurfactants have largely relied on patent literature or industry-sponsored studies, with insufficient independent clinical evidence to date.

From the formulation perspective, the combined application of two congeneric lipids may compensate for some of the limitations mentioned, for example, incompatibility or instability, however, it is complicated to predict their interaction with other substances in each case individually. From an economic point of view, according to the reviewed manuscripts, sophorolipids are the most promising variants due to their relative simplicity and cost-effectiveness of production, rhamnolipids are constrained by the pathogenicity of their producer organism, and MELs are the furthest from the stage of industrial production readiness. Moreover, the trend of regulatory harmonization also seems

relevant: it was noted that depending on the jurisdiction, specific documentation for each type of biosurfactant may be required, which could be simplified if their characteristics and quality requirements are comparable.

Thus, glycolipids represent a promising class of multifunctional ingredients well suited for leave-on cosmetics for the modern consumer. However, their implementation requires further research, documentation, and economic justification, depending on the intended use and concentration.

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