

# Antimicrobial Biosurfactants Towards the Inhibition of Biofilm Formation



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## 1 Introduction

Nowadays, infections associated with urinary tract medical devices, have become a common health issue. The fact that their surfaces are prone to microbial colonization and biofilm formation is certainly a problem. As a result, these medical devices usage can be a source of extreme concern, especially for critically ill patients [1].

Urinary tract related infections (UTIs) are among the most frequent HAIs comprising 27% in Europe and 36–40% in the USA [2, 3]. Unfortunately, intensive care units (ICU) also have become a stage of HAIs events where several reported infections among ICU patients can be attributed to catheter-related urinary tract infections (CRUTIs) [4, 5]. UTIs in ICUs have been reported as 1.1 per 1000 patient-days in Europe and most of these are, CRUTIs i.e.97.4% [3]. Nevertheless, device-associated UTI are not exclusively catheter-related. Consequently, among patients undergoing ureteral stents, 38% develop UTI while 45–100% of them have bacteriuria [3].

The incidence of UTIs calls for a well understanding of their pathogenesis, alongside with rapid interventions before and after bacterial colonization and biofilm formation to prevent such infections and to diminish its negative impacts.

Biofilm is a mono or multilayer of interconnected microorganisms surrounded with extracellular matrix (ECM) interfacing a liquid medium. Scientists have described biofilm formation as a process of multi-steps including adhesion, aggregation, maturation, and detachment. Drawbacks associated with biofilm development are substantial and compose a challenge for UTIs management and prevention. In addition to their ability to detach as planktonic to colonize on other surfaces inside the body systems, the diversity of biofilm microorganisms also contributes to

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the failure of antimicrobial treatment [6]. Additional potential protection of bacteria is provided by the biofilm composition which acts as a guard against antibiotics and immunity system.

Due to the resistance of mature biofilms and the risks associated to biofilm manipulation or eradication, prevention of biofilm generation is advantageous. Therefore, the majority of the strategies that have been proposed aim at preventing the early stages of biofilm formation on the catheter surface [7]. A possible strategy may be the use of surface active molecules with antimicrobial activity such as biosurfactants.

Biosurfactants are surface-active molecules that have granted priority in research and industrial studies. They are identified as amphiphilic biomolecules produced by a wide range of microorganisms as secondary metabolites, owning the ability of surface tension reduction like the industrial surfactants but with the advantage of being eco-friendly molecules that can be produced from renewable resources. Moreover features associated with biosurfactants include low toxicity, biodegradability, cost-effectiveness, and biocompatibility [8]. Due to their unique properties, biosurfactants can be used in several applications regarding pharmaceutical, food, agriculture, petroleum and cosmetic industries [9, 10].

According to their structure, biosurfactants have been classified into glycolipids (e.g. rhamnolipids and sophorolipids), lipoproteins or lipopeptides (e.g. surfactin), conjugated phospholipids and fatty acids (e.g. polymyxin) and polymeric biosurfactant (e.g. liposan) [8].

Glycolipids are the most used biosurfactants due to their surface-active properties, e.g. dispersion, emulsion, foaming, solubilization, wetting and penetration [8, 11]. In glycolipids monosaccharide residues are linked to an hydrophobic group [12] and this class comprises sophorolipids, rhamnolipids, trehalose lipids, cellobiose lipids and mannosylerythritol lipids, which are the most studied [8, 13].

Besides their surface-active properties, some biosurfactants also detain interesting biological activities and the most studied have been sophorolipids and rhamnolipids.

Among the glycolipid class, sophorolipids have been assigned for antimicrobial properties and are also considered as potential anticancer candidates considering their ability for apoptosis induction among different types of cells such as liver and leukemia cancer cells [14, 15]. Additional sophorolipids revealed sperm immobilization and death through micelles formation combined with anti-HIV via inhibition of virus duplication [16]. Also, rhamnolipids have been pointed to present antifungal, antimicrobial, antiviral and anti-adhesive properties which makes them suitable for a variety of industrial, environmental, agricultural or medical applications [17].

## 2 Sophorolipids and Rhamnolipids Antimicrobial Activity

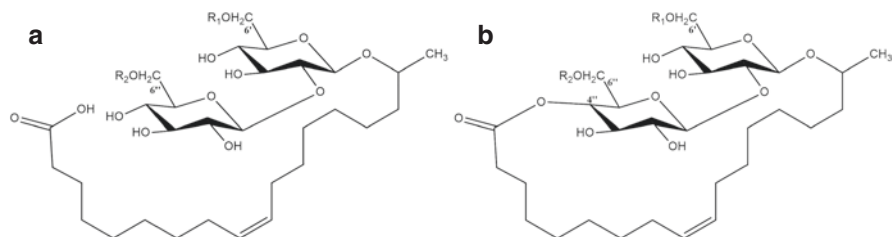
To understand why sophorolipids and rhamnolipids have been proposed for biofilm inhibition or disruption it is important to study their antimicrobial properties.

## 2.1 Sophorolipids

Sophorolipids can be produced by several microorganisms with a considerable yield [13] and present the favorable characteristics of being antibacterial, antiviral, antimycoplasma, antifungal and antialgal agents. Furthermore, sophorolipids can occur either in an acidic (non-esterified) or lactonic (esterified) form as illustrated in Fig. 1. Usually, lactonic sophorolipids present higher antimicrobial activity while acidic SLs display higher solubility and foaming characteristics [13, 18].

Sophorolipids' antimicrobial activity effect is assigned to their ability to change the hydrophobic properties of bacterial surfaces and to burst the cellular membrane resulting in the release of intracellular content and death. Sophorolipids may act also as antifungal since they are able to inhibit their movement and induce their lysis [14, 15].

An example of sophorolipids' antimicrobial activity can be verified in Lydon et al. studies [19] when investigating the antimicrobial potential of sophorolipids produced by *Starmerella bombicola*. The acidic sophorolipids proved to have antimicrobial activities against the nosocomial infective agents *Enterococcus faecalis* and *Pseudomonas aeruginosa*, with significant reduction in colony forming units (CFU) at concentrations of 5 mg/mL. In addition, *in vivo* experiments using a mouse skin wounding assay revealed that acidic sophorolipids could be used as a component of antimicrobial creams to reduce the risk of wound infection during healing [19]. Moreover, the antimicrobial activity of sophorolipids was also shown by Dangle-Pulate et al. [20]. The biosurfactants obtained from *Candida bombicola*, with glucose and lauryl alcohol media supplementation, were able to prevent bacterial colonization of *Escherichia coli* (30  $\mu\text{g}/\text{mL}$  and 2 h) and *P. aeruginosa* (1  $\mu\text{g}/\text{mL}$  and 4 h) as well as *Staphylococcus aureus* (6  $\mu\text{g}/\text{mL}$  and 4 h). The suggested mode of action of antibacterial sophorolipids was pointed out as cellular membrane disruption causing the loss of all cytoplasmic components leading to cellular death [20].



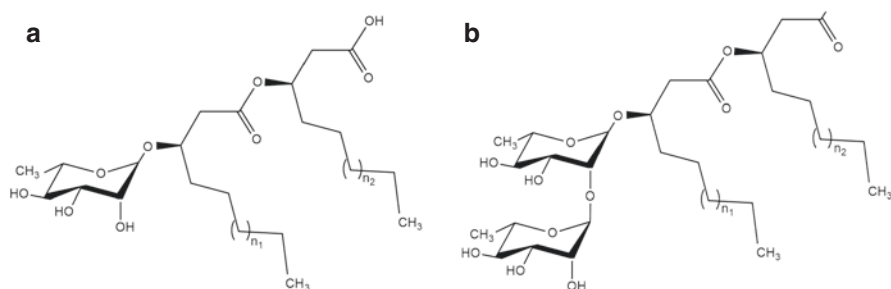
**Fig. 1** Illustration of the chemical structure of acidic (a) and lactonic (b) sophorolipids. R<sub>1</sub>=R<sub>2</sub>=H; R<sub>1</sub>=H and R<sub>2</sub>=COCH<sub>3</sub>; R<sub>1</sub>=COCH<sub>3</sub> and R<sub>2</sub>=H; R<sub>1</sub>=R<sub>2</sub>=COCH<sub>3</sub>

## 2.2 Rhamnolipids

In the past three decades, rhamnolipids have also acquired some recognition for presenting some valuable characteristics, such as antifungal, antimicrobial, antiviral and antimycoplasmal activity [21, 22]. Besides presenting antimicrobial activity, rhamnolipids also present antiadhesive properties that can be used as an antimicrobial strategy by coating the surface of medical devices and perform changes on surface's hydrophobicity [18].

Rhamnolipids have structures (Fig. 2) and properties similar to that of detergents and have been reported to intercalate into the membrane phospholipid bilayer, facilitating the permeability of the membrane and flow of metabolites [23].

Their antimicrobial mechanism can explain the results of the antimicrobial activity of the rhamnolipid extract, obtained by Ndlovu et al. [23], observing pronounced activity against a broad spectrum of opportunistic and pathogenic microorganisms, including antibiotic resistant *S. aureus* and *E. coli* strains and the pathogenic yeast *Candida albicans*, when using the agar disc susceptibility method [23]. Moreover, the antimicrobial properties of these compounds were also evaluated by Lotfabad et al. [24] who studied rhamnolipids produced by two indigenous *P. aeruginosa* strains. In this study, preliminary disc diffusion assay showed that all examined Gram-positive bacteria (i.e. *S. aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12228 and *Bacillus cereus* ATCC 6051) were inhibited by biosurfactants produced by both MR01 and MASH1 strains [24]. Another study, conducted by de Freitas Ferreira et al. [25] investigated the antimicrobial activity of rhamnolipids under different pH values and assessed an antimicrobial activity against the Gram-positive pathogens, *Listeria monocytogenes*, *B. cereus* and *S. aureus*. *B. cereus* was the most sensitive bacteria showing a MIC value of 19.5  $\mu\text{g/mL}$ , and a bactericidal activity at 39.1  $\mu\text{g/mL}$  of rhamnolipids [25].



**Fig. 2** Illustration of chemical structure for mono-rhamnolipids (a) and di-RLs (b). Fatty acid moieties may present a length that usually ranges from 8 to 14 carbon atoms ( $1 < n_1$  and  $n_2 < 7$ )

### 3 Fighting Biofilm Formation with Biosurfactants

Biosurfactants are molecules that have amphipathic structures, which allow the interaction with cellular membranes, such as the bilayer membrane [24, 26]. The interaction of the biosurfactants with the cellular membrane causes changes and perturbations that will lead eventually to the disruption of the cellular membrane and ultimately the release of the cytoplasmic content of the cell and consequently important metabolites [24, 27]. These properties can be used to prevent biofilm formation on medical devices surfaces with the intention of reducing their related infections.

Due to presenting antimicrobial activity, sophorolipids have been explored on biofilm inhibition studies (Table 1). These studies have been developed mostly *in vitro* (e.g. using common microtiter plates) by evaluating the ability of sophorolipids' biofilm disruption or biofilm formation inhibition. Examples include the study of Mukherji and Prabhune [28] that observed the ability of sophorolipid mixtures, produced by *C. bombicola* when the media was supplemented with different plant essential oils, to inhibit *Vibrio cholerae* biofilm formation on glass slides [28]. Moreover, Sen et al. [29] investigated the efficacy of a sophorolipid mixture (SL-YS3) produced by *Rhodotorula babjevae* YS3 towards *Trichophyton mentagrophytes* biofilm. In this study a biofilm eradication around 80% was observed on microtiter plate assays when a concentration of 2 mg/mL was used. Moreover, when observing biofilms disruption on pre-sterilized glass coverslips by scanning electron microscopy (SEM) or confocal laser scanning microscopy (CLSM) a considerable reduction was also observed. The therapeutic efficacy of this sophorolipid mixture on experimentally induced dermatophytosis in mice infected with *T. mentagrophytes* was also evaluated. SL-YS3 showed therapeutic effects and also its ability to regulate collagen deposition together with proper matrix and spatial arrangement, thereby contributing to the healing of the infected skin tissue as compared to the untreated control [29].

The use of these natural biosurfactants to prevent biofilm formation on the surface of medical grade silicone, a common material used in catheters and stents fabrication has also been studied in order to evaluate its potential to reduce related infections. This was first investigated by Pontes et al. [30] who observed that sophorolipids when adsorbed to silicone could reduce *S. aureus* and *E. coli* biofilm formation. Comparing to plain silicone a reduction of 3 log units on *S. aureus* surface colonization was observed when using a solution with a concentration of 1.5 mg/mL to promote sophorolipids adsorption. Moreover, a 50% decrease on *E. coli* biofilm formation was also observed (Fig. 3, [30]).

More recently, Ceresa et al. [31] studied the effect of acidic congeners, C18 lactic sophorolipids and mixture of acidic and lactonic sophorolipids on the disruption of *S. aureus* ATCC 6538, *P. aeruginosa* ATCC 10145 and *C. albicans* IHEM 2894 pre-formed biofilms on medical grade silicone. All three tested mixtures (when at a concentration > 0.1% w/v) were able to disrupt biofilms up to 70%, 75%

**Table 1** Examples of research studies presenting the potential application of the biosurfactants (BS) sophorolipids (SLs) and rhamnolipids (RLs) in preventing biofilm formation

| BS  | BS Producer              | Biofilm producer   | Method   | Results  | Refs. |
|-----|--------------------------|--|--|--|-------|
| SLs | <i>R. babjevae</i> YS3   | <i>T. mentagrophytes</i>   | Biofilm eradication. Crystal violet stain, SEM or CLSM<br><i>In vivo</i> assay: experimentally induced dermatophytosis in mice       | Biofilm eradication. Around 80% with of 2 mg/mL<br><i>In vivo</i> assay: SLs contributed to the healing of the infected skin tissue comparing to untreated control | [29]  |
| SLs | <i>S. bombicola</i>      | <i>S. aureus</i> ATCC 25923 and <i>E. coli</i> ATCC 25922  | Biofilm inhibition. Crystal violet staining and CFU counts. Silicone coated with SLs, static assay. Concentration range 0.10–3 mg/mL | 3 log units reduction <i>S. aureus</i> colonization 1.5 mg/mL to promote adsorption. A 50% decrease on <i>E. coli</i> biofilm formation with all concentrations    | [30]  |
| SLs | <i>C. bombicola</i>      | <i>C. albicans</i> IHEM 2894, <i>S. aureus</i> ATCC 6538 and <i>P. aeruginosa</i> ATCC 10145     | Anti-adhesion and antibiofilm activity. SLs-coated discs were evaluated using the crystal violet assay                               | 75% and 68–70% inhibition on the cell attachment for <i>S. aureus</i> and <i>C. albicans</i> . No anti-adhesive effect on cells of <i>P. aeruginosa</i>            | [31]  |
| SLs | <i>C. bombicola</i>      | <i>P. aeruginosa</i> PAO1 (WT) and $\Delta$ <i>wspF</i> deletion mutant (PAO1)                   | Biofilm eradication. Addition of SLs to formed biofilms, 5 h incubation. Response through OD <sub>600</sub> and CLSM                 | SLs tested against a EPS overexpression mutant biofilms disrupts ~ 70% of the biofilm at a concentration of 0.1% and nearly 90% at 1%                              | [32]  |
| RLs | <i>P. aeruginosa</i> LBI | <i>L. monocytogenes</i> ATCC 19112 and <i>S. aureus</i> ATCC 25923                               | Adhesion test. Crystal Violet staining. Different intervals, static. Concentration 0.25%, 0.5% and 1.0% (w/v)                        | Concentration 1.0% reduced 57.8% adhesion of <i>L. monocytogenes</i> and by 67.8% adhesion of <i>S. aureus</i>   | [39]  |
|     |                          | <i>L. monocytogenes</i> ATCC 19112 <i>S. aureus</i> ATCC 25923 and <i>S. enteritidis</i> PNCQ030 | Disruption of biofilms. 24 h, static. Concentration 0.25% and 1.0% (w/v) aqueous solutions   | At 0.25% RLs removed 58.5% the biofilm of <i>S. aureus</i> , 26.5% of <i>L. monocytogenes</i> , 23.0% of <i>S. enteritidis</i> and 24.0% of the mixed culture      | [39]  |
| RLs | <i>P. aeruginosa</i>     | <i>H. pylori</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> and <i>S. mutans</i> | Biofilm inhibition   | Biofilm inhibition for five bacterial strains in a dose-dependent manner   | [43]  |

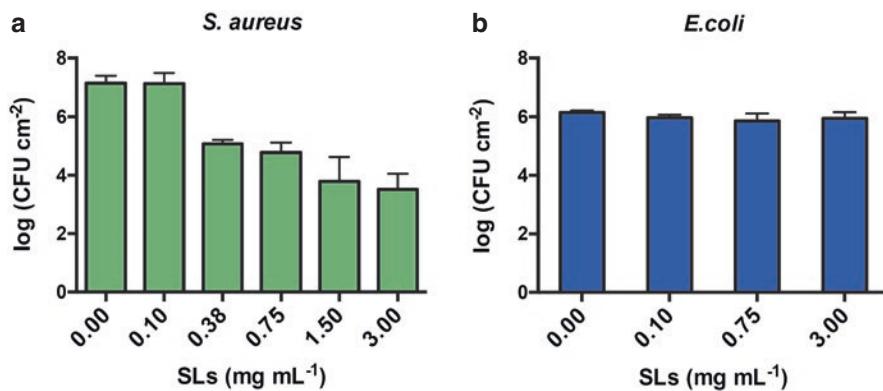
**Table 1** (continued)

| BS  | BS Producer             | Biofilm producer   | Method  | Results   | Refs. |
|-----|-------------------------|--|---|---|-------|
| RLs | <i>P. aeruginosa</i>    | <i>S. epidermidis</i> , <i>S. salivarius</i> , <i>S. aureus</i> , <i>C. tropicalis</i> , <i>C. albicans</i> , and <i>R. dentocariosa</i> | Biofilm inhibition and anti-adhesion. Crystal violet staining and phase-contrast microscopy   | Reductions of 50% on bacteria was achieved for <i>S. epidermidis</i> , <i>S. salivarius</i> , <i>S. aureus</i> and <i>C. tropicalis</i> . <i>C. albicans</i> , <i>R. dentocariosa</i> showed a decrease after 4 h of 20–28%                         | [44]  |
| RLs | <i>P. aeruginosa</i>    | <i>S. epidermidis</i>  | Biofilm inhibition. Flow-cell model in combination with CLSM and AFM  | 90% of biofilm inhibition   | [45]  |
| RLs | <i>P. aeruginosa</i> 89 | <i>S. aureus</i> ATCC® 6538 and <i>S. epidermidis</i> ATCC® 35984  | Biofilm disruption and inhibition. Crystal Violet staining and MTT assay. RLs at a concentration 0.06–2 mg/mL for disruption and 2 mg/mL for inhibition assays. End points at 24, 48 and 72 h of incubation | Biofilm disruption ranged from 68 to 89% for <i>S. aureus</i> and from 44 to 96% for <i>S. epidermidis</i> . Pre-treatment of silicone with R89BS resulted in a biofilm inhibition of 76% for <i>S. aureus</i> and of 63% for <i>S. epidermidis</i> | [46]  |
| RLs | <i>P. aeruginosa</i>    | <i>S. aureus</i> ATCC 25923  | Biofilm inhibition. After incubation at 37 °C for 24 h, biofilm assessment was performed by colony forming units (CFU) count  | A biofilm inhibition of 99% was achieved with rhamnolipid–chitosan nanoparticles  | [47]  |

and 80% regarding *S. aureus*, *P. aeruginosa* and *C. albicans*, respectively. Moreover, acidic sophorolipid (0.8% w/v) pre-coated silicone discs reduced *S. aureus* biofilm by 75% while *C. albicans* reached 68–70% [31].

It is also of great importance to study the development and ways to prevent biofilm formation onto microfluidic systems. Nguyen et al. [32] demonstrated that sophorolipids had a stronger effect than chemical surfactants such as sodium dodecyl sulphate, Tween20 and Tween80 when disrupting established *P. aeruginosa* PAO1 biofilms grown in microfluidic channels. The authors noticed that although presenting antibiofilm properties, sophorolipids did not seem to have antibacterial effects on PAO1. When testing these compounds on a mutant strain that overexpresses extracellular polymeric substances they observed that sophorolipids detached and disintegrated biofilms from glass surfaces [32].

Rhamnolipids have been recognized for their antiadhesive and biofilm dispersion effects. It is suggested that the antibiofilm activity of rhamnolipids occurs through



**Fig. 3** Anti-sessile activity of silicone specimens adsorbed with sophorolipids towards *S. aureus* (a) and *E. coli* (b). Sessile cells CFU counts were performed when different concentrations of SLs were tested (0.1–3 mg/mL). (Reproduced with permission [30] Copyright 2016, Elsevier)

interference with quorum sensing of biofilm cells, which leads to detachment of microorganisms. This interference has been attributed to the inhibition of intracellular lipidic signals, however, it is also reported that rhamnolipids solubilize ECM proteins via micelles formation [8, 33]. Furthermore, other investigations have pointed out that rhamnolipids can manipulate biofilm-associated channels, altering the oxygen and nutrient supply for sessile microorganisms. Moreover, it has been observed that they may enhance interconnections changes as well, so they affect not only quorum sensing of bacteria but also, they do not allow them to develop genetic mutations or resistance [34]. A previous study of Davey et al. [35] mentioned that rhamnolipids can inhibit both intracellular contact and cell–surface contact allowing the detachment and preventing attachment of microorganisms [35]. Other studies pointed out that the mechanism of action of rhamnolipids is through modification of bacterial surface components. These studies proved that rhamnolipids could sharply increase the hydrophobicity of the cell surface by removing out the lipopolysaccharides parts from the outer membrane. Also, they showed that a low concentration of rhamnolipids is required to induce the disruption of cells [36, 37]. Similarly, the antifungal activity of rhamnolipids was explained by the disruption of the cytoplasmic membrane [38]. Additional investigations regarding the antibacterial effect of rhamnolipid showed that monorhamnolipids exhibit bacteriostatic effect while dirhamnolipids were able to kill the bacteria and show bactericidal effect [34].

Due to their antimicrobial and antiadhesive properties rhamnolipids have been the target of many studies focused on diminishing biofilm formation in different surfaces such as polystyrene, silicone and medical devices surfaces.

Different studies aiming the investigation of rhamnolipids antibiofilm, antiadhesive and biofilm dispersion effects have been performed and some examples can be found in Table 1. Gomes and Nitschke [39] used different concentrations of



rhamnolipids from *P. aeruginosa* to evaluate their capacity in reducing the adhesion and biofilm formation on polystyrene surfaces. When using a rhamnolipids solution at 1% an adhesion reduction of 57.8 and 67.8% was observed for *L. monocytogenes* and *S. aureus*, respectively. Moreover, rhamnolipids were also effective in preventing the adhesion of bacterial mixed cultures. When at a concentration of 0.25%, rhamnolipids removed 58.5% of *S. aureus* biofilm, 26.5% of *L. monocytogenes* biofilm, 23.0% of *Salmonella enteritidis* and 24.0% of the mixed culture biofilm [39].

Moreover, Aleksik et al. [40] compared the antibiofilm ability against *P. aeruginosa* PAO1 of di-rhamnolipids produced by *Lysinibacillus* sp. BV152.1 with the commercial di-rhamnolipids. The authors observed that di-rhamnolipids produced by *Lysinibacillus* sp. BV152.1 were more effective in reducing biofilm than the commercial ones and an inhibition of 50% was observed with 50 µg/mL and 75 µg/mL, respectively. The authors also observed that amide derivatization of both di-rhamnolipids improved the inhibition of biofilm formation and dispersion, and that the morpholine derivative was the most active causing more than 80% biofilm inhibition at concentrations of 100 µg/mL [40].

Besides their activity towards bacterial biofilms, rhamnolipids, also have revealed activity on *C. albicans* biofilms. Di-rhamnolipids produced by *P. aeruginosa* when at a concentration of 0.16 or 5 mg/mL were able to reduce pre-formed biofilms on polystyrene by 50% and 90%, respectively. In this study the influence of rhamnolipids in disrupting *C. albicans* biofilms was proven and the authors suggested their exploration as a potential alternative to the available conventional therapies [41].

Comparison of rhamnolipids with other antimicrobial compounds or surfactants has also been performed. For example, Quinn et al. [42] compared rhamnolipids with antibiotics antibiofilm activity. The effect of a rhamnolipid mixture, containing mono- and di-rhamnolipids (20 µg/mL) in pre-existing biofilms was observed as a reduction of  $88.4 \pm 5.8$ ,  $74.5 \pm 6.6\%$  and  $85.6 \pm 3.9\%$  against *B. subtilis*, *Micrococcus luteus* and *S. aureus*, respectively. A lower antibiofilm effect was observed with the antibiotics ampicillin, chloramphenicol and kanamycin (5 µg/mL) [42].

Moreover, Shen et al. [43] evaluated sodium lauryl sulfate, rhamnolipids, and N-acetylcysteine ability to eradicate mature biofilms and inhibit new biofilm formation of *Helicobacter pylori*, *E. coli*, *P. aeruginosa*, *S. aureus*, and *Streptococcus mutants*. The authors observed that sodium lauryl sulfate and rhamnolipids successfully inhibited the formation of those five bacterial biofilms in a dose-dependent manner even at concentrations below the minimal inhibitory concentrations. This suggests that their antibiofilm activities are unrelated to their antibacterial activities and that had already been observed by Quinn et al. [42] when comparing rhamnolipids antibiofilm activity to antibiotics [43].

These results have led to the hypothesis of using these biosurfactants on medical devices to prevent their related infections. Therefore, some papers have also investigated the potential of rhamnolipids inhibition of different strain biofilms on silicone rubber or medical grade silicone. For example, Rodrigues et al. [44] studied the ability of rhamnolipids to interfere in the adhesion of bacteria and yeasts

isolated from explanted voice prostheses onto silicone rubber. The authors concluded that the number of cells adhering onto silicone rubber treated with biosurfactant was reduced and that declines of 50% on the number of cells were attained for *S. epidermidis*, *Streptococcus salivarius*, *S. aureus* and *C. tropicalis*. Nevertheless, *C. albicans* and the bacterial strain *Rothia dentocariosa* showed a lower decrease in the number of attached cells after 4 h (20–28%) [44].

Studies on antibiofilm activity of rhamnolipids have also been realized on other medical devices such as catheters. Biofilm formation by *S. epidermidis* is a cause of infections related to peritoneal dialysis. Pihl et al. [45] used a peritoneal dialysis catheter flow-cell model in combination with confocal scanning laser microscopy and atomic force microscopy to study biofilm formation by *S. epidermidis* and observed a reduction in the covering of biofilm with exposure to the supernatant from two *P. aeruginosa* strains (i.e. rhamnolipids). The exposure to this supernatant originated a coverage of only 10% in biofilm when compared to untreated samples [45].

Additionally, when adsorbed to silicone elastomeric discs the rhamnolipids 89, produced by *P. aeruginosa* 89, were able to reduce *Staphylococcus* spp. biofilm formation, by 70 and 50% regarding biomass and 72 and 63% regarding cell metabolic activity (at 72 h) for *S. aureus* and *S. epidermidis*, respectively. SEM analysis also corroborated these results making R89 a promising antibiofilm coating for silicon catheters [46].

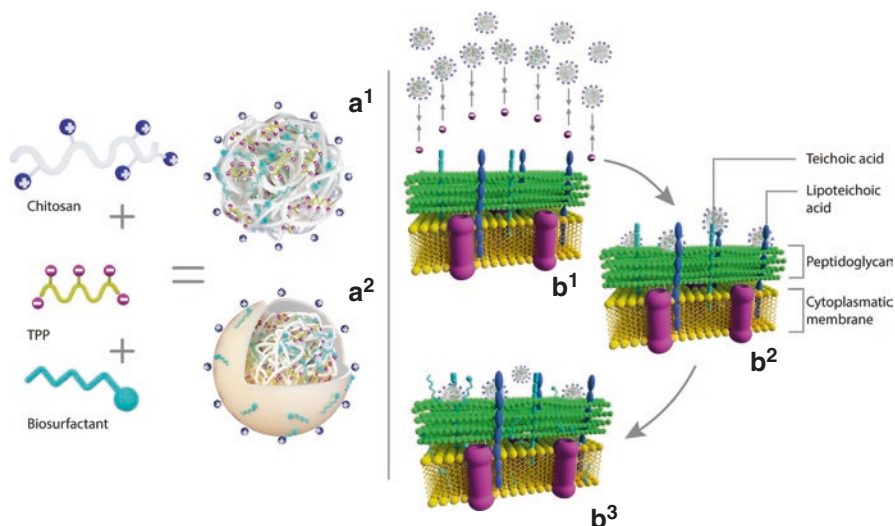
Recently, Bettencourt et al. [47] developed chitosan–rhamnolipid nanoparticles intended to fight *S. aureus* infections. The obtained particles showed an antimicrobial synergic effect between chitosan and rhamnolipids produced by *P. aeruginosa* when testing their antimicrobial activity towards *S. aureus*. Regarding antibiofilm activity of the produced particles a reduction of 99% on biofilm formation on medical grade silicone could be observed making these particles an interesting approach to prevent *S. aureus* related infections such as the medical devices-related (Fig. 4) [47].

## 4 Conclusion

Infections associated with urinary tract medical devices are a common health concern, in particularly, when associated to biofilm formation on their surfaces.

Among multiple strategies to fight those infections, biosurfactants as glycolipids can be a valuable tool for biofilm inhibition or disruption. In particularly, multiple *in vitro* studies concerning sophorolipids and rhamnolipids confirms the antimicrobial activity of those compounds.

Further, sophorolipids or rhamnolipids potential role to prevent biofilm associated infections, using different surfaces like medical grade silicone as example of



**Fig. 4** Illustration of rhamnolipids–chitosan particles (RLs–CSp) antimicrobial mechanism of action towards *S. aureus*. Particles may deliver rhamnolipids as encapsulated onto RLs–CSp. (**A1**) or/and adsorbed to its surface (**A2**). First, electrostatic attraction of RLs–CSp (negatively charged) to *S. aureus* membranes (positively charged) takes place (**B1**, **B2**). Later, RLs are released from the particles, enter into membranes leading to cell damage and death (**B3**). (Reproduced with permission [47] Copyright 2021, Elsevier)

common material used in catheters and stents fabrication, shows the capacity of those biosurfactants in reducing the adhesion and biofilm formation.

Finally, new trends in the delivery of these biosurfactants, namely by their inclusion in nanoparticulate systems paves the way for newer clinical applications.

Overall, sophorolipids and rhamnolipids due to their multiple antimicrobial/anti-adhesive effects might be an interesting approach to fight urinary tract medical devices associated infections.

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