BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, December 2018. Vol. **15**(4), p. 767-781

Rhamno Lipids Biosurfactants from *Pseudomonas aeruginosa* - A Review

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http://dx.doi.org/10.13005/bbra/2685

(Received: 21 September 2018; accepted: 27 November 2018)

Studies addressing for ecological compatible products have been increased along time, especially, on biosurfactant field. Biosurfactants are extracellular amphiphilic compound that are mainly produced by microorganisms and are classified into five main groups, including the glycolipids one. Rhamnolipids are included in the latter and are anionic biosurfactants produced predominantly by *Pseudomonas aeruginosa*being classified as mono- and di-rhamnolipids. In addition, their production may occur from different carbon sources, which may be obtained from renewable and low-cost residue. Therefore, it is possible to reduce the rhamnolipids production cost, since this has been the main bottleneck for replacing the chemical surfactants. In addition, to meeting a *bona fide*industrial application some limitations such as low productivity as well as recovery and/or purification that represent from 60 to 80% of total production cost should be improved. Therefore, this review covers different ways for producing rhamnolipids covering their application in many fields such as pharmaceutical, agricultural, petrochemical and so on; demonstrating the versatility of these biological compounds.

Keywords: rhamnolipid; synthesis; agro-industrial waste; application.

Surfactants are chemical compounds synthesized by petroleum derivatives and capable of reducing the surface tension between two immiscible phases due to their amphiphilicity. Structurally, a surfactant molecule is composed of a hydrophilic and a hydrophobic moiety[1,2]. The polar moiety can be formed by carbohydrates, amino acids, carboxylic acids, phosphates or alcohols, while the apolar portion consists of carbon chains[3]. This characteristic is essential in applications requiring emulsification, lubrication, foaming, solubilization of immiscible compounds or phase dispersion[4].

In contrast, biosurfactants are metabolites produced by bacteria, filamentous fungi or yeasts. These amphiphilic and extracellular compounds were discovered in the 1960s through the fermentation of hydrocarbons and have many advantages compared to chemical surfactants. In the last 10 years, the biosurfactants received a lot of attention due to their low toxicity, high selectivity and biodegradability, low critical micellar concentration (CMC) and stability in drastic conditions of pH, salinity and temperature[5–7].

Although biological surfactants have a wide range of structures, can be produced by

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different strains of microorganisms and water immiscible and miscible substrates, its low productivity and recovery hinders industrial scale production. Their upstream process costs can represent up to 30% of the total production cost. Meanwhile, recovery and purification steps amount between 60 and 80% of the total operating value, which explains the high values of marketable products based on biosurfactants (BS) and bioemulsifiers (BE). Thus, the use of renewable and low-cost substrates appears as an alternative to reducing these costs[8–10].

Biosurfactants are divided into five main groups: glycolipids, phospholipids, lipopeptides, fatty acids and polymeric biosurfactants[11]. Rhamnolipids (RLs) are one of the glycolipids, whose molecules are formed by a hydrophilic portion, containing one or two rhamnoses, and a lipophilic region, consisting of saturated or unsaturated fatty acids. In addition, depending on the amount of rhamnoses they can be classified into mono- and di-rhamnolipids[12].

RLs are produced by different strains of Pseudomonas e.g. *P. chlororaphis, P. plantarii*, *P. putida*, *P. fluorescens* and *P. aeruginosa*. The latter being the most used in the studies. In order to produce the RLs, the submerged fermentation is a mode of production extensively explored. However, solid-state fermentation has advantages such as lower energy expenditure during cultivation, less use of solvent for extraction and no need for agitation unit. In this mode, the nutrient source is a solid residue, so the choice of the substrate is a very relevant point, since it will have to contain all the nutrients the microorganism needs to express the biosurfactant[13,14].

The biosynthesis of RLs in *Pseudomonas aeruginosa* is controlled by environmental factors and the quorum sensing system (QS)[15]. This system is responsible for the regulation of approximately 10% of the *P. aeruginosa* genes. It coordinates several functions, including the formation of virulence agents, motility and production of exopolysaccharides. The QS also controls the synthesis of fundamental compounds for biofilms, such as rhamnolipids, lectins and siderophores[16].

Among the properties of RLs, they are able to emulsify oils, reduce water surface tension from 72 mN/m to approximately 25-30 mN/m, reduce the interfacial tension between compounds of different polarities, and decrease the CMC to values between 10 and 200 mg/L[17–19]. Due to these characteristics, the bio-product can be applied in agriculture and in the pharmaceutical, food, cosmetic and petrochemical industries. Studies have also shown that these compounds exhibit antimicrobial activities against Gram-positive and Gram-negative bacteria and fungi, and many of these micro-organisms are pathogenic[19–21].

Thus, this study aims to highlight important points in the production of rhamnolipids by *Pseudomonas aeruginosa*, emphasizing the use of renewable and low-cost substrates, production methods (submerged and solid state), as well as their main applications.

Fermentative process

The choice of the fermentative process is of great importance, given that the conditions employed directly influence the productivity of the target biomolecule[22]. The conditions of the applied fermentation process must be optimized and controlled so that the process can succeed and its increase of scale is favorable for the production of the biosurfactants, being economically feasible when compared to chemical surfactants[23].

Submerged Fermentation (SmF)

SmF is a fermentative process that uses a liquid fermentative medium, composed of soluble nutrients, where the microorganisms develop and release the biomolecules of interest[24].

For the most part, the production of biosurfactants is developed through this process. The volume of biosurfactants produced by SmF varies according to the type and the magnitude of the process, the reaction medium and the culture conditions involved[25].

Some difficulties have been found in pilot or large-scale reactors in the production processes of these molecules [25,26]. A great amount of foam is formed, when the biosurfactant are produced, as they are conducted with agitation and forced aeration, leading to the loss of biomass, nutrients and products contained in the foam that is expelled from the reactor, which decreases the production parameters or in extreme cases it makes the process unfeasible[27,28].

Solid-State Fermentation (SSF)

SSF is a process that simulates the natural habitat of microorganisms. It occurs in the absence or near absence of free water, so the substrate must

have sufficient moisture to maintain and grow the microorganism[29]. The substrates used in SSF are quite diverse, namely, wheat bran, lemon and orange peel[30], sugar cane bagasse and coffee husk[31], corn bran[25], among others.

The differences between this process and the SmF are in the restricted availability of water, which may stimulate the excretion of some specific metabolites that are not produced in a liquid medium[29].

This process presents several advantages, higher yields and volumetric productivity, lower operating costs, inexpensive culture medium (the use of agroindustrial waste as a substrate), greater oxygen distribution and, in general, lower energy demand[32,33].

Thus, SSF presents a viable alternative for the production of high added value metabolic products, among them are biologically active secondary metabolites (toxins, antibiotics), enzymes, organic acids, amino acids, vitamins, ethanol and biopesticides[29,31–34].

There are few papers in the literature addressing the production of biosurfactants by SSF, the only records found are related to the production of biosurfactants by bacteria or filamentous fungi[25,35,36]. SSF is a technique of simple application, especially in bench scale. In surfactant production, higher concentrations can be achieved, and the formation of foam is avoided as in SmF. However, there are obstacles to overcome, the increase of scale is hampered by heat and mass transfer in bioreactors because materials' heterogeneity. Thereby, this process should be further explored to improve the application and production of biosurfactants. The development and projection of bioreactors capable of operating under the conditions the closest to optimal is ideal to the strengthening of SSF[14,37,38].

Agroindustrialwaste

Researchers are increasingly interested in biosurfactants, since they present physicochemical and surfactant characteristics that allow them to be applied to several areas such as petroleum (recovery, emulsification and refining), cosmetic. They also can act as antimicrobial and biomedical agents, in bioremediation, as food additives, in cleaning products and others[39–41].

The successful implementation of biosurfactants in the industrial field is due to the efforts made by JeneilBiosurfactant Co. (Saukville, Wisconsin), which carried out a batch fermentation process of up to 20,000 gallons [41,42].

Interestingly, microorganisms are versatile to mediate the transformation of complex residues even under extreme conditions of pH, high salinity, pressure and temperature[43]. It is recognized that the nutritional composition and the environment exposed to the microorganism directly influence its growth and, indirectly, the synthesis and ratio of the type of synthesized RLs[39,44,45].

The use of biosurfactants from bioprocesses brings benefits to the environment and industrial process, since it is possible to reduce the cost of receiving the substrate, acquiring the agroindustrial residue (unexpensive and available in large quantities), and making use of sources of renewable carbon[42,44,46,47]. Among the various agroindustrial residues (effluents from the refining of soybean oil, sunflower oil and palm oil), coconut and cashew residues, which presented promising results for the production of rhamnolipids[44,48,49].

Other agroindustrial residues for the production of rhamnolipids targeting substrates of renewable and widely available origin are vegetable oils, sugars and glycerol. The use of glycerol is highlighted among these substrates, since it is highly consumed by yeasts and bacteria, and because of the excessive Brazilian production[39,46].

Looking for alternatives to reduce costs of production of rhamnolipids, some authors reported data using lignocellulosic and agricultural residues[50], residues from the dairy industry, molasses and starch residues[51], crude oil [52], soybean sludge, chicken and hydrogenated vegetable fat[53].

The use of biosurfactants in advanced oil recovery wells is an ancient technique discovered in the mid-1930s, but it has been improved and better understood in recent decades. This allowed the advances of the research in relation to the factors that favored the emulsification of the oil in the wells from the culture of the microorganisms. However, several difficulties prevent diffusion of biosurfactants, such as low yields, scale up for bioreactors, high production cost, among others[11].

Among those agroindustrial residues, the use of soybean oil (37 g / L) in the cultivation of *P. aeruginosa* E03-40 for the production of RL was promising when compared to the use of glycerol

(20 g / L). After optimization, the concentration of 42.1 g / L with an estimated yield of 47.3% was obtained under optimal conditions (10% dissolved oxygen and pH 5.7)[54].

Recent studies investigated the use of two or more agroindustrial residues for the production of biosurfactants based on RLs. A culture medium containing 5% animal fat and 2.5% corn steep liquor was used in the production of biosurfactants by *Candida lipolytica*, obtaining satisfactory results in the treatment of sites contaminated by heavy metals and petroleum derivatives[9]. Among the emerging biotechnologies with application in the petroleum industry, there are those that make use of biosurfactants with the purpose of coordinating, reducing and treating the effluents generated from the oil processing[55].

In light of what has been discussed previously, Table 1 shows the influence of different low-cost substrates and different strains of *Pseudomonas aeruginosa* on RL production. From this, it can be seen that most studies use SmF in the production of this biosurfactant. Thus, it is interesting that future works may approach SSF as an alternative to the production of RLs.

Rhamnolipidbio synthesis

Microorganisms and pathways

Pseudomonas aeruginosa is a pathogenic Gram-negative bacterium responsible for producing virulence agents, toxins, alginates and lipopolysaccharides (LPS)[63]. The biosynthesis of RLs by *P. aeruginosa* occurs by means of three sequential enzymatic reactions, giving rise to mono-rhamnolipids or di-rhamnolipids, as shown in Figure 1.

In general, microorganisms consume hydrophilic substrates in the synthesis of the polar portion of the biosurfactant molecule, while the hydrophobic substrates are used exclusively in the hydrocarbon moiety[22]. The production of RLs occurs by two metabolic pathways, which are responsible for forming the portions of that molecule. The hydrophobic region is formed by a long chain fatty acid, a hydroxy acid or an á-alkyl-â-hydroxy fatty acid, on the other hand the hydrophilic part may be a carbohydrate, a carboxylic acid, an alcohol or an amino acid[64].

Hydrophilic substrates such as glucose or glycerol are degraded to form intermediates from glycolytic pathways, such as glucose 6-phosphate, which is one of the main precursors of carbohydrates present in the hydrophilic portion of biosurfactants. For the production of lipids, glucose is oxidized to pyruvate by means of glycolysis, and pyruvate is then converted to acetyl-CoA, which, together with oxaloacetate, produces malonyl-CoA and then fatty acid, one of the precursors for the synthesis of lipids[22].

Figure 1 shows that the fatty acid is catalyzed by the enzyme Rh1G, responsible for diverting fatty acid synthesis intermediates into the biosynthetic pathway of RLs in *P. aeruginosa*. However, more recent studies have indicated that there is no enzyme above the rhamnosyltransferase (RhlA)[65]. This finding was based on the biochemical properties of the purified RhlA protein and its products when expressed heterologously in an *E. coli* host[66]. Thus, RhlA catalyzes the formation of an ester bond between the fatty acid intermediates, 3-hydroxyalkyl-ACP, forming 3- (3-hydroxyalkanoyloxy) alkanoate (HAA), the lipid component of the RLs[66,67]. Then RhlB catalyzes the formation of mono-rhamnolipids using trimethophosphate (dTDP) -L-rhamnose and HAA as precursors[68]. For the synthesis of the di-rhamnolipids, a further rhamnosil (Rh1C) group is added to the structure using another molecule of (dTDP) -L-rhamnose, by an á-1,2-glycosidic bond[63].

Rhamnose is found in several strains of *Pseudomonas spp.* as a component of LPS present in the cell wall of several Gram-negative bacteria. It is also present in exopolysaccharides (EPS)[63,65]. The formation of the hydrophilic portion of the RL molecule is initiated by the conversion of glucose-6-phosphate into glucose-1-phosphate through the action of the enzyme phosphoglyceromutase (AlgC). Followed by the action of rmlBDAC genes producing dTDP-L-rhamnose that will be precursor to the synthesis of RLs, as shown in Figure 1.

Regulation by quorum sensing (QS)

The QS corresponds to a bacterial signaling medium that is based on the production, during the cellular growth phase, of mediating molecules called auto-inducers. When a concentration limit is reached, these autoinducers interact with a transcriptional regulator, allowing the specific expression of a group of genes. One of the most studied intraspecies autoinducers is the N-acyl homoserine lactones (AHL) released by Gram-

negative bacteria. There are more than 70 species of Gram-negative bacteria known to use AHL as a signaling molecule[69].

Pseudomonas aeruginosa are able to grow within the host cells without damaging them until their population density reaches a sufficiently high value, necessary for biofilm formation. From this point, the microorganisms become aggressive to the host's immune system causing diseases[16]. The quantum detection system of *P. aeruginosa* regulates the production of several essential compounds in the formation of biofilms and acts on the release of extracellular DNA (eDNA). This bacterium has three known systems for the detection of quorum sensing, LasI / LasR, RhI / RhRR and *Pseudomonas* quinolone signaling system (PQS)[70–72].

In QS the main systems of regulation are las and rhl. Las and RhlI, catalytic enzymes in the synthesis process, produce the homoserine lactones 3OC12-HSL and C4-HSL signaling molecules, which bind and modulate their corresponding transcriptional regulators LasR and RhRR respectively. The system also requires the RsaL protein, and lasR, which negatively regulates the expression of both genes and indirectly affects the biosynthesis of RLs[73,74].

A third signaling system based on 2-heptyl-3-hydroxy-4-quinolone, designated the signal *Pseudomonas* quinolone (PQS), was shown to be part of the quorum sensing regulatory network in *P. aeruginosa*[75]. The biosynthesis of PQS is promoted by the pqsABCD gene products and binds to the LysR-type regulator PqsR (or MvfR). The expression of PqsR is directed by las and repressed by the rhl QS system, in a typically complex regulatory network. The production of PQS has a profile similar to that of RLs because it reaches its maximum in the stationary phase. Mutant genes of pqsR and pqsE decreased the levels of RLs synthesis, even when supplied with exogenous C4-HSL, indicating a direct relation of PqsR and PQS in the biosynthesis of RLs[76,77].

Understanding the biosynthesis of RLs allows us to have conditions to solve everyday problems. For example, due to the high resistance of bacteria against most of the antibiotics on the market, it is necessary to develop techniques that inhibit this resistance. Therefore, recently, some studies have demonstrated anti-QS properties of natural herbal medicinal substances. Inhibition of the QS molecules requires the specific screening of several molecules with different chemical natures[69].

Rhamnolipid isoforms

The structural variety of the isoforms of RLs is defined by the presence of rhamnose and / or fatty acids as their chain length may vary from C8 to C14. There are 4 types of isoforms that can be classified as mono (RL1 and RL3) or di-rhamnolipid (RL2 and RL4), as can be seen in Figure 2[12,78].

The properties presented by the RLs vary according to the composition of the homologues present in the medium and their distribution depends on the culture conditions (composition of the substrates, pH, and temperature), strain used and culture medium[80].

Some studies show the formation of different isoforms. For example, when producing RLs from vegetable oils it was found that the mixture had di-rhamnolipid (Rha-Rha-C10-C10) and mono-rhamnolipid (Rha-C10-C10)[58]. In another investigation, the authors proved that the mixture of RLs synthesized by *Pseudomonas aeruginosa* MN1 and glycerol was composed of different homologues (Rha-C10, Rha-C8-C10, Rha-C10-C8, Rha-C10-C12: 1, Rha C10-C10, Rha-C10-C10, Rha-C10-C10, Rha-C10-C10, Rha-Rha-C8-C10, Rha-Rha-C10-C8, Rha-Rha-C8-C12: 1, Rha-Rha-C10-C10 , Rha-Rha-C10-C12: 1, Rha-Rha-C12: 1-C10, Rha-Rha-C10 -C12, Rha-Rha-C12 -C10, Rha-Rha-C8 -C8) 35% were mono-rhamnolipids. In addition, the homologue greater quantity had better CMC and surface tension results when compared to the isolated di-rhamnolipid and the mixture of the two homologues[80].

Numerous studies have shown that different strains of *Pseudomonas aeruginosa* when combined with several substrates have fairly variable amounts of homologues[81–85].

Biosurfactant application

Although the biosurfactants have some superior characteristics in relation to the chemical surfactants, they still have very limited applications, mainly because of the cost of production[11]. However, there are potential applications where the biological origin promises better biocompatibility and good microbial degradability[86]. Therefore, as the cost of production becomes lower, its application should become more generalized,

not surprisingly a large number of laboratory researches for the most diverse areas of application. The following topics explore the various uses of RLs proposed in the scientific literature.

Bioremediation

Bioremediation can be defined as a process whereby organic wastes are biologically removed or degraded for cleaning of oil spills and treatment of terrestrial and aquatic environments contaminated with xenobiotics[50]. These processes appear as an innovative technology in the removal of compounds derived from petroleum, among other pollutants, against chemical surfactants that have high toxicity and non-biodegradable properties[87].

It was shown that by adding RLs to pure P. aeruginosa cultures there was an increase in biodegradation of hexadecane, octadecane, n-paraffins and phenanthrene, as well as degradation in soil systems in the presence of hexadecane, tetradecane, pristine, creosote or hydrocarbon mixtures[88,89].

Table 1. Production of rhamnolipid by low-cost substrates

Strain	Fermentation	Substrates	Maximum yield (g/L)	Ref.
P. aeruginosa PAO1	Submerged (250 mL[1])	Palm fatty acid distillate(PFDA)	0,43	[48]
*P. aeruginosa*DR1	Submerged (250 mL)	Mango kernel	1,80	[56]
P. aeruginosa #112	Submerged (500 mL)	Corn steep liquor (CSL) + molasses	3,20	[19]
*P. aeruginosa*LBI	Submerged (2 L)	Soapstock	15,9	[49]
P. aeruginosa PAO1	Submerged (1 L)	Olive millwaste (OMW)	0,19	[57]
P. aeruginosa UFPEDA 614	Solid-state (250 mL)	Sugarcane bagasse + cornbran	45,0	[25]
*P. aeruginosa*LBI	Submerged (125 mL)	Braziliannutoil	9,90	[58]
P. aeruginosa DS10-129	Submerged (250 mL)	SoybeanOil	4,31	[59]
P. aeruginosa UCP092	Submerged (500 mL)	Glycerol	3,50	[60]
P. aeruginosa ATCC 10145	Submerged (250 mL)	Sugarcane bagasse	9,10	[61]
*P. aeruginosa*LBI 2A1	Submerged (1 L)	Crudeglycerol	2,55	[62]
P. aeruginosa #112	Submerged (5 L)	CSL + molasses + OMW	5,10	[4]

[1]Bioreactor volume.

Table 2. Rhamnolipid application

Strain	Carbon Source	Application	References
Pseudomonas aeruginosa AP 029/GLVIIA	Glucose	Enzymatichydrolysis	[108]
*Pseudomonas aeruginosa*L2-1	Casssava wastewater	Crude oil removal	[109]
Pseudomonas aeruginosa 1501	Water-soluble diesel	Antimicrobial agent	[110]
Pseudomonas aeruginosa PA1	Glycerol	Nano/micropheresformulations	[111]

Although there are some studies that report the positive effects on the biodegradation of petroleum hydrocarbons in the presence of biosurfactant, there are reports that both in pure addition as in soil systems there was an inhibition of biodegradation by the addition of RLs. This inhibition can occur due to the preference of RLs as carbon source for bacterial metabolism[90].

Some previous research suggested that increased degradation by the presence of RLs may occur by increasing the solubility of the hydrocarbon then increasing bioavailability for

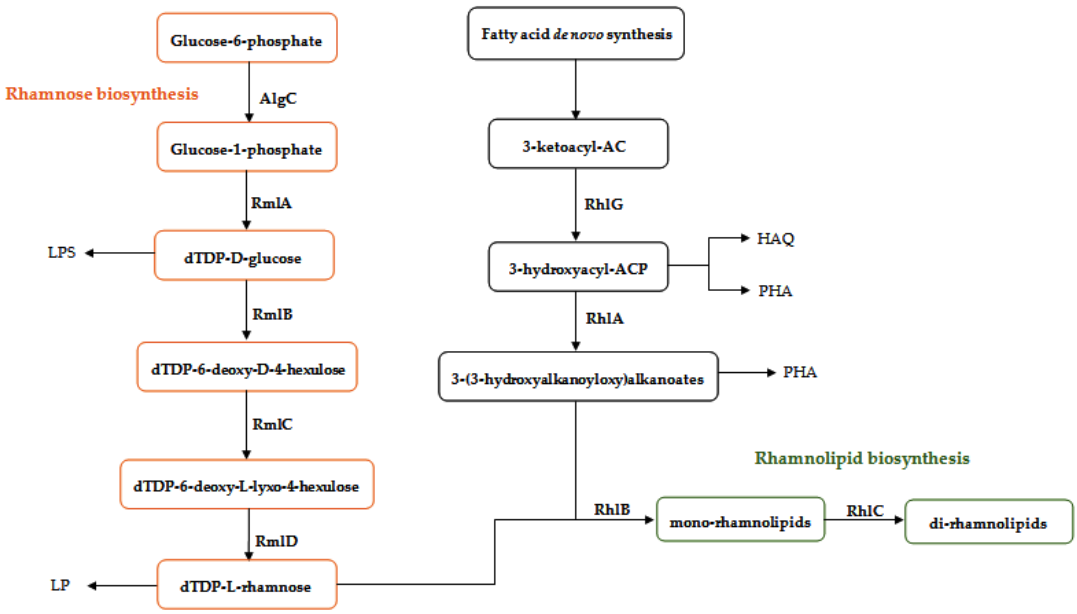

Fig. 1. Rhamnolipid production pathways[45]

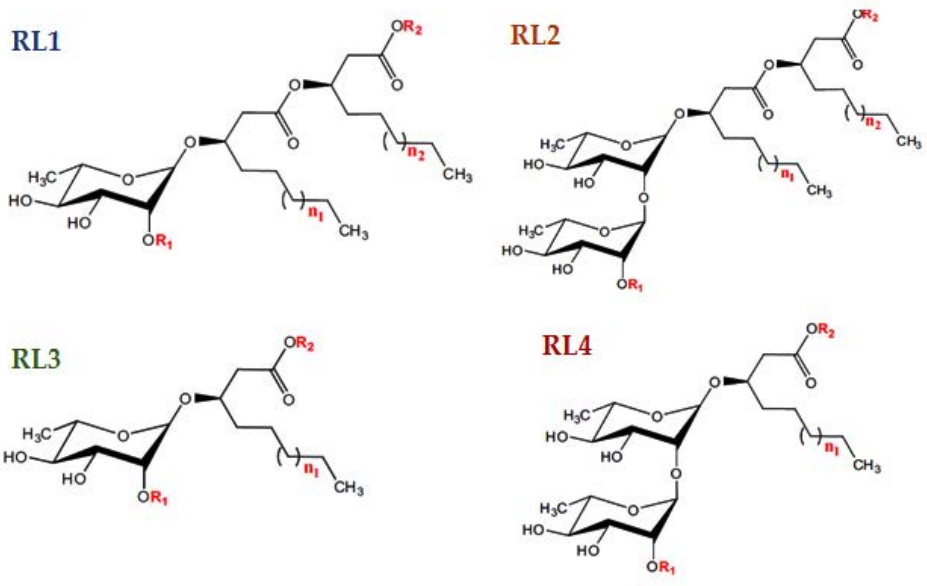

Fig. 2. Chemical structure of different isoforms.RL1 (mono-rhamno-di-lipidic),RL2 (di-rhamno-di-lipidic),RL3 (mono-rhamno-mono-lipidic), RL4 (di-rhamno-mono-lipidic)[78,79]

cell degradation or interaction with the degrading cell, causing the cell surface to become more hydrophobic and interacting more easily with the hydrophobic substrates[91]. This second mechanism becomes more economically and environmentally interesting, since a large amount of RLs is required to increase the solubility of the hydrocarbon, whereas to alter the cell surface the required amount is smaller. Indeed, as RLs are the preferred source of carbon, higher concentrations would decrease the degradation of the hydrocarbons.

The decontamination of areas contaminated with heavy metals is a relatively few explored field. The presence of these may inhibit degradation of organic compounds. In a research carried out on systems contaminated with organic compounds, cadmium and naphthalene in the presence of RLs, the cadmium toxicity reduced, which led to the increase of the biodegradation of naphthalene[92]. Another study observed a decrease in the inhibition of phenanthrene mineralization in the presence of cadmium by pulsed addition of RLs[90]. There are reports of higher copper and nickel removal rates from sediments by adding RLs to a 1% NaOH solution[93].

Food industry

RLs present some properties, such as formulation and stabilization of emulsions, as well as anti-adherence and antimicrobial activity, which makes them interesting for the food industry, particularly in increasing food shelf-life without concerning consumer, eliminating the need for addition of synthetic preservatives. RLs can be used directly to avoid contamination of food, as a food additive, or indirectly, as a detergent formulation to clean surfaces that come into contact with food[94].

Other functions performed in the food industry by RLs is acting to improve the stability of the dough, texture, volume and preservation of bakery products obtained by the addition of surfactants[94]. It is also possible to use them to improve the properties of frozen butter cream, croissants and confectionery[95]. They can also serve as a source of L-rhamnose for the synthesis of food flavors, which has already been successfully obtained by the hydrolysis of surfactants produced by *P. aeruginosa*[96].

In addition to their obvious role as surface and interfacial tension reducing agent, RLs may have other functions in foods aiding in the general blending of ingredients and may also retard the growth of fungi and some bacteria[97]. It has also been shown that they can be successfully exploited to break down biofilms from individual and mixed cultures of foodborne pathogens[98].

Agriculture

RLs influence nonspecific immunity in plants and induce resistance and are considered potential alternatives to reduce or replace pesticides in agriculture[99]. Some studies on the effect of RLs on plants and pests showed that they are capable of stimulating defense genes in tobacco and are potent protectors in monocotyledonous plants against biotrophic fungi Other studies proved that RLs could improve wettability of leaf surfaces[100]. Antifitoviral effects were observed for virus / host combinations of tobacco mosaic virus / *Nicotianaglutinosa* and potato X virus / *Nicotiana tabacum*[101].

Pure mono and di-rhamnolipids were tested in three species representatives of the zoosporicphytopathogen genera, namely, *Pythiumaphanidermatum*, *Phytophtoracapsici* and *Plasmoparalactucaeradicis*. They showed the ability to control certain pathogens. At concentrations of 5 to 30 mg L-1, both RLs caused a cessation of motility and lysis of the entire zoospora population within 1 min[102]. This observation led to the development of a biofungicide formulation containing RLs, used to avoid the contamination of crops by pathogenic fungi.

These molecules are also useful in the removal of polyaromatic hydrocarbons and pentachlorophenol from the soil and may facilitate the uptake of nutrients and fertilizers through the roots[103]. Due to their anionic nature, they are able to remove toxic metals from agriculture. However, the success in increasing the recovery of heavy metals will also depend on the amount of RLs present in the aqueous phase[104].

Agricultural lands containing petroleum hydrocarbons that are important contaminants can be remedied by an introduction of RLs in the soil due to their high solubilization and increase of the bioavailability properties in some inaccessible compounds[105]. Other applications of RLs found in the literature in the field involve eradication of the disease caused by *P. capsici* in pepper plants (*Capsicum annuum*) and control of a serious pathogen for certain tomato crops. In addition, it

has been suggested the application in the treatment and prevention of overwatering during irrigation due to its wettability properties facilitating the breaking of impenetrable barriers to the water and allowing the water to easily reach the soil spreading more evenly[99].

Pharmaceutical and cosmetic industry

Several cosmetic creams exhibit, in their formula, essential oils from plants due to their occlusive, emollient and moisturizing properties in the skin. Many of these oil-based substances requires the presence of a stabilizing agent as emulsifiers and / or surfactants in order to obtain good emulsions. Other functions of cosmetic surfactants are detergency, wetting, solubilization, dispersion and foaming effects[106]. Natural surfactants besides performing these functions have benefits such as biodegradability, low toxicity and acceptability, making them in high demand.

The application of RLs in cosmetics and pharmaceuticals as emulsifiers, penetrating agents and drug delivery systems is still an emerging area of research. Surfactants as emulsifiers, foaming agents, solubilizers, wetting agents, cleaning agents, antimicrobial agents and enzymatic mediators in various dosage forms such as creams, lotions, liquids, pastes, powders, sticks, gels, films and sprays can be replaced by biosurfactants. Patents were granted for cosmetics containing RLs for anti-wrinkle and anti-aging products[98], which were released as commercial cosmetics for skin care because of their skin compatibility and extremely low skin irritation[97].

Briefly, some applications of RLs produced by different strains of *Pseudomonas aeruginosa* are presented in Table 2.

CONCLUSIONS

The synthesis of rhamnolipids occurs mainly by submerged fermentation, however, solid-state fermentation presents advantages according to some studies. In addition, the use of renewable and low-cost substrates, such as agroindustrial waste, make the production process more interesting, economically. Another point corresponding to the diversity of chemical structures formed when working with different substrates and strains of Pseudomonas aeruginosa, the four existing isoforms constitute numerous homologs of rhamnolipids that vary according to the amount of rhamnose and extension of the carbonic chain. Finally, researches on applications of this bioproduct makes the study even more interesting, since it is possible to analyze its future commercial outcomes and, mainly, to substitute chemical surfactants by biological eco-friendly surfactants.

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