

Mini-review: Synthetic methods for the production of cationic sugar-based surfactants



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ABSTRACT

Surfactants are ubiquitously used and are currently indispensable in our daily life. However, the increased surfactant production has given rise to some environmental and health concerns making it imperative to look for new sustainable and viable alternatives. Sugar based surfactants, sourced from renewable sources are an excellent candidate to solve this problem. This class of surfactants has been developed in the last years, however, of these, cationic sugar-based surfactants have been the least studied which is unfortunate as they have excellent properties when compared to the other type of surfactants, such as antimicrobial activity, and high environmental and dermatological biocompatibility. These properties making them useful not only in disinfectant products but other applications as well such as for gene delivery. Therefore, the develop new methods to produce these compounds, preferably with sustainable synthetic procedures is of utmost importance. This is the first review on this topic and compiles and describes the available synthetic methods to produced cationic sugar-based surfactants with one single chain and geminis published so far.

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Contents

1. Introduction	1
2. Sugar-based surfactants	2
2.1. Cationic sugar-based surfactants	2
3. Synthetic methods for the production of cationic sugar-based surfactants	3
3.1. Cationic sugar-based surfactants with single chain	3
3.2. Cationic sugar-based gemini	7
4. Conclusion	8
Declaration of Competing Interest	8
References	8

1. Introduction

Surfactants are used globally, being indispensable molecules in life. Their importance in our daily life is reflected in the increased production of these compounds which has been growing since the

80 s. In 2014 the production of surfactants hit 16 million tons and it is expected to reach 24 million tons in 2022 [1]. This increase is directly related to their wide applicability in products such as cleaning supplies, personal hygiene products, cosmetics, and pharmaceutical products, to name a few. As key ingredients in the formulation of soaps and detergents, their demand has suffered an accentuated rise in the past months due to the COVID-19 pandemic outbreak and the subsequent health measures recommended by the World Health Organization adopted globally. The choice of surfactants as a universal ingredient in these products is due to their cleaning, dispersing, foaming and emulsifying properties [2].

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Surfactants are amphiphilic molecules composed of a polar headgroup and a nonpolar chain. Due to this constitution, the head is hydrophilic, and the chain is hydrophobic, which gives the surfactants the ability to auto aggregate in aqueous solution and form different structures such as spherical, cylindrical, and inverted micelles, hexagonal, and cubic phases, vesicles and bilayers [3]. The surfactant self-assembly can be influenced by many factors such as their structure and concentration, salt concentration (in the case of ionic surfactants), temperature and others [4]. Micelles are the smaller aggregates and are formed when very low concentrations of surfactants are present in water. The concentration at which micelles start to form is designated critical micelle concentration (CMC) and it is the most important property of a surfactant [5].

Surfactants can be characterized by the charge of their headgroup: anionic if the headgroup has a negative charge, cationic if the head has a positive charge, zwitterionic if the polar head has both charges (one negative and one positive), and nonionic if the headgroup has no charge at all. The hydrophobic part of a surfactant is a long hydrocarbon chain with a number of carbon atoms that can range from 8 to 22 being either branched or linear [5].

Besides being characterized by the charge of the molecule's headgroup, surfactants can also be classified as natural or synthetic, depending on their production method. As the name indicates, natural surfactants derive directly from natural sources. The strict definition for them implies that they can be obtained by separation, extraction, precipitation or distillation, but no organic synthesis should be involved in any step. An example of a natural surfactant is lecithin which can be sourced from soybean. The term has however grown a broader sense and surfactants that are synthesized from natural raw materials have also been designated by natural by some authors and users [6].

Biosurfactants in turn are natural surfactants that have a microbial origin [7–10]. Both strictly natural surfactants and biosurfactants, or truly natural surfactants, are however, hard to obtain easily with a great yield, with their production turning out to be slow and expensive, making their commercialization in large-scale difficult. Therefore, due to the ease of manufacture and the low cost implied, synthetic surfactants have been the answer to satisfy market demands. Synthetic surfactants can be produced by chemical [11,12], enzymatic [13–15] or chemical-enzymatic route [16,17]. They can be subclassified by the origin of the raw material and therefore synthetic surfactants can be of nonrenewable or renewable source. The increased interest for environmentally friendly solutions makes the renewable surfactants class especially compelling. Sugar-based surfactants are an example of this type of surfactants and are the focus of this review [18,19].

2. Sugar-based surfactants

The production of sugar-based surfactants has been increasing in the last years due to their properties such as high biodegradability, low toxicity and high environmental and dermatological compatibility [20–23]. Moreover, this novel class is more advantageous considering that they are sourced from natural and renewable raw materials. The hydrophilic part of the sugar-based surfactant contains a sugar molecule and the hydrophobic part is usually a fatty acid [18].

Concerning the synthesis and availability of sugar-based surfactants while both nonionic and anionic sugar-based surfactants seem to be more evolved, the cationic ones are still an underdeveloped area of this renewable class of surfactants. In fact, many classes of nonionic sugar-based surfactants are already being commercialized like alkyl polyglycosides (APG), sucrose esters and sorbitan esters [18,22,24–27]. Their synthesis has been described by

chemical and enzymatic routes [28]. While the chemical route is nonselective yielding several by-products [29], the enzymatic route is more specific and allows to obtain monosubstituted sucrose esters or ethers [18,30,31]. Regarding anionic sugar-based surfactants their synthesis also seems to be sorted out - they can be produced through the incorporation of different functional groups like sulfonate, carboxylate and phosphate, in nonionic sugar-based surfactants. The synthetic route for these has been described with two or more steps [18,32–36]. The chemical route of cationic sugar-based surfactants occurs frequently in two or more steps, equally to the anionic surfactants. In general, the route begins with the substitution of the sugar's hydroxyl group by a good leaving group like a halide and then the intermediate compound reacts with an amine, usually a tertiary amine, by nucleophilic substitution. Regarding these cationic surfactants, although their synthesis can be accomplished, these synthetic methods can still have many steps and resort to the use of toxic reagents and solvents, leaving room for improvement [18,37–40]. The focus of this review are however cationic sugar-based surfactants owing to the fact of their additional interesting properties that are currently very sought for, such as their antimicrobial properties which they share with their petrol-based counterparts but unlike the later, the use of these renewable-based surfactants poses a greater advantage for the environment. For this reason, cationic sugar-based surfactants have been more intensively developed in the last years [28,41].

2.1. Cationic sugar-based surfactants

Cationic surfactants constitute a small class of surfactants, but their use is widespread in several products such as shampoos, softener (fabric and hair), emulsifiers and dispersant auxiliaries. Cationic quaternary surfactants have the ability to disrupt the microorganisms' cell membranes, thus presenting antimicrobial activity, being quite popular in disinfectant formulations [5].

Since cationic sugar-based surfactants are constituted by sugar fatty amines they can be protonated in an acidic medium (i. e. tertiary amines) (Fig. 1a) or acquire permanent charge (i. e. quaternary amines) (Fig. 1b). Moreover, cationic sugar-based surfactants can also be esterquats (Fig. 1c). These surfactants are more biodegradable than sugar amines because esterquats have an ester bond allowing it to degrade more easily than their counterparts, due to the ready enzymatic hydrolysis of the ester group [28,42]. Furthermore, cationic sugar-based surfactants demonstrate promising properties in gene delivery systems [43].

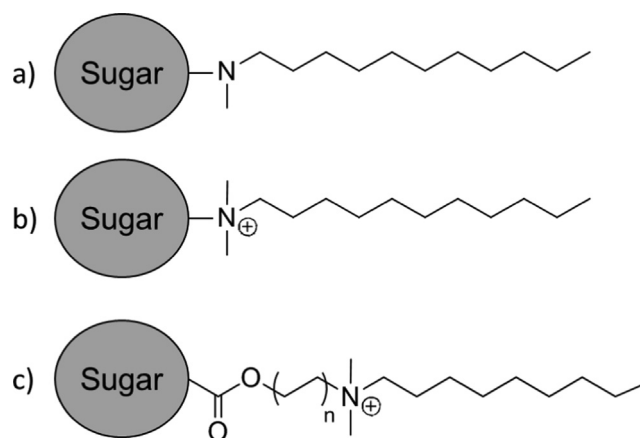
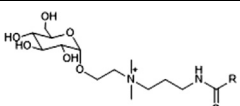
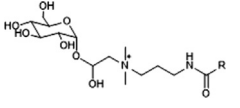
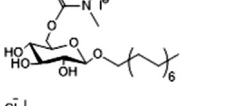
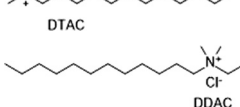
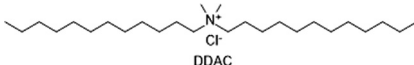


Fig. 1. Structural representation of cationic sugar-based surfactants: (a) sugar-based tertiary amine; (b) sugar-based quaternary amine and (c) sugar-based esterquats.

Table 1
Values of biodegradability of cationic sugar-based surfactants and common cationic surfactants.

Compound	Test	Time (days)	Biodegradability (%)	Reference
	Closed bottle	28	89	[48]
	Closed bottle	28	93	[48]
	Closed bottle	28	86	[49]
	MITI	10	59	[50]
	MITI	10	0	[50]

Usually, when dilute solutions of cationic and anionic petrol-based surfactants are mixed together in aqueous solutions, associative phase separation occurs. According to Gant et al. [38] this phase separation did not happen with the sugar-based surfactants they tested but no explanation was given for this effect. Further studies are needed to understand if this is a trend with this type of surfactants.

Additionally, these cationic surfactants show lower aquatic and dermatological toxicity than most surfactants [38,43,44]. In literature, the most documented cationic sugar-based surfactants have a glucose or glucose-based hydrophilic group [18,37,43–46]. The introduction of a glucose moiety in cationic surfactants influences positively their bacteriostatic activity, and at the same time it turns the surfactant more biodegradable (Table 1) [46]. As stated before, these sugar-based surfactants show more dermatological biocompatibility than common cationic surfactants [37] but this property can still be enhanced with the incorporation of an amide bond. This bond is similar to the peptide bond of amino acids and can be easily hydrolyzed enzymatically [44,47]. Also, compared to conventional cationic surfactants cationic sugar-based surfactants have improved interfacial properties, lower CMC values, and a greater ability to reduce superficial free energy [45–47]. Nonetheless, their synthesis process must be clearly described and optimized if a greener future with the industrial production of these compounds instead of petrol-based ones is aimed.

3. Synthetic methods for the production of cationic sugar-based surfactants

Nonionic sugar-based surfactants are aimed to be produced according to the principles of green chemistry. Raw materials like sugar, fatty acids and fatty alcohols are available from renewable sources, providing a greener and low-cost source. The synthetic process is quite simple, and atomic economy is observed once the reagents are incorporated in the final product.

The synthesis of cationic sugar-based surfactants is sparsely described in the literature. The synthetic methods used are frequently more complex than the ones currently used at the industrial scale having two or more steps. The commitment to a fully green process has also not yet been fulfilled as these methods still rely on toxic reagents and solvents, and finally, another challenge

to overcome are the low yields attained with some processes [37,38,51–53]

The synthesis of cationic sugar-based surfactants has been developing since the 40's with the reaction of glucose with amines [54]. Currently, synthetic methods to produce cationic single chain sugar-based surfactants and cationic sugar-based gemini are described in the literature [37–39,45–49,51–53,55–62]. In the following sections the synthesis of these surfactants will be discussed in detail with the respective yields presented for each reaction pathway after purification.

3.1. Cationic sugar-based surfactants with single chain

As the name suggests, single chain surfactants are constituted by a single hydrocarbon chain which can be branched or linear. Most cationic sugar-based surfactants bear a glucose molecule as their hydrophilic group [38,39,49,60], however, surfactants with other sugar molecules in their headgroup have also been described including glucose- δ -lactone [47,61], lactobionic acid [61] and lactose [60].

As stated previously, the production of cationic sugar-based surfactants involves two or more steps. One step consists of an amidation between the sugar molecule and a diamine. Afterwards, the alkylation of the previous intermediate with *n*-alkyl bromide, of different lengths can take place. Zhi et al. used this method to produce glucose- δ -lactone and lactobionic acid-based surfactants (Table 2, entry 7 and 8). The authors reported a two-step sequence initiated by the reaction glucose- δ -lactone or lactobionic acid with *N,N*-dimethyl-1,3-propanediamine in methanol (reflux for 8 h). After isolation, the product reacted with *n*-alkyl bromides (BrC₁₀H₂₁, BrC₁₂H₂₅ and BrC₁₄H₂₉) in ethanol, at reflux for 20 h. The surfactants were obtained in 80 and 85% yield, for glucose- δ -lactone-based surfactants, with C₁₀H₂₁ and C₁₂H₂₅, respectively. For lactobionic acid-based surfactants with C₁₀H₂₁, C₁₂H₂₅ and C₁₄H₂₉, yields of 64, 61 and 56%, respectively [61]. Aiming to increase the diversity of this class of surfactants, Zhi et al. studied the effect of the structure on the interfacial activity of cationic sugar-based surfactants, through the introduction of a hydroxyethyl group (Table 2, entry 6). Thus, using the same method, the authors produce a new type of glucose- δ -lactone-based surfactants, with yields greater than 80% [47]. The chemical routes described by Zhi et al. to produce glucose- δ -lactone and lactobionic acid-based surfactants, are represented in Fig. 2.

Table 2
Summary of the reaction conditions for the different chemical routes used for the synthesis of cationic sugar-based surfactants.

#	Substrate	Reaction conditions					CMC (mM)	γ (mN/m)	Ref.
		Reagent	Solvent	T (°C)	t (h)	(%)			
1	Glucose	i) K ₂ CO ₃ ; 2-Chloroacetyl chloride ii) Tertiary amine (n = 12 e 16)	CCl ₃ H	r. t.	3	–	C ₁₂ – 0.095	C ₁₂ – 24.5	[38]
2	Glucose	i) AcONa; acetic anhydride	n-propyl alcohol:water (1:2)	85	5	72/66	C ₁₆ – 0.079	C ₁₆ – 22.9	[39]
		ii) Bromoethanol; BF ₃	–	100	2	86	C ₈ – 16	C ₈ – 24.8	
		iii) Alkylated imidazole	CCl ₂ H ₂	r. t.	3	55	C ₁₂ – 1.5	C ₁₂ – 25.5	
		iv) NaOH	Xylene	125	1	95	C ₁₆ – 0.31	C ₁₆ – 39.8	
3	Lactose	i) Alkylamine (n = 12 e 14)	MeOH	r. t.	overnight	95	C ₁₂ – 3.01	C ₁₂ – 29.5	[46]
		ii) 1,3-propanesultone	Propan-3-ol	r. t.	24	90–92	C ₁₄ – 0.4	C ₁₄ – 27.6	
		iii) HCl	MeOH	–	–	94			
4	D-(+)-glucose- δ -lactone	i) N-Methyl-N-(2-hydroxyethyl)-1; 3-Propanediamine	MeOH	reflux	8	92	C ₁₀ – 12.62	C ₁₀ – 25.70	[47]
		ii) n-Alkylamine bromide (n = 12 e 14)	MeOH	reflux	20	87/89	C ₁₂ – 4.89	C ₁₂ – 27.42	
5	Glucose	i) AcONa; acetic anhydride	–	100	2	86	1.37x10 ⁻²	35.0	[49]
		ii) HBr, acetic acid	CCl ₂ H ₂	r. t.	–	91			
		iii) Tetradecanol; Ag ₂ CO ₃ ; I ₂	CCl ₂ H ₂	r. t.	overnight	43			
		iv) CH ₃ ONa	MeOH	r. t.	–	73			
		v) a) Glycine betaine methyl ester; SDS; NaHCO ₃ b) Glycine betaine methyl ester; NaHCO ₃	a) Water b) DMF	a) 70 b) 110	a) 4 b) 5	a) 56 b) 32			
6	Glucose	i) N-dodecylamine	MeOH	45	4	65	0.5	30.0	[60]
		ii) Bromoethane	EtOH	55	12	35			
7	D-(+)-glucose- δ -lactone	i) N,N-dimethyl-1,3-propanediamine	MeOH	reflux	8	91	C ₁₀ – 12.62	C ₁₂ – 30.26	[61]
		ii) Alkyl bromide (n = 12 e 14)	EtOH	reflux	20	83/80	C ₁₂ – 4.89	C ₁₄ – 28.36	
8	Lactobionic acid	i) N,N-dimethyl-1,3-propanediamine	MeOH	reflux	8	88	C ₁₀ – 12.62	C ₁₀ – 25.70	[61]
		ii) Alkyl bromide (n = 10, 12 e 14)	EtOH	reflux	20	64/61/56	C ₁₂ – 4.89 C ₁₄ – 1.83	C ₁₂ – 27.42 C ₁₄ – 25.70	

CMC – Critical micellar concentration; γ – superficial tension on CMC; r. t. – room temperature.

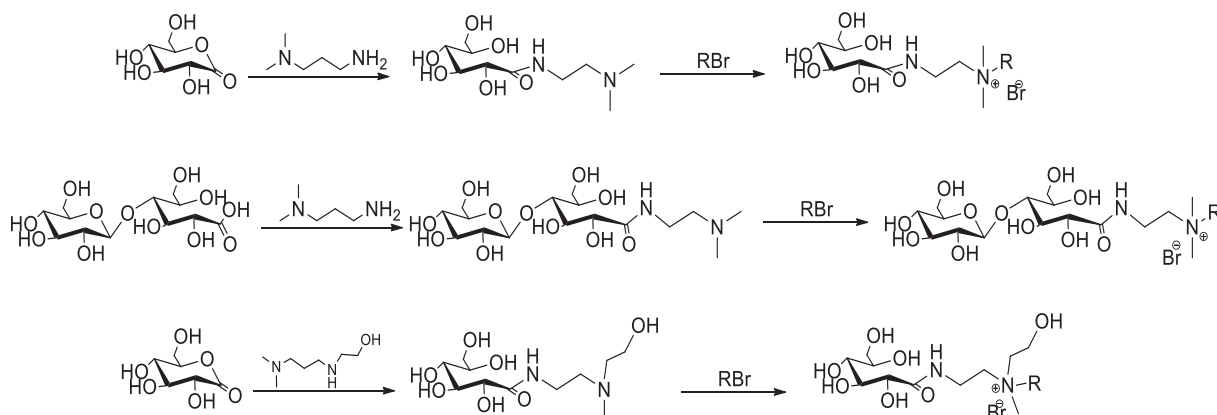


Fig. 2. Two-step chemical routes used by Zhi et al. [47,61] to produce cationic glucose- δ -lactone and lactobionic acid-based surfactants.

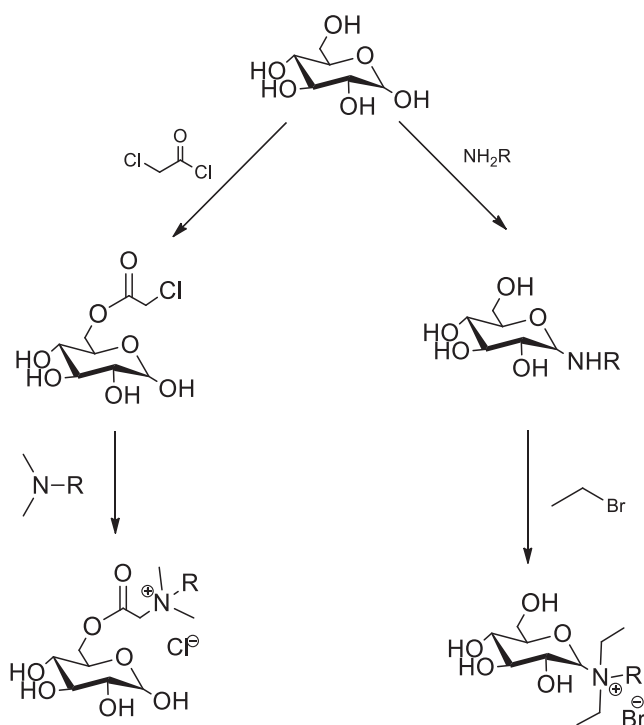


Fig. 3. Two-step chemical routes to produce cationic glucose-based surfactants with different anions.

Another two-step synthetic method was described to produce cationic sugar-based surfactants, based on a double nucleophilic addition or amine formation bond followed by ethylation. Gan et al. used double nucleophilic addition to produce cationic glucose-based surfactants (Table 2, entry 1). Using this method, the authors prepared cationic surfactants with different alkyl chains lengths (C_{12} and C_{16}). Firstly, glucose was reacted with chloroacetyl chloride in chloroform at room temperature for 3 h. Then, the previously synthesized intermediate was dissolved in a mixture of solvents (isopropanol: water) and reacted with tertiary fatty amines, C_{12} and C_{16} , at 85 °C for 5 h. The surfactants were obtained with a 72 and 66% yield, respectively [38]. Zhao et al. synthesized glucose-based surfactants in two steps (Table 2, entry 6) by the condensation of sugar's carbonyl group with an amine, followed by the ethylation of the amine group. Firstly, glucose and *n*-dodecylamine were added in methanol, at 45 °C for 4 h and the intermediate was obtained with a 65% yield. After isolation, *n*-bromoethane was added and the mixture was stirred in methanol at 55 °C for 12 h. The cationic glucose-based surfactant was obtained with a low yield, 35% [60]. These two-step chemical routes methods to produce cationic glucose-based surfactants, with different counterions are depicted in Fig. 3.

Other methods were developed, involving multi-step synthetic sequences including protection of the sugar's hydroxyl groups, nucleophilic substitution, condensation of sugar's carbonyl group with fatty amine, deprotection and transesterification. Salman et al. developed a four-step method to produce cationic glucose-based surfactant (Table 2, entry 2). This method begins with the

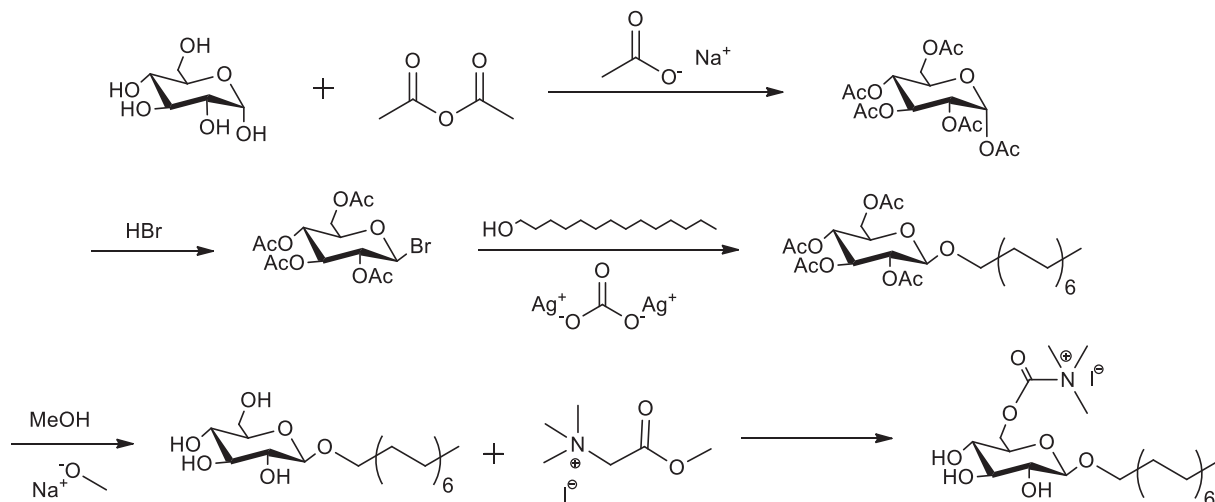


Fig. 4. Multi-step chemical route to produce glucose-glycine betaine based cationic surfactant described by Esmailian et al.

protection of glucose's hydroxyl groups, followed by the glycosylation with bromoethanol. After that, the prepared intermediate is reacted with an alkylated imidazole with different lengths. Finally, the resulting compound is reacted with NaOH to remove the hydroxyl protecting groups. The authors reported that this method is efficient, with a yield greater than 90%. However, they reported some difficulty in the preparation of the alkylated imidazole, once this reaction was not optimized [39].

Esmaeilian et al. also reported a multi-step chemical route to produce sugar-based surfactants combined with amino acids (Table 2, entry 5). This method begins with the protection of glu-

cose's hydroxyl groups with acetic anhydride in the presence of sodium acetate, at 100 °C under magnetic stirring for 2 h. Then, the protected glucose is dissolved in dichloromethane and HBr is added to form a 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide. Then, the bromide is substituted by tetradecanol in dichloromethane, at room temperature overnight. Subsequently, hydroxyl groups are deprotected, followed by reaction with glycine betaine pre-treated with an excess of iodomethane. This compound was prepared by two different methods. In the first one the reaction was made in water, using sodium dodecyl sulfate (SDS) as co-surfactant and NaHCO₃ as catalyst. The product was

Table 3
Summary of the reaction conditions for the production of cationic sugar-based gemini.

#	Substrate	Reaction conditions					CMC (mM)	γ (mN/m)	Ref.
		Reagent	Solvent	T (°C)	t (h)	(%)			
1	Lactose	i) K ₂ CO ₃ ; 2-Chloroacetyl chloride	CCl ₃ H	r. t.	2	–	C ₁₂ – 0.631	C ₁₂ – 27.58	[55]
		ii) Alkyl dimethylamine (n = 12, 14 e 16)	H ₂ O:Isopropanol (2:1)	90–100	24–36	–	C ₁₄ – 0.178 C ₁₆ – 0.056	C ₁₄ – 26.01 C ₁₆ – 27.33	
2	Isosorbide	i) 2-Chloroacetyl chloride	CCl ₂ H ₂	r. t.	4	–	C ₁₀ – 0.513	C ₁₀ – 31.7	[56]
		ii) Dimethylethanolamine	CCl ₂ H ₂	reflux	24	>85	C ₁₂ – 0.372 C ₁₄ – 0.234 C ₁₆ – 0.162	C ₁₂ – 33.5 C ₁₄ – 35.4 C ₁₆ – 37.4	
3	Glucose	i) N-dodecylamina	MeOH	25–30	10	70	N = 1 – 3.13	N = 1 – 30.5	[57]
		ii) Dicarboxylic acid	MeOH	50–55	2.5	–	N = 2 – 1.80	N = 2 – 33.5	
4	Fructose	i) Bromoacetic acid	Toluene	r. t.	48	60–68	N = 3 – 3.75	N = 3 – 32.9	[58]
		ii) TEA; fatty acid (C ₁₂ , C ₁₆ , C ₁₈ , C ₂₂); p-toluene sulfonic acid	Toluene	reflux	–	–	C ₁₂ – 0.468	C ₁₂ – 39	
5	Glucose	iii) TEA-fatty acid;	Acetone	reflux	80	–	C ₂₂ – 0.210	C ₂₂ – 32	[58]
		i) Bromoacetic acid	Toluene	reflux	–	–	C ₁₂ – 0.525	C ₁₂ – 36	
6	Isosorbide	ii) TEA; fatty acid (C ₁₂ , C ₁₆ , C ₁₈ , C ₂₂); p-toluene sulfonic acid	Toluene	40	–	–	C ₁₆ – 0.495	C ₁₆ – 34	[59]
		iii) TEA-fatty acid;	Acetone	reflux	80	–	C ₁₈ – 0.416	C ₁₈ – 33	
7	D-(+)-glucose- δ -lactone	i) 2-Chloroacetyl chloride	CCl ₂ H ₂	reflux	4	90	C ₁₂ – 0.859	C ₁₂ – 0.049	[62]
		ii) Alkyl dimethylamine (n = 12, 14 e 16)	AcEt: CCl ₂ H ₂ (8:2)	reflux	24–48	40–70	C ₁₄ – 0.108 C ₁₆ – 0.035	C ₁₄ – 0.042 C ₁₆ – 0.003	
7	D-(+)-glucose- δ -lactone	i) N-dodecyl-N,N-bis(3-aminopropyl) amine;	MeOH	reflux	8	85	C ₁₀ – 1.04	C ₁₀ – 28.31	[62]
		ii) n-Alkylamine bromide	EtOH	reflux	24	~30	C ₁₂ – 0.71 C ₁₄ – 0.51	C ₁₂ – 27.61 C ₁₄ – 27.12	

CMC – Critical micellar concentration; γ – superficial tension on CMC; r. t. – room temperature.

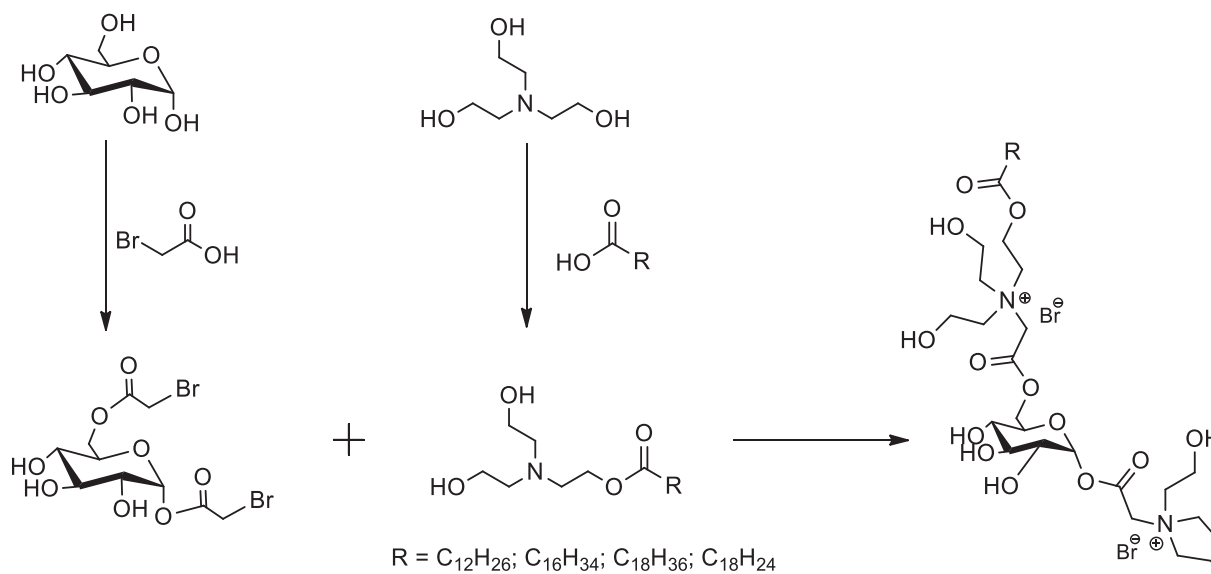


Fig. 5. Chemical route used by Negm and Mohamed [58] to produce cationic glucose/fructose-based gemini.

obtained with a 56% yield. The second method, dimethylformamide (DMF) was used as solvent, in the presence of NaHCO_3 as the catalyst. The product was obtained with a 32% yield [49]. A multi-step chemical route to produce sugar-amino acid based cationic surfactant is represented in Fig. 4.

Besides glucose, lactose was also used to produce cationic sugar-based surfactants as described by Michocka et al. (Table 2, entry 3). This route is initiated by the reaction of lactose's carbonyl group with N-alkylamine (C_{12} and C_{14}) in propan-3-ol, at room temperature for 24 h. The products were isolated with 90 and 92% yield, respectively. After that, the previously prepared intermediate was treated with 1,3-propanesultone in methanol. The authors observed that the product was insoluble in water, so it was treated with a solution of HCl, thus obtaining a novel class of cationic lactose-based surfactants [63].

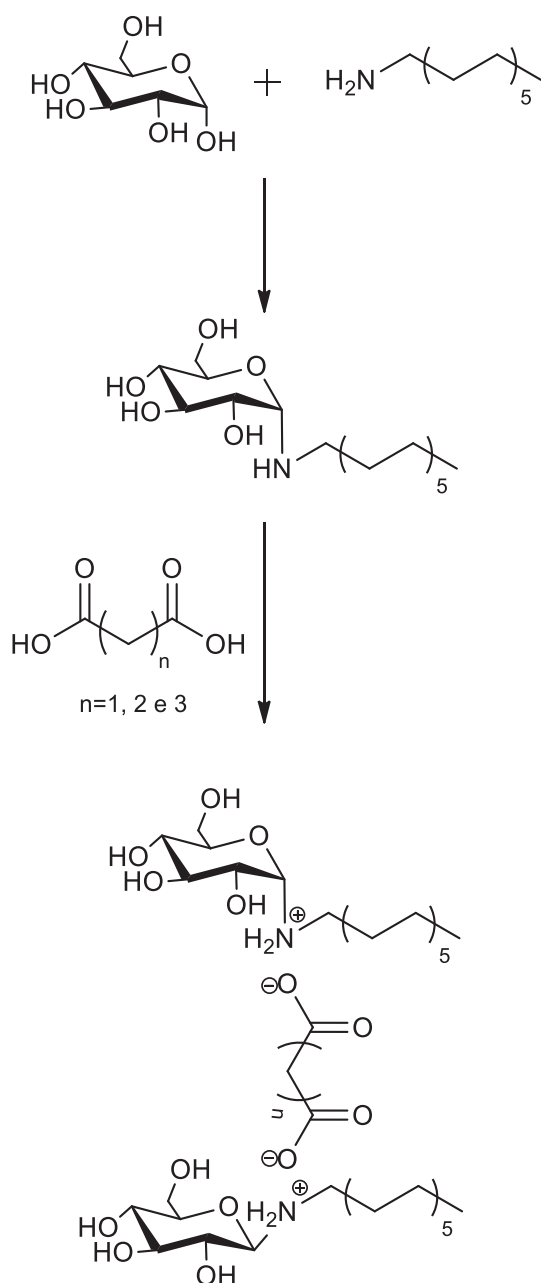


Fig. 6. Chemical route to produce cationic glucose-based gemini with different spacer lengths.

3.2. Cationic sugar-based gemini

In the last years, gemini surfactants have been getting a special focus due to their structure–activity and self-assembly capacity. This class of surfactants was synthesized for the first time in 1971 by Bunton et al. [64] and denominated “gemini” by Mener and Littau in 1991 [65]. Cationic gemini surfactants contain two hydrophobic chains and two positively charged hydrophilic groups covalently linked by a spacer being structurally similar to a dimeric cationic surfactant. The length and nature of the spacer works as a tool to manipulate the size, shape and morphology of the gemini, including the structural transitions from micelle to vesicle [66].

Gemini can be incorporated in cleaning products with bacteriostatic activity, in personal care and pharmaceutical products, and more recently, in micellar catalysis with high efficiency. It can also be applied in corrosion inhibitor agents, anti-aesthetic fabric, dyes adsorption, porous materials and enhanced oil recovery [67,68].

Like single chain cationic surfactants, gemini surfactants can be classified according to the charge of their headgroup. Gemini can thus be characterized as nonionic, anionic, cationic and zwitterionic. Nonionic and cationic gemini surfactants are the most described ones in the literature [69,70]. The interfacial properties of gemini are interesting since they have lower CMC values than other classes, giving them great potential for the application in many scientific and industrial areas [71]. Due to their biodegradable nature and natural source, sugar-based gemini are more interesting for bio applications, like DNA micellization and interaction,

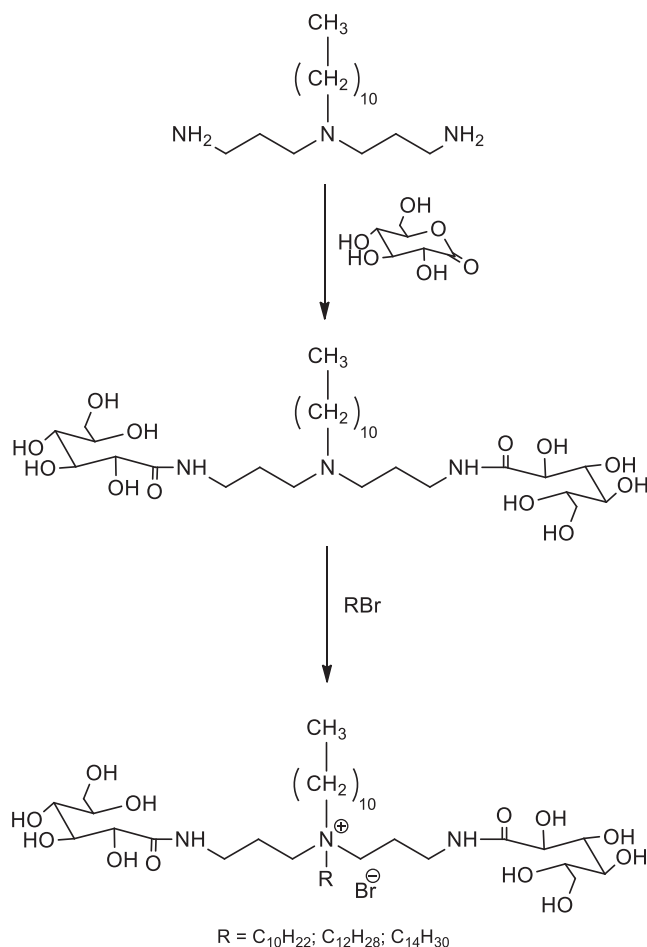


Fig. 7. Two-step chemical route described by Zhi et al to produce glucose- δ -lactone-based star surfactants.

than petrol-based gemini. Several cationic sugar-based gemini have been produced using different sugars in the headgroup including glucose [57,58], fructose [57], glucose- δ -lactone [62], isosorbide [56,59] and lactose [55].

Li et al. also prepared cationic glucose-based gemini with different dicarboxylic acid spacer lengths (Table 3, entry 3). The chemical route for the production of cationic glucose-based gemini is shown in Fig. 6. This method involves a two-step sequence. Firstly, glucose reacts with N-dodecylamine in methanol at 25–30 °C for 10 h, and then the mixture is heated to 50–55 °C and stirred for 2.5 h. Subsequently, the intermediate is dissolved in methanol, a dicarboxylic acid is added, and the reaction proceeds for 48 h, at room temperature. The cationic glucose-based gemini was obtained with a 60% yield [57].

Negm and Mohamed synthesized two series of cationic sugar-based gemini surfactants, with glucose and fructose (Table 3, entry 4 and 5). The authors developed a three-step method using several natural compounds, besides reduced sugars, they also used triethanolamine (TEA) and fatty acids with different chain lengths as reagents. Firstly, TEA was esterified with a fatty acid in toluene and *p*-toluene using sulfonic acid as a catalyst. Then, the triethanolamine monoalkanoates were added, in acetone, to the sugar which has been previously esterified with bromoacetic acid [58]. The three-step chemical route to produce cationic glucose and fructose-based gemini is represented in Fig. 5.

Still in the context of gemini surfactants the synthesis of a star surfactant was also described. While gemini have two principal hydrophilic groups linked to two hydrophobic chains, star surfactants possess a star-shaped configuration, with spacer groups that radiate from a central moiety, usually the central spot being nitrogen. Zhi et al. synthesized glucose- δ -lactone-based star-surfactants (Table 3, entry 7), this chemical route is represented in Fig. 7. The authors reported a two-step synthesis to produce cationic star-surfactants. Firstly, D (+)-glucose δ -lactone and N-dodecyl-N,N-bis(3-aminopropyl)amine were stirred in methanol at reflux temperature for 8 h. After isolation of the intermediate, *n*-alkyl bromides with different lengths (C₁₀, C₁₂ and C₁₄) were added in ethanol, at reflux temperature, for 24 h. A lower yield of approximately 30%, was obtained. Despite the low yield the authors reported that the synthesized surfactants showed excellent interfacial properties when compared with monomeric ones [62].

Sugar molecules can also be the spacer of cationic sugar-based gemini. These geminis are synthesized using methods like those used for the preparation of cationic sugar-based surfactants with single chain. One of those methods involves the substitution of sugar's primary hydroxyl groups by other functional groups, followed by nucleophilic substitution with tertiary fatty acid. Parikh et al. reported the synthesis of a cationic isosorbide gemini (Table 3, entry 6). Isosorbide is obtained by sorbitol dehydration, and sorbitol is produced by glucose hydrogenation. The authors reacted isosorbide with chloroacetyl chloride, at reflux for 24 h, and the product was obtained with a 90% yield. Then, the synthesized intermediate was added to a tertiary fatty amine in a mixture of solvents (diethyl ether: dichloromethane), in reflux for 24–48 h, and the resulting product was obtained with a 40–70% yield [59]. Cho and Joeng used a similar method to produce cationic isosorbide gemini (Table 3, entry 2), that was used to evaluate interfacial properties and antimicrobial activities of cationic sugar-based gemini. Firstly, they reacted dimethylethanolamine with octanoyl chloride, in dichloromethane at room temperature for 4 h. Then, isosorbide was modified with chloroacetyl chloride in dichloromethane at room temperature for 4 h. Finally, both intermediates were added in acetone and the reaction mixture was refluxed for 24 h. Yields greater than 80% were obtained [56]. Cai et al. used the same method to produce cationic lactose-based gemini (Table 3, entry 1) [55].

4. Conclusion

Cationic sugar-based surfactants are a new class of cationic surfactants that are less toxic and more biodegradable than petrol-based ones. These surfactants are more advantageous because their raw materials are of renewable origin and their properties are superior to those of oil-based surfactants. However, this class of surfactants is not yet very widespread. Regarding these synthesized cationic sugar-based surfactants the most common sugars used to prepare them are glucose, glucose- δ -lactone, lactobionic acid and lactose, and for cationic gemini, glucose, fructose, glucose- δ -lactone, isosorbide and lactose. The synthetic processes have two or more steps that usually begin with an amidation between the sugar molecule and a diamine followed by alkylation with *n*-alkyl bromide or a double nucleophilic addition, for single cationic surfactants. For gemini, most of the processes have two steps that involve the substitution of the sugar's primary hydroxyl groups by other functional groups, followed by a nucleophilic substitution with a tertiary fatty acid. The reason why these surfactants are not yet being adopted at an industrial level are mainly two. The first one is that a simple method to synthesize these molecules has not yet been described since these methods have in general more steps than the ones currently being made. The second reason relies on the fact that industry survives on profit and in some cases the reactions lead to low or reasonable yields. Even if these two challenges were overcome more work needs to be done to reduce or eliminate the use of toxic reagents and solvents in these processes to effectively assure green surfactants. However, there have been several efforts and developments to overcome this handicap, with different types of surfactants being synthesized with different types of sugars and with different methods for the introduction of long chains and positive charge. While alternative green chemical routes do not emerge, other options may be presented such as the reuse of natural residues to produce these surfactants, namely the sugary residues from sugar extraction. We are confident that further efforts are being made at the moment to establish green chemical routes to produce this class of surfactants.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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