Development of amino acid-based surfactants: from synthesis to applications

Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in
Colloid & Interface Science

Development of amino acid-based surfactants: from synthesis to applications

Krister Holmberg, Frida Bilén and Romain Bordes

The diversity of both natural and non-natural amino acids provides a strong foundation for the synthesis of a wide array of surfactants and offers the possibility to control the interactions at interfaces and within self-assembly processes. This review provides an overview of the latest developments of amino acid-based surfactant over the past decade, with a particular focus on the past five years. A detailed overview of the synthesis is first given, and physicochemical properties of surfactants derived from both standard amino acids, and non-natural amino acids are discussed. From enhancing foaming to controlling rheological properties, these surfactants meet a wide range of application-specific requirements. This is illustrated in various fields, such as drug delivery or mineral ore flotation.

Although single amino acid derivatives have been deeply explored, surfactants based on multiple amino acids are also discussed for the new possibilities in self-assembly and potential various applications they offer.

Addresses
Department of Chemistry and Chemical Engineering, Chalmers University of Technology, 41296 Gothenburg, Sweden

Corresponding authors: Bordes, Romain (bordes@chalmers.se); Holmberg, Krister (kh@chalmers.se)

Current Opinion in Colloid & Interface Science 2025, **75**:101884

This review comes from a themed issue on **Surfactants**

Editors: **Romain Bordes**, **Yilin Wang**, **Rico Tabor**

For a complete overview see the Issue and the Editorial

https://doi.org/10.1016/j.cocis.2024.101884

Keywords
Amino acids, Self-assembly, Surface activity, Adsorption, Foams, Rheology, Biological activity.

Introduction

Surfactants having an amino acid residue as polar headgroup have been around for several decades and surface-active derivatives of standard amino acids, such as glycine and glutamic acid, as well as of non-natural amino acids not used in the biosynthesis of proteins, such as sarcosine and betaine, are produced in large quantities today. There are several comprehensive overviews of this class of surfactants [1–3], as well as more focused reviews [4] and the aim of this opinion is not to compete with these. Instead, the intention of this paper is to cover the development during the last decade, particularly the last five years. Surfactants based on natural raw materials, often referred to as green surfactants, and surfactants with a good biodegradability profile are very much in focus today. Amphiphiles based on amino acids are both green and rapidly biodegradable and are, in addition, mild to the skin. It is therefore understandable that there is a large research activity in the area which is reflected in the number of papers that appear every year.

Furthermore, the scope of this review is limited to papers that provide a well-defined chemical structure of the amphiphile. This means that most oligopeptide surfactants and surface-active protein derivatives are not included. We have excluded papers that deal with taurine derivatives and similar compounds; only derivatives of amino acids that have amino and carboxyl groups are included.

This review gives a detailed overview of amino acid-based surfactants, starting with their synthesis methods and then exploring their physicochemical properties. It further discusses various applications arising from these properties in fields like enhanced oil recovery, personal care, or corrosion inhibition. The final section further covers potential future research directions.

Synthesis aspects

Many recent papers deal with novel procedures for synthesis of amino acid surfactants. The papers can be divided into two main subsections: syntheses based on organic chemistry, which are the most common, and enzymatic syntheses. These will be treated separately below.

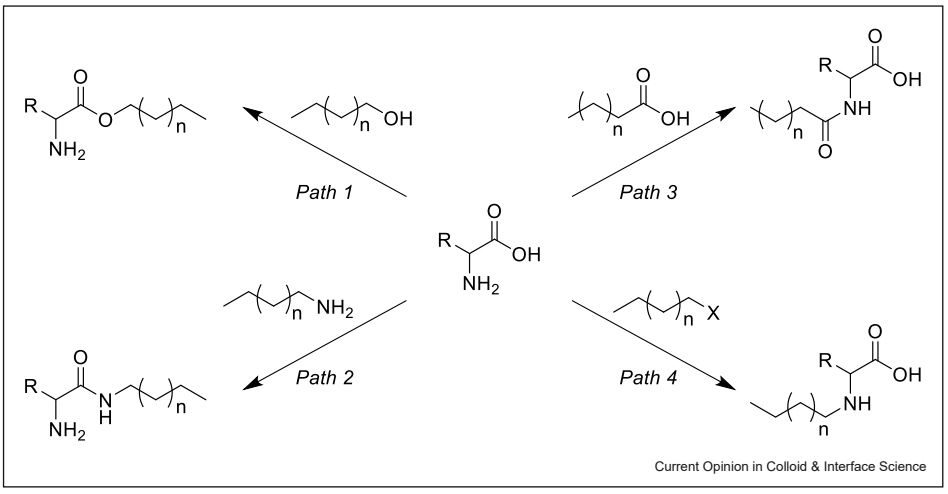
There are four main routes to amino acid-based surfactants, and these are illustrated in Figure 1.

Organic chemistry routes

Apart from these four synthesis routes, there are examples in the literature where an amino acid is used as a

Given the role as Guest Editor, Romain Bordes had no involvement in the peer review of the article and has no access to information regarding its peer review. Full responsibility for the editorial process of this article was delegated to Yilin Wang.

Figure 1



Four routes for synthesis of amino acid-based surfactants from an amino acid. Reproduced with permission from Ref. [3].

building block for surfactants with a very different structure, without neither an ester nor an amide bond in the molecule [5]. Such amphiphiles, which lack a bond susceptible to enzyme catalyzed cleavage, are less attractive from an environmental perspective.

In Figure 1, paths 1 and 2 give a cationic surfactant (except at high pH when the amino group is not protonated), path 3 gives an anionic surfactant (except at low pH when the carboxyl group is protonated), and path 4 gives an amphoteric surfactant. Path 3 is the most important synthesis route, and all the commercially important amino acid surfactants are made by this path, usually by reacting the amino acid with a long-chain acyl chloride, the so-called Schotten–Baumann reaction.

The N-alkylation of path 4 is normally made with alkyl chloride. Yan et al. developed ruthenium-catalyzed N-alkylation of an ester or an amide of the amino acid using a long-chain alcohol instead of a long-chain alkyl halide as alkylating agent [6]. This is advantageous from a green chemistry perspective since fatty alcohols are natural raw materials, while fatty halides are not. The reaction is shown in Figure 2.

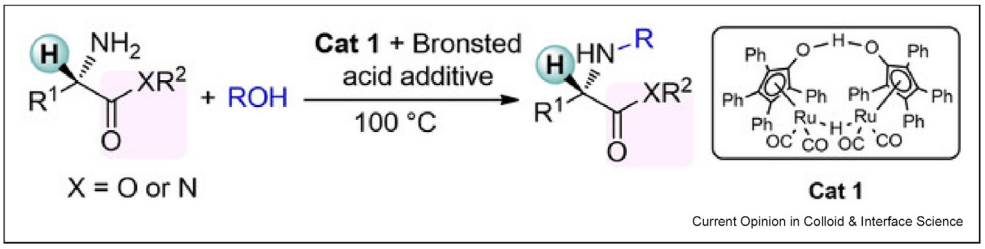
Another example of a new synthesis route according to path 4 of Figure 1 was described by Zhao et al. [7]. They reacted an amino acid with an α,β-unsaturated fatty acid ester using $SiCl_4$ as catalyst. The reaction, an aza-Michael addition, resulted in N-alkylation, as shown in Figure 3a.

Several papers describe a modified Schotten–Baumann reaction in which the long-chain acyl chloride is replaced by a triglyceride, such as coconut, peanut, soybean, or palm kernel oil. A broad range of amino acids were used as reactants, including glycine, alanine, lysine, leucine, threonine, and methionine. Sodium methylate was used as a catalyst [8,9]. The methyl ester of the fatty acid may also be used as electrophilic species. The amidation is then performed with a zeolite catalyst [10]. The use of a triglyceride or a fatty acid methyl ester instead of an acyl chloride is advantageous from a toxicity and an environmental point of view.

An alternative to an acid chloride, a triglyceride, or a fatty acid methyl ester as acyl donor for path 3 in Figure 1 is to use a fatty acid together with dicyclohexylcarbodiimide (DCC) as the coupling agent. Several amphiphilic N-acyl derivatives of amino acids have been prepared by that procedure [11]. There is an environmental benefit in using the fatty acid rather than the fatty acid chloride as starting material, but a drawback of the procedure is that DCC is not a catalyst, it is a coupling agent that is converted to dicyclohexylurea and used in equimolar amount to the amino acid. This part is simply aligned with traditional peptide syntheses.

Alkylsuccinic anhydrides are another possible group of acyl donors for reactions according to path 3. Lysine was N-acylated exclusively at the α-amino group with long-chain alkylsuccinic anhydrides as the reagent [12]. The reaction, shown in Figure 3b, is environmentally benign but the product obtained is not a normal N-acylated amino acid; it contains an extra carboxyl group, which is likely to substantially change its physical chemical properties. In addition, it may not be regarded as an entirely green surfactant because the hydrophobic part of the amphiphile does not have a natural origin.

Figure 2

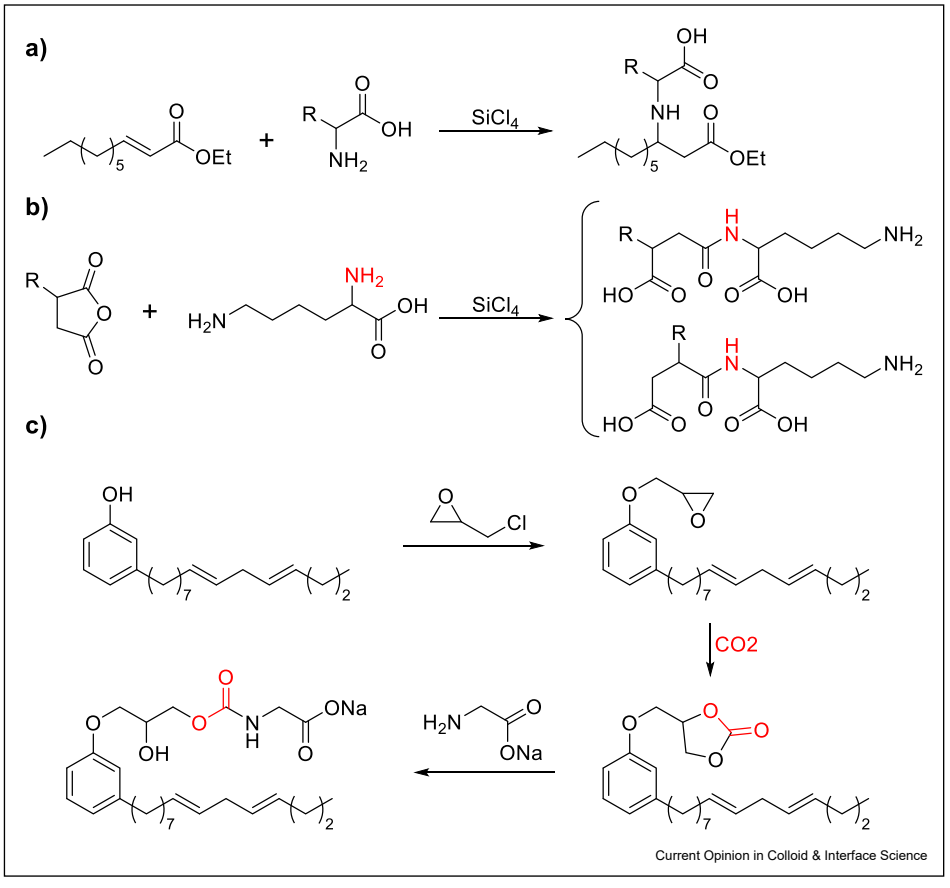


N-alkylation of an ester or an amide of an amino acid using a fatty alcohol as an alkylating agent. Adapted from Ref. [8].

Aspartic acid, which has two carboxyl groups, can form a five-membered anhydride. This anhydride, with a protective group at the nitrogen atom, was used as acylating reagent in a reaction with a hydrophobic alcohol [13]. After removal of the protecting group, an aspartic acid monoester was obtained. However, the use of a protective group limits the practical use of such a synthesis procedure.

Carbamate-functional amino acid surfactants constitute another innovative approach and were synthesized by Zhu et al. The synthesis, which consisted of three steps, is shown in Figure 3c for the derivative based on glycine [14]. Surfactants containing a carbamate linkage are not new and it has been shown that the carbamate bond is slightly more stable to alkali than an ester bond in the same environment [15]. However, this may be the first

Figure 3



(a) Synthesis of a surface-active amino acid derivative through N-alkylation. **(b)** Synthesis of N-acylated lysine using an alkylsuccinic anhydride as acylating agent. **(c)** Synthesis of a surface-active carbamate derivative of glycine.

time that carbamate-containing amino acid surfactants have been reported.

Enzymatic synthesis

Enzymatic routes have historically been attractive for the synthesis of amino acid surfactants and are well documented. Despite not meeting the requirements of industrial relevance, they are central in the preparation of new species with high molecular complexity. Pérez et al. used a bioorganic route to synthesize a dimeric arginine surfactant [16]. The molecule, which can be seen as a gemini surfactant, consists of two N-acylated arginine moieties linked together by a diaminoalkane spacer. The enzyme papain was used as catalyst for the formation of the amide bonds between the carboxyl group of arginine and the amino groups of an α,ω-diaminoalkane. The structure of the surfactant is shown in Figure 4a.

More recently Faustino et al. synthesized surfactants from the amino acids cystine, lysine, and phenylalanine using porcine pancreatic lipase as catalyst for amidation of the amino acids with dodecylamine [17]. The enzyme was encapsulated in a gel and the yields were around 85 %. The products obtained from lysine and phenylalanine were normal amphiphiles with one hydrophobic tail attached to the amino acid residue, while the amphiphile obtained from cystine was a dimer, i.e. a gemini surfactant. The structure is shown in Figure 4b.

Bourkaib et al. used an aminoacylase from *Streptomyces ambofaciens* to catalyze N-acylation of several amino acids with fatty acids of varying chain length [18]. The conversion of amino acids into the N-acylated derivative decreased in the order lysine > arginine > leucine > methionine > phenylalanine > valine > cystine > isoleucine > threonine. Addition of a small amount of $CoCl_2$ increased the reaction rate considerably.

Physical–chemical investigations

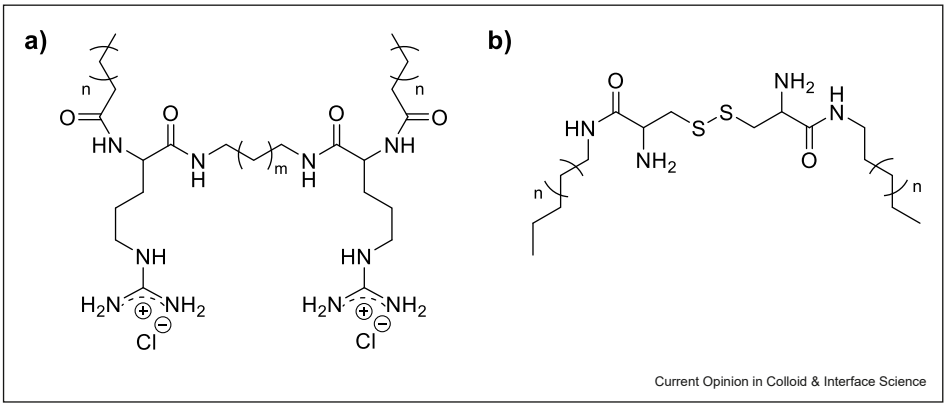
The work on the synthesis of amino acid-based surfactants has led to the production of numerous new surface-active agents, which has expanded their field of application significantly. Consequently, there has been a substantial increase in the number of reports on the physicochemical properties of these molecules. Figure 5 illustrates the most commonly studied molecules in this context.

Foams and foaming

There is a large research activity on foams and foaming behavior of amino acid surfactants, which is not surprising considering the importance of foaming and lathering for the most important application of the surfactants: personal care. Several studies have dealt with the foaming behavior of single N-acyl amino acid surfactant, such as N-acyl glycinate and N-acyl phenylalaninate [19], N-acyl serinate [20], and N-acyl glutamate [21]. In a detailed study of the effect of hydrocarbon chain length (C12, C14, C16, and C18) of two types of surfactants, N-acyl glutamate and N-acyl phenylalaninate, it was found that the foamability decreased but the foam stability increased with increasing number of carbon atoms in the acyl chain. Whereas the foam stability was relatively unaffected by the concentration of surfactant used (within the range investigated), the foamability showed a maximum at a certain concentration. Both foamability and foam stability were better for the glycinate than for the phenylalaninate surfactant [19].

Another work dealt with the effect of the structure of the fatty acyl chain on the foam characteristics of N-acyl serinate surfactants. A series of amphiphiles with different lengths of a straight hydrocarbon chain (C14, C16, and C18), with different number of unsaturated bonds in the chain (0, 1, and 2) and with or without a

Figure 4



(a) A gemini surfactant from arginine [16]. **(b)** A gemini surfactant from cystine [17].

hydroxyl group in the 12-position of a C18 chain with a C9–C10 double bond, *i.e.* the ricinoleic acid structure [20]. The main structure is shown in Figure 5.

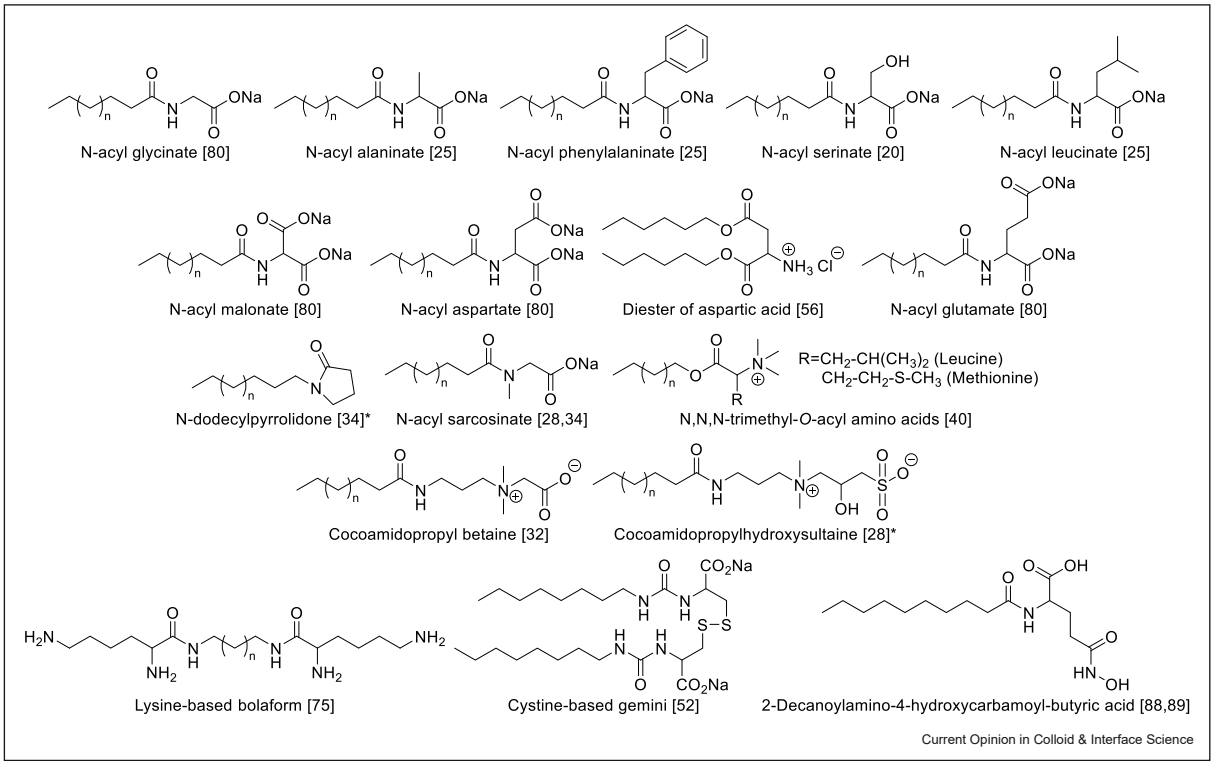
It was found that the foam stability increased with increasing length of the acyl chain. This is according to expectations because longer chains mean stronger van der Waals interaction, which, in turn, leads to closer packing at the air–water interface. Foamability, on the other hand, decreased with increasing acyl chain length because of decreasing water solubility. Introduction of one double bond in the acyl chain improved the surface activity and enhanced the water solubility. However, two double bonds resulted in a decrease in surface activity, probably due to less favorable packing at the interface, and to a decrease in foam stability. The hydroxyl group in 12-position hindered close packing of the chains, resulting in a decrease in foam stability.

Glutamate surfactants contain two carboxyl groups with different pK_a values, 2.1 and 4.5. This means that the physical–chemical properties have different pH dependence than for surfactants based on glycine and other amino acids with just one carboxyl group. Foaming and foam properties of sodium lauroyl glutamate was investigated in some detail [21]. It was found that there was a minimum in surface tension and a maximum in foam stability at neutral pH. At low pH, a gel was formed in solution, and it was also present in the foam film. A weak gel seemed to enhance the duration of the foam, while a strong gel was detrimental to the foam stability.

Wang et al. studied the pH dependent foaming of surfactants from the dicarboxylic amino acids aspartic and glutamic acid [22]. At pH 6–7, where one of the carboxyl groups is protonated, the surface activity was high and so was the foam stability. However, the foamability was approximately the same over the pH range 6–10. The authors speculate that dimers, held together by hydrogen bonds, may form at pH 6–7. At this pH, the aspartate and the glutamate surfactants were good emulsifiers for W/O systems, while at pH 9–10, the surfactants gave O/W emulsions. At a pH below 6, solutions of the surfactants become unstable due to the increasing amount of the fully protonated dicarboxylate derivatives. Comparing the two dicarboxylate surfactants, the aspartate had higher surface activity, gave better foam stability, and was a better emulsifier. This difference was attributed to the glutamate surfactant with two carbons between the carboxyl groups having a too large headgroup to pack tightly at interfaces.

Intermolecular hydrogen bonds are known to improve the packing of amino acid-based surfactants, as was shown by comparing the behavior of a glycine-based surfactant (which can form hydrogen bonds) and a sarcosine-based

Figure 5



Common amino acid-based surfactants that have been studied for their physicochemical properties. Please note that the molecules with an asterisk are not amino acid-based surfactants.

surfactant (which cannot form hydrogen bonds) with the same length of the hydrocarbon tail. Hydrogen bonding also enhances foam stability as was demonstrated by comparing foaming of the same glycine-based and sarcosine-based surfactants [23]. In a more recent paper, the effects of different salts, ranging from kosmotropic to chaotropic, on foams made from the two surfactants were described. The salts had almost no effect on foams created by the sarcosine surfactant but a substantial effect on foams from the glycine surfactant. The stability of the foam from the glycine-based amphiphile decreased in the order NaF > NaCl > NaSCN, which is in accordance with NaF promoting and NaSCN breaking intermolecular hydrogen bonds. NaCl is in-between in this respect [24].

Amino acid-based surfactants are often used in combination with a fatty alcohol. Borkowski et al. studied the influence of n-octanol on the surface activity, foamability, and foam stability for the N-lauroyl derivatives of alanine, leucine, and phenylalanine and conducted molecular dynamics simulations to complement the experimental work [25]. As expected, addition of n-octanol gave a reduction of the surface tension for all three surfactants, but the effect differed. It was most pronounced for N-lauroyl alanine and least pronounced for N-lauroyl phenylalanine. In the foamability experiments, there was a very strong effect for all three surfactants with respect to foam height. None of the mixtures gave a very stable foam; however. The strong synergistic effect on foamability seen in all the octanol-surfactant systems, as well as the difference between the surfactants in the surface tension experiments, were explained as differences in hydrogen bonding capabilities. Hydrogen bonds formed in all three systems, but the octanol-surfactant hydrogen bonding decreased in the order N-lauroyl alanine > N-lauroyl leucine > N-lauroyl phenylalanine, a trend that corresponds to that of synergy in surface tension reduction. The authors postulated that the strong foamability-enhancing effect seen in all three systems is mainly due to hydrogen bonding between octanol and the surfactant. Addition of octanol also drastically lowered the critical micelle concentration (CMC), i.e. increased the number of micelles in the system. During the highly dynamic foaming experiments, the micelles are transported to the foam surface by convection, where they supply their surrounding with new surface-active molecules. According to the authors, this explains why the octanol addition gave such a strong effect in the dynamic foamability experiments compared to the surface tension experiments, which reflect an equilibrium situation.

Bae et al. studied mixtures of two amino acid surfactants, one glycinate and one glutamate, with respect to foam properties [26]. They found a strong synergistic effect on interfacial viscosity and on foam rigidity when the mixture was diluted with tap water but not with distilled water. The authors concluded that divalent ions in the tap water mediated binding between the head groups of surfactants aligned at the air–water interface.

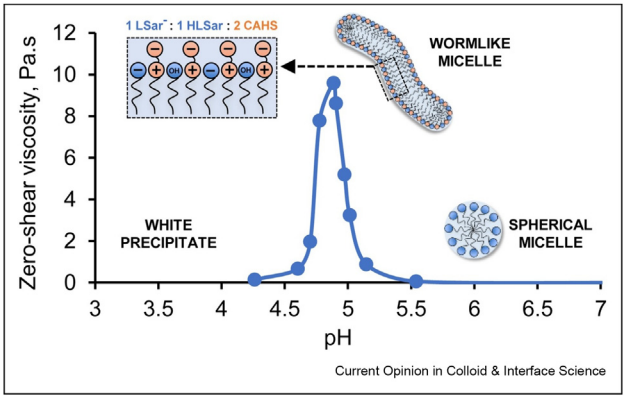
Rheology

Proper control of rheology is imperative for many surfactant applications. It is very important in many personal care products and since amino acid-based surfactants are common ingredients in such formulations, it is not unexpected that there are many papers dealing with rheological effects of these amphiphiles.

N-acyl amino acid surfactants having a carboxyl group in the polar head are inherently pH sensitive. In this, they differ from the amphiphiles with a sulfate or sulfonate polar headgroup, which are the most common anionic surfactants. The pH sensitivity can be a problem, but it can also be an asset if the formulation is properly done. Zhang et al. studied how the viscosity changed with pH for solutions of N-oleoyl sarcosine, an amino acid surfactant with an unusually long tail. Raising the pH from 9.0 to 12.4 gave an increase in viscosity from 3 to 10 000 mPa s, a clear indication of a transition from spherical to worm-like micelles [27].

In related papers, Vu et al. describe the use of pH and nonionic cosurfactants to control the rheology of a mixture of an amino acid surfactant, sodium N-lauroyl sarcosinate, and the zwitterionic amphiphile cocoamidopropylhydroxysultaine [28,29]. This surfactant combination is practically relevant since such mixtures of an anionic and a zwitterionic surfactant are commonly used in personal care formulations. As shown in Figure 6, there is a pronounced maximum in viscosity at a pH just below 5 and the high viscosity is caused by worm-like micelles. The rheological behavior is very much governed by micelle dynamics, in particular reptation and breakage time. Comparing the behavior with that of a system based on a sulfate surfactant, sodium laurylethersulfate, for

Figure 6



Effect of pH on the zero shear viscosity of a 1:1 M ratio solution of sodium lauroyl sarcosinate and cocoamidopropylhydroxysultaine. Reproduced with permission from Ref. [28].

which the viscosity is regulated by salt instead of pH, the authors concluded that the micelle dynamics is more important in the amino acid surfactant system.

The same research group also studied the effect on the viscosity of several inorganic and organic counterions—including the cationic surfactant cetyltrimethylammonium chloride (CTAC)—on the surfactant system discussed above [30]. The viscosity was found to be strongly dependent on the choice of counterion and decreased in the following order: CTAC > LiCl = NaCl > triethanolamine = arginine = no additive > trimethylphenylammoniumchloride. Thus, CTAC gave a strong viscosity enhancing effect while the large organic counterion trimethylphenylammonium gave a decrease in viscosity.

Aqueous solutions of worm-like micelles are often used in personal care formulations. They can give a high zero shear viscosity and at the same time have a marked shear-thinning behavior. This is the rheological behavior that formulators of rinse-off personal care products, such as shampoos and body washes, want. Rajput et al. studied the rheology of sodium cocoyl glycinate, a common amino acid surfactant, in combination with a nonionic surfactant of the type used in personal care products. The nonionic surfactants were cocamide diethanolamine and lauryl glucoside, which are both good at stabilizing foams and are mild to the skin [31]. Sodium cocoyl glycinate is a hydrophilic surfactant with a high CMC value. Addition of the nonionic surfactants resulted in a drastic reduction of the CMC. A 1:1:1 mixture of the three had a CMC three orders of magnitude lower than the glycinate only. Sodium cocoyl glycinate alone forms spherical micelles and the ternary mixture forms short rod-like mixed micelles under neutral conditions. By lowering the pH to 5.5—6.0, the mixed micelles grew into long rods or worm-like micelles. This, in turn, leads to high viscosity. Thus, the rheology of the surfactant system can be fine-tuned by pH.

In formulation science, both salt and pH are important parameters that govern solution behavior, including rheology. Jamadagni et al. investigated how the zero shear viscosity was affected by salt and temperature for a mixture of two surfactants commonly used in personal care formulations, the zwitterionic lauramidopropyl betaine (LAPB) and the anionic sodium dodecyl sulfate (SDS), a combination of surfactants that is known to exhibit "synergy", i.e. give a much lower CMC value than those of the single surfactants [32]. The structure of LAPB is shown in Figure 5.

Using proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) as the main experimental tool, the authors could demonstrate that the energetically favorable formation of mixed micelles triggered the betaine surfactant to pick up a proton and become cationic even at a pH well above the pKa of its carboxyl group. This means that at pH values around 5, which are common in many formulations, the amphiphile system is not a binary one but a ternary one composed of the anionic SDS, the zwitterionic LAPB, and the cationic protonated-LAPB, This, in turn, leads to elongation of the micelles and to an increase in viscosity. They could also demonstrate that salt concentration and pH governed the micelle size and structure and, consequently, the viscosity of the solution.

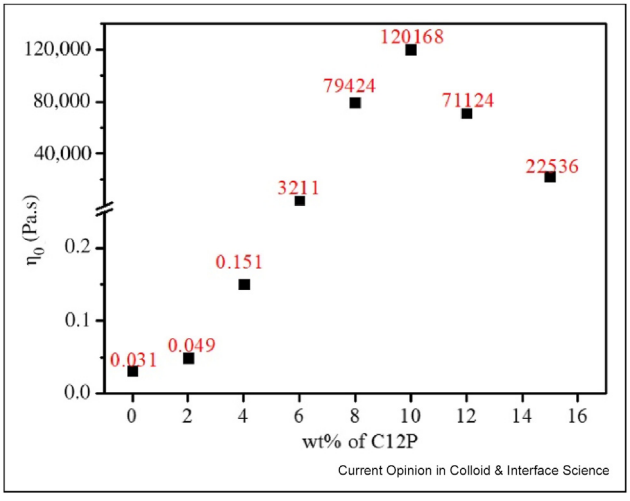
Ullah et al. investigated how the rheological behavior of potassium N-cocoyl glycinate varied with the electrolyte [33]. The salts used in the study were KCl, $CaCl_2$, and tetrabutylammonium bromide; thus, there was a monovalent inorganic cation, a divalent inorganic cation, or a large organic cation as counterion to the anionic surfactant. All three electrolytes improved the packing density at the oil—water interface because of screening of the electrostatic forces. However, the bulky butyl groups prevented real tight packing, which, in turn, gave a more viscoelastic surface film as compared with the films obtained with the inorganic counterions.

The rheological behavior can also be governed by the ratio of the surfactants in the formulation. Sodium lauroyl sarcosinate was combined with the hydrophobic nonionic surfactant N-dodecylpyrrolidone (see Figure 5) in a work by Liu et al. [34]. Figure 7 shows the viscosity as a function of added amount of N-dodecylpyrrolidone. The strong viscosity increase is due to formation of worm-like mixed micelles.

Biological activity

The antimicrobial effect of amino acid-based surfactants has been the topic of many studies. Cationic surfactants in general exhibit antimicrobial activity so cationic amino

Figure 7



Zero shear viscosity of a formulation containing 30 % sodium lauroyl sarcosinate and varying amounts of N-dodecylpyrrolidone (C12P) at a pH of 7.2. Reproduced with permission from Ref. [35].

acid surfactants, *i.e.* those based on arginine and lysine, are the obvious candidates. The hydrophobic chain is usually attached via an ester linkage at the carboxyl group of the amino acid. The fact that such substances contain a hydrolyzable bond, easily degraded by the action of, *e.g.*, pancreatic lipase, makes them fall into the category of cleavable surfactants or soft antimicrobial agents [35], *i.e.* substances that lose their biological effect with time, which may be advantageous. Reference [36] gives an overview of the representative examples of papers describing arginine- and lysine-based esters, respectively, that have been investigated for antimicrobial activity. More recently, Qi et al. have studied the antimicrobial effect and cytotoxicity of gemini surfactants with various cationic amino acid-based spacers [37,38], and Shen et al. showed a prolonged antimicrobial effect for an arginine-based surfactant when combined with gallic acid in hierarchical assemblies [39].

Traditional antibacterial agents are often "quats", *i.e.* amphiphilic quaternary ammonium compounds. Perinelli et al. synthesized such surfactants from leucine and methionine and evaluated them as antimicrobial agents [40]. The synthesis was a two-step procedure, and the product is shown in Figure 5. As can be seen, also these substances have the hydrophobic tail connected to the amino acid residue via an ester bond, *i.e.* they belong to the category of soft antimicrobial agents.

Antibacterial tests were conducted on both Gram-positive and Gram-negative bacteria, as well as on one fungus, *Candida albicans*. An established disinfectant, benzalkonium chloride, was used as reference. The tests showed that the polar headgroup did not matter; leucine and methionine derivatives with the same length of the hydrocarbon chain gave similar biological activity. The antibacterial activity increased with the length of the tail. The effect was very good on Gram-positive bacteria and less good on Gram-negative bacteria. This is the common pattern for amphiphilic quaternary ammonium compounds and the leucine and methionine derivatives with the optimal hydrocarbon chain length (C14) had approximately the same antibacterial spectrum as the reference compound, benzalkonium chloride.

Mixtures of anionic and cationic surfactants can give vesicles and the charge of such vesicles will be governed by the ratio of the amphiphiles. Pérez et al. mixed a cationic long-chain histidine derivative with an anionic surfactant, either a lysine derivative, where both amino groups had been transformed into amide groups, or sodium myristate and investigated the bactericidal activity, as well as the cytotoxicity and the hemolytic activity [41]. The vesicles showed good antibacterial activity against Gram-positive bacteria and the effect increased with increasing cationic charge of the vesicles. The cytotoxicity and the hemolytic activity also increased with increasing cationic charge.

Kapitanov et al. used a three-step procedure to synthesize cationic surfactants from phenylalanine [42]. The carboxyl group was first esterified with a fatty alcohol and then the reaction with bromoacetylbromide gave the N-bromoacetyl derivative. The bromine was subsequently substituted by a tertiary amine to form the bromide salt of a cationic surfactant. In total, three series of substances were made with pyridinium, imidazolium, or cholinium as polar head and with bromide as counterion. For each series, eight homologs were prepared with 2 to 16 carbon atoms in the side chain. The surface-active species, *i.e.* those with a long enough hydrocarbon tail, had the expected antimicrobial activity against bacteria and fungi. However, a drawback with these amphiphiles is that the synthesis is more demanding than other procedures to make cationic amino acid surfactants, for instance, esterification of arginine or lysine with a fatty alcohol as discussed above.

Even if amino acid surfactants are considered atoxic, they are not completely free from toxicity. In order to improve our understanding of the relationship between chemical structure and toxicity of these surfactants, Perinelli et al. investigated the toxicity of surfactants based on alanine and serine, both with different lengths of the hydrocarbon tails [43]. The toxicity was found to increase with increasing length of the N-acyl chain as expected. However, the toxicity differed between alanine and serine surfactants with the same chain length, the serine surfactants generally being the least toxic. It is interesting that there was a clear difference in toxicity between these two classes of surfactants although the only structural difference is that $-CH_3$ in alanine is replaced by $-CH_2OH$ in serine. As the authors point out, the toxicity was very small for all the amino acid-based surfactants, much smaller than for the regular surfactant sodium dodecyl sulfate, which was included as reference. At concentrations below the CMC, the amino acid surfactants were completely without toxicity.

Kalebic et al. studied the environmental effects of N-acyl derivatives of the amino acids methionine, glutamic acid, and aspartic acid with the length of the acyl chain varying from 10 to 16 carbon atoms [44]. The aquatic toxicity was evaluated using zebrafish larvae as experimental animals. Comparing surfactants with the same length of the hydrophobic tail showed that the methionine derivative was the least and the aspartate derivative the most toxic. The toxicity increased with the length of the tail and the most toxic of the tested amphiphiles was the N-hexadecyl derivative of aspartic acid. This surfactant had a lower value of maximum tolerable concentration (MTC) than the common anionic surfactant SDS indicating that it had a higher fish toxicity. All the other amino acid surfactants had similar or higher MTC values than SDS.

Long-chain esters of arginine are dicationic surfactants. Song et al. mixed the dodecyl ester of arginine with alkyl polyglucosides and studied the physical chemical behavior as well as the antimicrobial activity [45]. The antibacterial and antifungal activity found were mainly attributed to the effect of the arginine derivative.

Many amino acids are known to have antioxidant activity and amphiphilic antioxidants are of interest for some applications, *e.g.* to prevent lipid oxidation in food products and pharmaceuticals where there can be a large oil-water interface. Hossain et al. studied the antioxidant effect of N-dodecanoyl derivatives of tryptophan, tyrosine and histidine, as well as N-dodecanoyl derivatives of three dipeptides [46]. The dipeptide amphiphiles had much higher water solubility than the regular amino acid surfactants, which may be advantageous for some applications. The N-acyl derivatives had approximately the same antioxidant activity as the parent amino acids and the dipeptide surfactants had the same activity as the regular surfactant based on the same amino acid. The authors conclude that the N-dodecanoyl derivatives of the amino acids are the products of choice for emulsion-based food or pharmaceutical products, while the dipeptide derivatives may be preferable for water-borne products.

Adsorption

Combining theory with experimental work, Borkowski et al. made an in-depth study of the adsorption behavior of the N-lauroyl derivates of the amino acids alanine, valine, leucine, proline, and phenylalanine at the air—water interface [47]. Without pH adjustment, the surfactants in practice are a mixture of an anionic (*i.e.* deprotonated) and a nonionic (*i.e.* protonated) amphiphile. The nonionic form has a stronger driving force to get out of solution and will dominate the interface. Density functional theory (DFT) calculations showed that intermolecular hydrogen bonding between amide bonds of the surfactants contributes to the formation of dimers, which affects the surface activity of the amphiphiles.

Molecular dynamics simulations of N-acyl amino acid surfactants at the air—water interface were performed by Wu et al. [48]. The calculations showed that intermolecular hydrogen bonds were the main factors behind close packing at the surface. A methyl group on the amide nitrogen atom, which sarcosine has, affected the packing considerably, as has been demonstrated before [49]. For dicarboxylic amino acid surfactants, the intermolecular hydrogen bonding was weaker because of charge repulsion between the head groups.

Sakai et al. used quartz crystal microbalance with dissipation monitoring (QCM-D) to study adsorption of disodium dodecanoylglutamate at a hydrophobic surface [50]. Exposure to a $CaCl_2$ solution resulted in partial desorption, as also monitored by QCM-D. The remaining calcium-containing surfactant film was rigid and elastic and had good lubricating properties.

Adsorption at the solid—water interface was also studied by Bonini et al. They investigated adsorption of a range of amino acids on imogolite, an aluminum silicate clay mineral, and found that the dicarboxylic glutamic acid had the strongest affinity for the mineral surface. Based on this observation, disodium N-lauroyl glutamate was chosen as surfactant for studies of adsorption on imogolite [51]. The authors claim that it is likely that glutamate surfactants will adsorb strongly also on other aluminum oxide surfaces.

Miscellaneous

Almost all amphiphiles based on an amino acid contain one hydrophobic tail and one polar headgroup. This is, for instance, the general structure of N-acylamino acid salts, the most common type of amino acid surfactants. The headgroup is usually just one carboxyl group but N-acyl derivatives of aspartic acid and glutamic acid contain two carboxyl groups in the polar head. Dimeric, or gemini, surfactants, *i.e.* surfactants with two tails and two headgroups have also been described. Faustino et al. have published several papers in which they study synthesis, characterization, and applications of cystine derivatives with long N-acyl chains. The disulfide bridge constitutes a very short spacer unit in the anionic gemini surfactant [52]. Use of this surfactant for drug delivery is discussed briefly below in the section Drug delivery. The same group has also synthesized a cationic gemini surfactant based on cystine [53].

Anionic gemini surfactants have also been made from aspartate. The surfactant had long-chain N-acyl groups and an α,ω-diaminoalkane acted as spacer, connecting the two aspartate moieties via amide bonds [54]. The group of Infante has published several papers on cationic gemini surfactants based on arginine with an α,ω-diaminoalkane moiety as spacer [55].

However, there are only few reports on amino acid surfactants with two hydrophobic chains and one polar head. Olutas et al. have synthesized such surfactants by esterifying aspartic acid with medium-chain alcohols and the products formed are shown in Figure 5 [56]. The cationic double-tailed amphiphiles were characterized with respect to physical chemical properties. The surfactant with two octyl chains, but not the one with two hexyl chains, formed vesicles in solution.

Fletcher et al. have used NMR to study how a wide range of such organic counterions bind to the micelles of an amino acid-based [57] and a dipeptide surfactant, undecyl-ll-leucinevalanate [58]. The effect of different tetraalkylammonium counterions on micelles of N-lauroyl alanine was recently investigated by Sun et al.

and the same research group has also studied vesicle-to-micelle transition of sodium lauroyl glycinate induced by tetraalkylammonium ions [59]. Ullah et al. made a similar study with N-cocoyl glycinate as amphiphile, but with a focus on the dilational rheological behavior [60].

Ikeda and Aramaki used glutamate-based gelators to form a hydrogel [61]. The gelator, which was a 1:1 mixture of N-lauroyl-glutamic acid dibutylamide and N-2-ethylhexanoyl-glutamic acid dibutylamide, was added to a micellar solution of the anionic sodium lauroyl glutamate and the cationic cetyltrimethylammonium chloride. Hydrogels were formed with less than 1 % added gelator. Angulo-Pachón et al. reported the use of alkali ions as gelator for an anionic valine derivative [62]. They found that the cations promoted micelle head crystallization with subsequent aggregation into fibrils and that the gelation efficiency decreased in the order Li > Na > K.

Chen et al. explored the use of the same amphiphile, ethyl N^{α}-lauroyl arginate, as a switchable surfactant [63]. Switchable surfactants are amphiphiles that in a reversible mode change their characteristics under the influence of a trigger. The most common trigger is CO_2, and the concept is for instance of interest for emulsification-demulsification and flocculation-redispersion. Figure 8 shows the principle applied to ethyl N^{α}-lauroyl arginate. Passing CO_2 through a solution of the surfactant transforms the hydrophobic nonionic surfactant to a more hydrophilic cationic amphiphile. Removing CO_2 by N_2 reverses the process.

Applications

Personal care

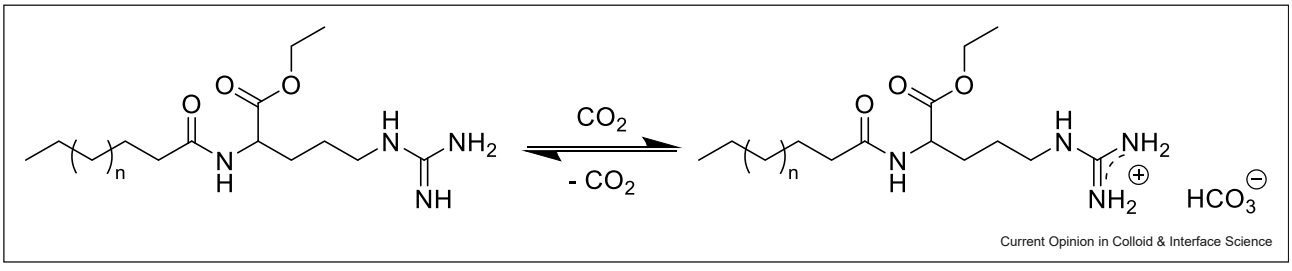
Amino acid-based surfactants have an established use in the personal care sector [64]. The most common N-acyl amino acid-based surfactants in the personal care segment are glycinates, sarcosinates, alaninates and glutamates. The hydrocarbon tail is usually C12, and the commercial surfactants are usually referred to as cocoyl derivatives but sometimes as lauroyl derivatives. They are usually sold as sodium salt, but potassium cocoyl glycinate is also a commercial product.

Glycine, sarcosine, and alanine have one carboxyl group while glutamic acid has two, which means that glutamate surfactants may exist either as the monosodium (or monopotassium) salt or as the disalt. In solution, the ratio between the two will depend on the pH. pKa_1 and pKa_2 for glutamic acid are 2.19 and 9.67, respectively.

Besides the N-acyl surfactants mentioned above, cocamidopropyl betaine (or lauramidopropyl betaine) is frequently used in personal care formulations. One may note that betaine is not one of the 20 standard amino acids; however, it is ubiquitous in biological materials. The same applies to sarcosine. Figure 5 shows the amino acid-based surfactants that are most popular in personal care applications, namely sodium cocoyl glycinate, sodium cocoyl sarcosinate, sodium cocoyl alaninate, (mono) sodium cocoyl glutamate, and cocamidopropyl betaine.

The increasing popularity of amino acid-based surfactants in this segment is largely due to their good compatibility with skin and hair, which is well documented, although a case of allergic contact dermatitis has been reported for the amino acid derivative N-capryloyl glycine [65]. However, "skin compatibility" has often been used in a vague sense, without much scientific foundation. There has been an assumption that skin cleansers should be formulated at the same pH as human skin, which is in the range 4.5–6.0. Relatively recently, Hawkins et al. have shown that this is not necessarily true. For products predominantly based on anionic surfactants—amino acid-based and others—those formulated to give skin pH gave increased skin dryness and irritation compared to those formulated at more neutral pH. The results were believed to be due to increased electrostatic interaction of anionic surfactants with stratum corneum under low pH as compared to neutral conditions [66]. The authors concluded that the mildness of the cleanser will be determined by the

Figure 8



Switching of ethyl N^{α}-lauroyl arginate by CO_2.

interaction of its surfactants and other ingredients with stratum corneum under the conditions of the formulated pH.

α-Gels are surfactant-based structures that resemble lamellar liquid crystals but where all the surfactant alkyl chains are fully stretched and in a solid state with all-*trans* configuration. They are of interest for shampoo formulations and other personal care products. However, α-gels have traditionally required surfactants with a minimum of 14 carbon atoms in a straight hydrocarbon chain [67]. Surfactants with a tail of 14 or more carbon atoms are problematic due to low Krafft temperature and are therefore normally not used in personal care formulations. Ren et al. have developed a formulation based on sodium lauroyl sarcosinate together with a mixture of two long-chain alcohols, cetyl alcohol and stearyl alcohol. The formulation was found to be an α-gel at room temperature. The concept was also extended to several other C-12 amino acids [68].

Microemulsions based on components that are green and mild to the skin are of interest for some cosmetics products. In a paper by Manyala and Varade, microemulsions of fatty acids and water were made with sodium lauroyl sarcosinate as surfactant. Without cosurfactant, the microemulsion region in a ternary phase diagram was small but it grew markedly with addition of a short-chain alcohol such as propanol or butanol. The same research group later used the lauroyl sarcosinate-based microemulsion as a nanocarrier for encapsulation and delivery of α-tocopherol [69].

Hair shampoos are often formulated with a combination of an anionic surfactant and a cationic polyelectrolyte. The dilution during the rinsing process leads to formation of a coacervate, which adheres to the hair and provides the smooth, lubricating effect that is expected from a conditioning shampoo. Aramaki et al. used an anionic amino acid-based surfactant, potassium cocoyl glutamate or potassium cocoyl glycinate, in combination with high molecular weight cationic cellulose ether to study the formation of coacervate. They could demonstrate that the coacervate was formed through electrostatic interaction between the different charged groups and that it was composed of fibrous aggregates [70].

Combinations of an anionic and a cationic surfactant are also common in personal care formulations. A problem with such mixtures is that they tend to precipitate if the hydrocarbon chains are long. Zhang et al. have studied a mixture of the anionic sodium lauroyl glutamate and the cationic amphiphile dodecyltrimethyl ammonium chloride. The mixture had a low Krafft point and did not show any signs of precipitation. The mixed micelles formed were worm-like and could be used to control the viscosity of the formulation [71].

Drug delivery

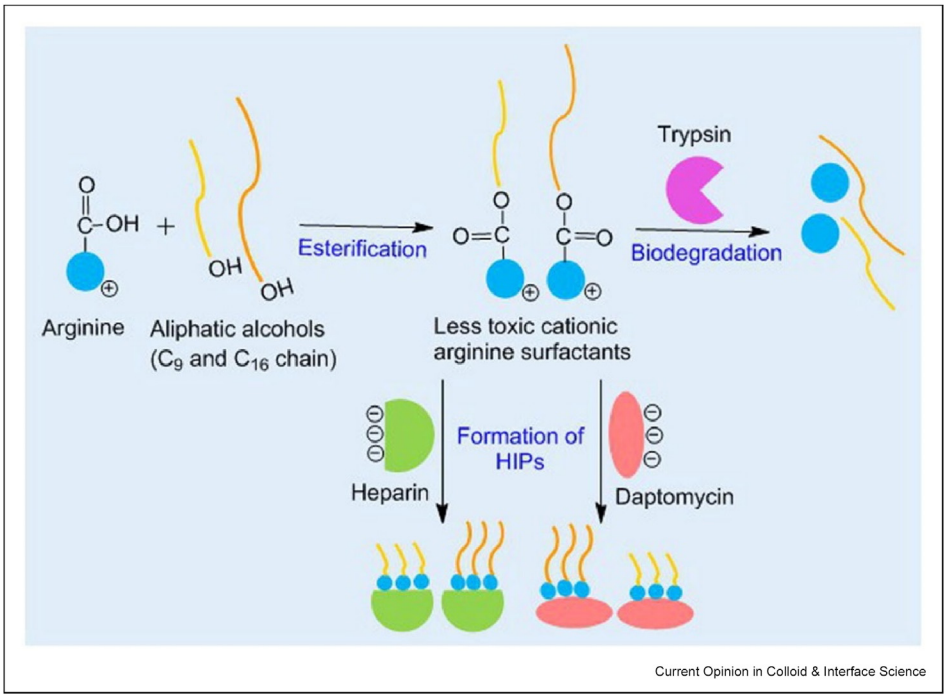
Being easily degradable, having low cytotoxicity [43], and being made from natural building blocks, amino acid-based surfactants are of interest in drug delivery applications. Arginine has a net positive charge at neutral pH due to its guanidino group. Thus, arginine esters of long-chain fatty alcohols can be regarded as dicationic surfactants. Shahzadi et al. prepared such esters by reacting the fatty alcohol with boc-protected arginine using DCC as coupling agent followed by deprotection with HCl [11]. The motivation for the work was to find a more benign cationic amphiphile for ion pairing with hydrophilic macromolecular drugs. In drug delivery, hydrophobic ion-pairing is seen as a promising approach to modulate the solubility of charged hydrophilic drugs ranging from small molecules to peptide- and protein-based therapeutics. The arginine ester was found to efficiently precipitate heparin and daptomycin, as representatives of polysaccharide and peptide drugs, respectively, from aqueous solution [72]. The concept is promising for a variety of anionic drugs. It is illustrated in Figure 9.

The arginine surfactants were found not to be cytotoxic at concentrations below the CMC. Above the CMC, the cytotoxicity depended on the length of the alkyl chain, the hexadecanol ester being less toxic than the nonanol ester. However, compared to standard cationic microbicides, such as benzalkonium chloride, the two arginine-based surfactants had very low cytotoxicity. Trypsin-induced degradation was fast for both esters.

A similar approach was taken by Jörgensen et al., who synthesized a cholesterol ester and a diosgenin ester of arginine for ion pairing with hydrophilic drugs. These cationic steroid esters were also efficient in forming hydrophobic ion pairs and had very low cytotoxicity [73]. In a similar work by the same research group, a series of hydrophobic esters of lysine was found to form complexes with insulin by hydrophobic ion pairing [74].

Bolasurfactants are amphiphiles that have two polar head groups, one on each side of a hydrocarbon chain. At an oil—water or an air—water interface, they will fold and orient the two polar ends into the aqueous phase and the hydrocarbon segment into the oil. Hu et al. synthesized the bolaform surfactant shown in Figure 5 from lysine and 1,12-diaminododecane [75]. The molecule is a diamide with a lysine residue at both ends and since both the α-amino and the ε-amino group of the lysine are intact, the molecule is strongly cationic, but the charge is pH dependent. Vesicles were made by combining the bolaform surfactant with the nonionic surfactant Tween 60 and the vesicles were loaded with the anticancer drug 5-fluorouracil. The therapeutic efficacy of the active vesicles was investigated on H_{22} tumor-bearing mice and was found to be high. Another type of vesicle, based on one cationic and one anionic

Figure 9



Long-chain arginine esters can form hydrophobic ion pairs with hydrophilic drugs such as heparin and daptomycin. HIP stands for hydrophobic ion pair. Reproduced with permission from Ref. [72].

amphiphile, both with serine as polar headgroup, was used as carrier for the anticancer drug doxorubicin [76]. The catanionic vesicles were found to have low cytotoxicity *in vitro* and give a high uptake of doxorubicin by cells.

Gemini surfactants are dimeric amphiphiles with the two moieties connected at the polar heads and several amino acid-based gemini surfactants have been synthesized either by organo-chemical routes or by enzymatic synthesis [55]. Serafim et al. synthesized a gemini surfactant based on cystine as polar head and used it as a delivery vehicle for the antibiotic amphotericin B (AmB) [52]. AmB is widely used in the therapy of systemic fungal infections, but its poor water solubility puts demands on the formulation. The paper describes the use of micelles of the gemini surfactant as a carrier for AmB, as well as for combinations of AmB and different bile salts. The micelles had a high solubilization capacity for monomeric AmB and the formulation showed high antifungal activity. The structure of the cystine-based gemini surfactant is shown in Figure 5.

The hydrophobic ion-pairing concept for drug delivery can also be applied to incorporation of DNA into lipophilic delivery systems. Wolf et al. synthesized hexadecyl lysinate from boc-protected lysine and with DCC as coupling agent [77]. This cationic ester surfactant was shown to be easily degraded by both trypsin and pancreatic lipase and have low cytotoxicity. The ion pairing between the surfactant and plasmid DNA was investigated and an optimal ratio was established. At this ratio, an effective transfection of HEK-293 cells was obtained.

Faustino et al. studied the interaction between DNA and long-chain amides of the amino acids phenylalanine, lysine, and cysteine [17]. The phenylalanine and the lysine surfactants were regular single-chain amphiphiles, while the cysteine-based was double-tailed because the cysteine residue had spontaneously oxidized to a cystine derivative. This means that it had become a gemini surfactant with a disulfide spacer unit. All three surfactants interacted with DNA and the complexes formed were considerably stronger for the cystine surfactant than for the two other amphiphiles, presumably due to the stronger hydrophobicity of this double-tailed surfactant. One may conclude that cationic and rapidly degradable amino acid-based surfactants should be regarded as attractive alternatives to the conventional and more toxic cationic amphiphiles normally used for transfection.

Hydrogels are also of interest for drug delivery. Oliveira et al. prepared hydrogels by combining a lysine derivative in which the two amino groups had been reacted with long-chain fatty acids and a cationic cellulose derivative. The hydrogels, which consisted of honeycomb-

like structures of surfactant and polymer moieties, were temperature sensitive, and may be candidates as vehicles for temperature-triggered release of actives [78].

Drugs can also be transported through the skin, usually with the help of so-called skin permeation enhancers. Hermet et al. tested amphiphilic arginine derivatives as skin permeation enhancers and found that these became incorporated into the stratum corneum-mimicking membrane and altered its rheological and structural properties by disordering the lipid chains. This, in turn, enhanced the membrane elasticity and caused thinning of the membrane layer [79].

Flotation

Amino acid-based surfactants have been explored as collectors in mineral ore flotation, also called froth flotation. The collector in froth flotation is a molecule that binds to the value mineral and renders it hydrophobic so that it can be removed by the froth, *i.e.* finely dispersed air bubbles. The collector is often an amphiphilic compound with the polar headgroup having a specificity for the surface of a specific mineral. The choice of a headgroup is typically guided by the hard and soft Lewis acid and base concept. The versatility of amino acid surfactants—there are many amino acids to choose from as headgroup—makes them candidates as collectors.

Patra et al. synthesized and evaluated a series of N-dodecanoyl dicarboxylic amino acid salts with one, two, or three carbon atoms between the carboxyl groups for flotation of calcium minerals [80]. The monocarboxylic N-dodecanoyl glycinate was also included in the test. The surfactants are shown in Figure 5.

The malonate surfactant was found to be an apatite and a fluorite specific collector while the glycinate derivative was calcite specific. The aspartate and the glutamate surfactants, with longer distance between the two carboxyl groups, did not float apatite at all at high pH. However, these substances were active, although not very efficient, as collectors for calcite and fluorite. The results were explained by matching the distance between the carboxyl groups with the distance between adsorption sites at the mineral surface.

The above series of three dicarboxylic amino acid-based surfactants were later the subject of an NMR study of the solution behavior at concentrations just below the CMC [81]. Sodium and calcium were used as counterions. NMR diffusometry clearly indicated the presence of premicellar aggregates. The most stable aggregate was the calcium salt of the glutamate surfactant, probably because of formation of an intermolecular complex with calcium. The stability of all the premicellar aggregates declined with temperature.

Guo et al. synthesized a modified amino acid surfactant, 2-carbamoylaminolauric acid, and investigated it as a collector for quartz flotation. Quartz is traditionally floated either with a cationic amphiphile such as a long-chain quaternary ammonium compound or a fatty amine or by an anionic collector such as sodium oleate together with divalent cations which act as activators [82]. Very good flotation results were obtained with the novel anionic surfactant after activation with a calcium salt [83]. Computational simulations based on DFT indicated that the collector attached to bound calcium ions at the mineral surface and that the binding was augmented by hydrogen bonding between surface sites and the amide bond of the collector. Amide bonds in amino acid-based surfactants are known to play an important role in the self-assembly of the amphiphiles [49].

In a recent work by Li et al., quartz and dolomite were separated from collophane, an apatite ore, by flotation using a novel anionic collector, sodium N-dodecyl-β-amino propionate [84]. The selectivity for dolomite was particularly good and X-ray photoelectron spectroscopy (XPS) analysis indicated that the collector interacted with magnesium ions at the surface of the dolomite. In another system, fluoroapatite was separated from dolomite by the use of the anionic amino acid-based collector N-hexadecanoyl glycine [85]. DFT calculations showed that the collector interacted with two calcium ions at the fluoroapatite surface to generate a tridentate binding in which hydrogen bonding between amido-NH in the collector and $-PO_4$ groups at the mineral surface was the third binding mode. In the hydrogen bonding, $-NH$ was the donor and $-PO_4$ at the surface the acceptor. The calculations showed that the collector could also bind to two metal ions at the dolomite surface, either two calcium or one calcium and one magnesium, in a bidentate fashion. The pronounced flotation selectivity for fluoroapatite over dolomite indicated that the collector adsorbed preferentially at the fluoroapatite surface due to the tridentate binding being a stronger mode of interaction than the bidentate binding.

Peng et al. used sodium lauroyl glutamate as a collector in cassiterite flotation and obtained very high selectivity [86]. The headgroup of lauroyl glutamate contains two carboxyl groups and one amido-NH group that may all interact with cassiterite, which is a tin oxide mineral. A possible chemisorption mode for sodium lauroyl glutamate at the mineral surface has been proposed, based on XPS and fourier transform infrared spectroscopy (FTIR) analyses. In the suggested arrangement, one carboxylate oxygen atom and the amide nitrogen atom chelate a surface Sn atom to form a five-membered ring.

The importance of amide bonds for the self-assembly of collector molecules via hydrogen bonds was also shown by Sun et al. They used a long-chain amide of glutamic acid for flotation of rhodochrosite, a manganese carbonate mineral, and obtained good selectivity for rhodochrosite against quartz and calcite. They could demonstrate a "weak to medium" hydrogen bonding between amide groups or between amide and carboxyl groups of closed-packed amphiphiles [87].

Fine particle flotation is a well-known challenge in the mineral processing industry. Recently, Fei et al. synthesized the surface-active compound 2-decanoylamino-4-hydroxycarbamoyl-butyric acid, which can be regarded as a glutamic acid derivative, and tested it as collector for fine rhodochrosite, a manganese carbonate mineral. The structure of the collector is shown in Figure 5. As can be seen, it contains a hydroxamate group, which is known to have strong affinity for rhodochrosite.

The synthesized surfactant turned out to be a very efficient collector for fine rhodochrosite. As can be seen from the structure, there are many possibilities for intermolecular hydrogen bonding when the amphiphile has aligned at the mineral surface. The good effect obtained is believed to be due to strong hydrogen bonds in combination with efficient binding through chelation to the surface [88,89].

Conclusion and perspectives

The interest in amino acid-based surfactants has experienced a significant growth that was originally driven by the transition from petrochemically based systems to bio-based systems. However, the possibility offered by the library of amino acids to fine-tune the interactions at play in self-assembly and at interfaces has also enabled the design of surfactants towards specific applications.

In fact, the ability to regulate intermolecular interactions in detail enables a strong control of their physicochemical properties, with amino acid-based surfactants demonstrating interesting properties across a wide range of applications. From enhancing foaming and controlling rheological properties to regulating surface activities and forming interesting self-assembled structures, these surfactants have proven to be able to meet a large number of requirements on the application side.

Beyond their initial use in personal care products, amino acid-based surfactants have demonstrated appealing features in fields such as drug delivery and mineral ore flotation. Their versatility and effectiveness have also sparked interest in areas such as enhanced oil recovery and metal corrosion inhibition.

Currently, they are mostly based on a single amino acid and the modulation of the interactions relies on parameters such as the type of coupling with the hydrophobe and the structure and length of the hydrophobic moiety. Considerable potential remains when considering exploring more complex structures of the headgroups that would incorporate multiple amino acids. This could unlock new frontiers in complex self-assembly and lead to intriguing properties, further expanding the scope of applications for amino acid-based 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.

Data availability

No data was used for the research described in the article.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Guo J, Sun L, Zhang F, Sun B, Xu B, Zhou Y: **Review: progress in synthesis, properties and application of amino acid surfactants**. *Chem Phys Lett* 2022, **794**, 139499, https://doi.org/10.1016/j.cplett.2022.139499.

2. Tripathy DB, Mishra A, Clark J, Farmer T: **Synthesis, chemistry, physicochemical properties and industrial applications of amino acid surfactants: a review**. *Compt Rendus Chem* 2018, **21**:112–130, https://doi.org/10.1016/j.crci.2017.11.005.

3. Bordes R, Holmberg K: **Amino acid-based surfactants - do they deserve more attention?** *Adv Colloid Interface Sci* 2015, **222**, https://doi.org/10.1016/j.cis.2014.10.013.

4. * Kelleppan VT, King JP, Butler CSG, Williams AP, Tuck KL, Tabor RF: **Heads or tails? The synthesis, self-assembly, properties and uses of betaine and betaine-like surfactants**. *Adv Colloid Interface Sci* 2021, **297**, 102528, https://doi.org/10.1016/j.cis.2021.102528.
A comprehensive review on the betaine and betaine-like surfactants, illustrating the the importance of the effect of the molecular structure on the properties.

5. Wang Z, Yao S, Song K, Gong X, Zhang S, Gao S, Lu Z: **A bio-based benzoxazine surfactant from amino acids**. *Green Chem* 2020, **22**:3481–3488, https://doi.org/10.1039/D0GC00218F.

6. Yan T, Feringa BL, Barta K: **Direct catalytic N-alkylation of α-amino acid esters and amides using alcohols with high retention of stereochemistry**. *ChemSusChem* 2021, **14**: 2303–2307, https://doi.org/10.1002/cssc.202100373.

7. Zhao W, Cheng Y, Lu S, Zhao Y, Zhang Z: **Synthesis and surface activity of novel amino acid surfactants**. *J Surfactants Deterg* 2024, **27**:93–102, https://doi.org/10.1002/jsde.12705.

8. Wang C, Zhang P, Chen Z, Liu Y, Zhao L, Wang N, Xu B: **Effects of fatty acyl chains on the interfacial rheological behaviors of amino acid surfactants**. *J Mol Liq* 2021, **325**, 114823, https://doi.org/10.1016/J.MOLLIQ.2020.114823.

9. Wang N, Yao K, Wang Y, Ti J, Tan J, Liu C, Zhang G, Wang C, Xu B: **Green synthesis, characterization, and properties of acyl lysine, serine, threonine, and methionine derived from three types of natural oils**. *J Surfactants Deterg* 2020, **23**: 239–250, https://doi.org/10.1002/jsde.12365.

10. Yang J, Zhou Y, Yang B, Huang L, Liu C, Han F, Xu B: **Comparative study on the syntheses and properties of three N-lauroyl aromatic amino acid surfactants**. *J Surfactants Deterg* 2020, **23**:687–695, https://doi.org/10.1002/jsde.12405.

11. Shahzadi I, Asim MH, Dizdarević A, Wolf JD, Kurpiers M, Matuszczak B, Bernkop-Schnürch A: **Arginine-based cationic surfactants: biodegradable auxiliary agents for the formation of hydrophobic ion pairs with hydrophilic macromolecular drugs**. *J Colloid Interface Sci* 2019, **552**:287–294, https://doi.org/10.1016/j.jcis.2019.05.057.

12. Cheng W, Anankanbil S, Pérez B, Ilyasoğlu H, Liu G, Guo Z: **Water-mediated catalyst-free synthesis of lysine-based ampholytic amphiphiles for multipurpose applications: characterization and pH-responsive emulsifying properties**. *J Colloid Interface Sci* 2019, **554**:404–416, https://doi.org/10.1016/j.jcis.2019.06.104.

13. Cheng W, Anankanbil S, Pérez B, Pedersen JN, Liu G, Guo Z: **Aspartic-acid-based ampholytic amphiphiles: synthesis, characterization, and pH-dependent properties at air/water and oil/water interfaces**. *J Agric Food Chem* 2019, **67**:2321–2330, https://doi.org/10.1021/acs.jafc.8b05122.

14. Zhu T, Qian D, Duan T, Li J, Yu H, Huang W, Zhou Y, Zhang Z, Sun J: **Carbamate-functional, biobased surfactants derived from cardanol, carbon dioxide, and amino acids: their synthesis and properties**. *J Surfactants Deterg* 2024, **27**:103–113, https://doi.org/10.1002/jsde.12707.

15. Stjerndahl M, Lundberg D, Chauhan V, Bordes R, Holmberg K: **Cleavable surfactants: a comparison between ester, amide, and carbonate as the weak bond**. *J Surfactants Deterg* 2019, **22**:1139–1145, https://doi.org/10.1002/jsde.12247.

16. ** Pinazo A, Pérez L, del Carmen Morán M, Pons R. In *Chapter 13 - arginine-based surfactants: synthesis, aggregation properties, and applications*. Edited by Hayes DG, Solaiman DKY, B.S RDBT, Ashby Second E, AOCS Press; 2019:413–445, https://doi.org/10.1016/B978-0-12-812705-6.00013-7.
A review on gemini surfacatants using amino acids as headgroups. It illustrates the potential benefits for the properties when designing geminis.

17. Faustino C, Martins T, Duarte N, Ribeiro MH: **Self-assembly of lipoaminoacids-DNA based on thermodynamic and aggregation properties**. *J Surfactants Deterg* 2020, **23**:581–593, https://doi.org/10.1002/jsde.12391.

18. Bourkaib MC, Delaunay S, Framboisier X, Hôtel L, Aigle B, Humeau C, Guiavarc'h Y, Chevalot I: **N-acylation of L-amino acids in aqueous media: evaluation of the catalytic performances of Streptomyces ambofaciens aminoacylases**. *Enzym Microb Technol* 2020, **137**, 109536, https://doi.org/10.1016/J.ENZMICTEC.2020.109536.

19. Zhao H, He C, Zhou Y, Yang J, Luo C, Xu B: **Study on foaming properties of N-acyl amino acid surfactants: sodium N-acyl glycinate and sodium N-acyl phenylalaninate**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2019, **567**:240–248, https://doi.org/10.1016/J.COLSURFA.2019.01.073.

20. Zhang Y, Li Y, Ran Z, Wang N, Mekkaoui A, Wang C, Zhao L, Xu B: **Effect of fatty acyl structure on the foam properties of N-acyl serinate surfactants**. *J Oleo Sci* 2023, **72**:715–723, https://doi.org/10.5650/jos.ess23028.

21. Zhang D, Sun Y, Deng Q, Qi X, Sun H, Li Y: **Study of the environmental responsiveness of amino acid-based surfactant sodium lauroylglutamate and its foam characteristics**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2016, **504**:384–392, https://doi.org/10.1016/J.COLSURFA.2016.05.097.

22. Wang Q, Song Z, Han F, Xu B, Xu B: **Synthesis and properties of pH-dependent N-acylglutamate/aspartate surfactants**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2022, **640**, 128474, https://doi.org/10.1016/J.COLSURFA.2022.128474.

23. ** Stubenrauch C, Hamann M, Preisig N, Chauhan V, Bordes R: **On how hydrogen bonds affect foam stability**. *Adv Colloid Interface Sci* 2017, **247**:435–443, https://doi.org/10.1016/j.cis.2017.02.002.
Review discussing the importance of H-bonds between headgroups in foaming, completed by experimental results showing that stable foams are generated with head groups capable of having intersurfactant H-bonds.

24. Preisig N, Schad T, Jacomine L, Bordes R, Stubenrauch C: **How promoting and breaking intersurfactant H-bonds impact foam stability**. *Langmuir* 2019, **35**:14999–15008, https://doi.org/10.1021/acs.langmuir.9b02407.

25. Borkowski M, Batys P, Demchuk OM, Kowalczuk PB, Zawala J: **Amino-acids surfactants and n-octanol Mixtures–Sustainable, efficient, and dynamically triggered foaming systems**. *Ind Eng Chem Res* 2023, **62**:13498–13509, https://doi.org/10.1021/acs.iecr.3c01972.

26. Bae J-E, Kim K, Kang N-G: **Ideal and nonideal mixing effects of amino acid based-surfactant on interfacial rheology and foam properties**. *Korea Aust Rheol J* 2021, **33**:113–122, https://doi.org/10.1007/s13367-021-0010-4.

27. Zhang D, Zhang M, Chen C, Su X: **Responsive wormlike micelles from oleoyl sarcosine triggered by pH and temperature**. *J Mol Liq* 2023, **385**, 122342, https://doi.org/10.1016/J.MOLLIQ.2023.122342.

28. Vu T, Koenig P, Cochran BM, Ananthapadmanabhan KP, Weaver M, Reeder B, Hutton HD, Kasting GB: **Thickening mechanisms for an amino acid-derived surfactant composition**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2020, **589**, 124424, https://doi.org/10.1016/J.COLSURFA.2020.124424.

29. * Vu T, Weaver MR, Kasting GB, Koenig P: **Effect of pH on the structure and dynamics of wormlike micelles in an amino acid-derived surfactant composition**. *Langmuir* 2021, **37**:4112–4120, https://doi.org/10.1021/acs.langmuir.0c03582.
Detailed study of the rheology of the system sodium lauroyl sarcosinate and cocamidopropyl hydroxysultaine (CAHS) and of the effect of the pH on the formation of rodlike micelles.

30. Vu T, Koenig P, Weaver M, Hutton HD, Kasting GB: **Effects of cationic counterions and surfactant on viscosity of an amino acid-based surfactant system**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2021, **626**, 127040, https://doi.org/10.1016/J.COLSURFA.2021.127040.

31. Rajput G, Janni DS, Subramanyam G, Ray D, Aswal V, Varade D: **Novel approach for tuning micellar characteristics and rheology of a sulfate-free anionic surfactant sodium cocoyl glycinate**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2022, **648**, 129426, https://doi.org/10.1016/J.COLSURFA.2022.129426.

32. Jamadagni SN, Ko X, Thomas JB, Eike DM: **Salt- and pH-dependent viscosity of SDS/LAPB solutions: experiments and a semiempirical thermodynamic model**. *Langmuir* 2021, **37**:8714–8725, https://doi.org/10.1021/acs.langmuir.1c00964.

33. Ullah S, Zhang P, Wang Y, Chen Z, Wang C, Liu C, Xu B: **Effect of electrolytes on the interfacial rheological behaviors of N-cocoyl glycinate**. *J Dispersion Sci Technol* 2022, **43**:649–657, https://doi.org/10.1080/01932691.2020.1844736.

34. Liu X, Wu K, Song W, Lei Q, Zhang H, Pan J, Ge X: **Aqueous solution thickening of amino acid-based surfactant by alkylpyrrolidone**. *J Surfactants Deterg* 2022, **25**:7–15, https://doi.org/10.1002/jsde.12544.

35. Gonçalves RA, Holmberg K, Lindman B: **Cationic surfactants: a review**. *J Mol Liq* 2023, **375**, 121335, https://doi.org/10.1016/J.MOLLIQ.2023.121335.

36. * Pinazo A, Manresa MA, Marques AM, Bustelo M, Espuny MJ, Pérez L: **Amino acid–based surfactants: new antimicrobial agents**. *Adv Colloid Interface Sci* 2016, **228**:17–39, https://doi.org/10.1016/J.CIS.2015.11.007.
An overview giving the potential use of amino acid-based surfactants as antibacterial agents. It discusses how the balance between hydrophobicity and hydrophilicity, along with cationic charge density, influences antimicrobial effectiveness.

37. Qi R, Zhang N, Zhang P, Zhao H, Liu J, Cui J, Xiang J, Han Y, Wang S, Wang Y: **Gemini peptide amphiphiles with broad-spectrum antimicrobial activity and potent antibiofilm capacity**. *ACS Appl Mater Interfaces* 2020, **12**:17220–17229, https://doi.org/10.1021/acsami.0c01167.

38. Qi R, Zhang P, Liu J, Zhou L, Zhou C, Zhang N, Han Y, Wang S, Wang Y: **Peptide amphiphiles with distinct supramolecular**

nanostructures for controlled antibacterial activities. *ACS Appl Bio Mater* 2018, **1**:21–26, https://doi.org/10.1021/acsabm.8b00005.

39. * Shen Y, Lin H, Yang M, Gong X, Guan B, Han Y, Wang S, Wang Y: **Hierarchical superstructure of plant polyphenol and arginine surfactant for long-lasting and target-selective antimicrobial application**. *Adv Mater* 2023, **35**, 2210936, https://doi.org/10.1002/adma.202210936.
A study reporting the use of arginine based surfactants combined with polyphenol towards antibacterial propoerties.

40. Perinelli DR, Petrelli D, Vitali LA, Vllasaliu D, Cespi M, Giorgioni G, Elmowafy E, Bonacucina G, Palmieri GF: **Quaternary ammonium surfactants derived from leucine and methionine: novel challenging surface active molecules with antimicrobial activity**. *J Mol Liq* 2019, **283**: 249–256, https://doi.org/10.1016/J.MOLLIQ.2019.03.083.

41. Pérez L, Pinazo A, Morán MC, Pons R: **Aggregation behavior, antibacterial activity and biocompatibility of catanionic assemblies based on amino acid-derived surfactants**. *Int J Mol Sci* 2020, **21**, https://doi.org/10.3390/ijms21238912.

42. V Kapitanov I, Jordan A, Karpichev Y, Spulak M, Perez L, Kellett A, Kümmerer K, Gathergood N: **Synthesis, self-assembly, bacterial and fungal toxicity, and preliminary biodegradation studies of a series of l-phenylalanine-derived surface-active ionic liquids**. *Green Chem* 2019, **21**:1777–1794, https://doi.org/10.1039/C9GC00030E.

43. Perinelli DR, Cespi M, Casettari L, Vllasaliu D, Cangiotti M, Ottaviani MF, Giorgioni G, Bonacucina G, Palmieri GF: **Correlation among chemical structure, surface properties and cytotoxicity of N-acyl alanine and serine surfactants**. *Eur J Pharm Biopharm* 2016, **109**:93–102, https://doi.org/10.1016/J.EJPB.2016.09.015.

44. Kalebic D, Binnemans K, de Witte PAM, Dehaen W: **Synthesis, physicochemical characterization and aquatic toxicity studies of anionic surfactants derived from amino and α-hydroxy acids**. *RSC Sustain* 2023, **1**:1995–2005, https://doi.org/10.1039/D3SU00189J.

45. Song Y, Gao S, Yao Y, Zheng H, Niu Y: **Synergism and properties of binary mixtures based on an arginine dodecyl ester surfactant**. *New J Chem* 2022, **46**:18342–18350, https://doi.org/10.1039/D2NJ02680E.

46. Hossain F, Ohta A, Yamane Y, Shizuka A, Asakawa H, Asakawa T: **Study of antioxidative properties of some mono amino-acid-type and dipeptide-type surfactants**. *J Surfactants Deterg* 2018, **21**:733–744, https://doi.org/10.1002/jsde.12180.

47. Borkowski M, Orvalho S, Warszyński P, Demchuk OM, Jarek E, Zawala J: **Experimental and theoretical study of adsorption of synthesized amino acid core derived surfactants at an air/water interface**. *Phys Chem Chem Phys* 2022, **24**:3854–3864, https://doi.org/10.1039/D1CP05322A.

48. Wu R, Qiu X, Shi Y, Deng M: **Molecular dynamics simulation of the atomistic monolayer structures of N-acyl amino acid-based surfactants**. *Mol Simulat* 2017, **43**:491–501, https://doi.org/10.1080/08927022.2016.1261289.

49. Bordes R, Tropsch J, Holmberg K: **Role of an amide bond for self-assembly of surfactants**. *Langmuir* 2010, **26**:3077–3083, https://doi.org/10.1021/la902979m.

50. Sakai K, Sawada M, Ikeda N, Akamatsu M, Sakai H: **Adsorption and lubrication of glutamic acid-based surfactant with calcium ions**. *J Oleo Sci* 2023, **72**:709–714, https://doi.org/10.5650/jos.ess23049.

51. Bonini M, Gabbani A, Del Buffa S, Ridi F, Baglioni P, Bordes R, Holmberg K: **Adsorption of amino acids and glutamic acid-based surfactants on imogolite clays**. *Langmuir* 2017, **33**, https://doi.org/10.1021/acs.langmuir.6b04414.

52. Serafim C, Ferreira I, Rijo P, Pinheiro L, Faustino C, Calado A, Garcia-Rio L: **Lipoamino acid-based micelles as promising delivery vehicles for monomeric amphotericin B**. *Int J Pharm* 2016, **497**:23–35, https://doi.org/10.1016/J.IJPHARM.2015.11.034.

53. Branco MA, Pinheiro L, Faustino C: **Amino acid-based cationic gemini surfactant–protein interactions**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2015, **480**:105–112, https://doi.org/10.1016/J.COLSURFA.2014.12.022.

54. Anchev BA, Tsekova DS, Mircheva KM, Grozev NA: **Monolayer formed by l-Asp-based gemini surfactants self-assembled in 1D nanostructures**. *RSC Adv* 2019, **9**:33071–33079, https://doi.org/10.1039/C9RA06390K.

55. Pérez L, Pinazo A, Pons R, Infante Mr: **Gemini surfactants from natural amino acids**. *Adv Colloid Interface Sci* 2014, **205**: 134–155, https://doi.org/10.1016/j.cis.2013.10.020.

56. Olutas EB, Taskesen T, Kartal NB: **Double-tailed single-head amino acid-based chiral cationic amphiphilic molecules: synthesis, characterization, and physicochemical properties**. *J Surfactants Deterg* 2020, **23**:153–168, https://doi.org/10.1002/jsde.12341.

57. Lewis C, Hughes BH, Vasquez M, Wall AM, Northrup VL, Witzleb TJ, Billiot EJ, Fang Y, Billiot FH, Morris KF: **Effect of pH on the binding of sodium, lysine, and arginine counterions to l-undecyl leucinate micelles**. *J Surfactants Deterg* 2016, **19**: 1175–1188, https://doi.org/10.1007/s11743-016-1875-y.

58. * Fletcher J, Mahant G, Witzleb T, Busche R, Garcia M, Fang Y, Billiot EJ, Billiot FH, Morris KF: **NMR investigation of counterion binding to undecyl LL-leucinevalanate micelles**. *J Dispersion Sci Technol* 2024, **45**:284–295, https://doi.org/10.1080/01932691.2022.2145303.
A study reporting the influence of the chemical structure on the counterion binding to undecyl LL-leucinevalanate micelles.

59. Sun L, Gong J, Xu B, Wang Y, Ding X, Zhang Y, Liu C, Zhao L, Xu B: **Ion-specific effects on vesicle-to-micelle transitions of an amino acid surfactant probed by chemical trapping**. *Langmuir* 2022, **38**:6295–6304, https://doi.org/10.1021/acs.langmuir.1c03415.

60. Ullah S, Yao K, Zhang P, Wang Y, Chen Z, Liu C, Wang C, Xu B: **Effect of added tetraalkylammonium counterions on the dilational rheological behaviors of N-cocoyl glycinate**. *J Oleo Sci* 2020, **69**:883–891, https://doi.org/10.5650/jos.ess20031.

61. * Ikeda N, Aramaki K: **Hydrogel Formation by glutamic-acid-based organogelator using surfactant-mediated gelation**. *J Oleo Sci* 2022, **71**:1169–1180, https://doi.org/10.5650/jos.ess22080.
A study on the potential use of amino acid based surfactant as organogelator, where the role of the amide bond is visible on the gelling.

62. Angulo-Pachón CA, Pozo V, Miravet JF: **Alkaline cations dramatically control molecular hydrogelation by an amino acid-derived anionic amphiphile**. *J Colloid Interface Sci* 2023, **635**:524–534, https://doi.org/10.1016/J.JCIS.2022.12.134.

63. Chen C, Luan H, Lei Z, Li L, Feng Z, Zhang D, Su X, Feng Y: **Lauroyl arginate ethyl: a novel bio-based CO2-switchable surfactant**. *J Surfactants Deterg* 2023, **26**:761–769, https://doi.org/10.1002/jsde.12692.

64. Ananthapadmanabhan KP: **Amino-acid surfactants in personal cleansing**. *Tenside Surfactants Detergents* 2019, **56**:378–386, https://doi.org/10.3139/113.110641.

65. Navarro-Triviño FJ, Ayén-Rodríguez Á, Ruiz-Villaverde R: **Allergic contact dermatitis caused by capryloyl glycine in an atopic dermatitis patient**. *Australas J Dermatol* 2022, **63**: e259–e261, https://doi.org/10.1111/ajd.13853.

66. Hawkins S, Dasgupta BR, Ananthapadmanabhan KP: **Role of pH in skin cleansing**. *Int J Cosmet Sci* 2021, **43**:474–483, https://doi.org/10.1111/ics.12721.

67. Wang FC, Marangoni AG: **Effect of intrinsic and extrinsic factors on the stability of the α-gel phase of a glyceryl monostearate–water system**. *RSC Adv* 2015, **5**:43121–43129, https://doi.org/10.1039/C5RA05045F.

68. Ren H, Tang X, Chen M: **Preparation and characterization of alpha gel formed by fatty alcohol and amino acid surfactants**. *J Surfactants Deterg* 2021, **24**:865–870, https://doi.org/10.1002/jsde.12539.

69. Manyala DL, Ghosh M, Dalai S: **Novel microemulsions formulated from sodium N-Lauroyl sarcosinate as nanocarrier for encapsulation of α-Tocopherol**. *J Mol Liq* 2023, **384**, 122323, https://doi.org/10.1016/J.MOLLIQ.2023.122323.

70. Aramaki K, Shiozaki Y, Kosono S, Ikeda N: **Coacervation in cationic polyelectrolyte solutions with anionic amino acid surfactants**. *J Oleo Sci* 2020, **69**:1411–1416, https://doi.org/10.5650/jos.ess20159.

71. Zhang W, Gao Z, Zhu H, Zhang Q: **Mixed micellization of cationic/anionic amino acid surfactants: synergistic effect of sodium lauroyl glutamate and alkyl tri-methyl ammonium chloride**. *J Dispersion Sci Technol* 2022, **43**:2227–2239, https://doi.org/10.1080/01932691.2021.1929289.

72. Shahzadi I, Asim MH, Dizdarević A, Wolf JD, Kurpiers M, Matuszczak B, Bernkop-Schnürch A: **Arginine-based cationic surfactants: biodegradable auxiliary agents for the formation of hydrophobic ion pairs with hydrophilic macromolecular drugs**. *J Colloid Interface Sci* 2019, **552**:287–294, https://doi.org/10.1016/J.JCIS.2019.05.057.

73. * Matteo Jörgensen A, Knoll P, Haddadzadegan S, Fabian H, Hupfauf A, Gust R, Georg Jörgensen R, Bernkop-Schnürch A: **Biodegradable arginine based steroid-surfactants: cationic green agents for hydrophobic ion-pairing**. *Int J Pharm* 2023, **630**, 122438, https://doi.org/10.1016/J.IJPHARM.2022.122438.
A study that highlights the potential of arginine-based surfactants in forming ion pairs to promote lypophilicity of peptide for drug delivery systems.

74. Kurpiers M, Wolf JD, Spleis H, Steinbring C, Jörgensen AM, Matuszczak B, Bernkop-Schnürch A: **Lysine-based biodegradable surfactants: increasing the lipophilicity of insulin by hydrophobic ion paring**. *J Pharmaceut Sci* 2021, **110**:124–134, https://doi.org/10.1016/J.XPHS.2020.07.024.

75. Hu B, Yuan Y, Yan Y, Zhou X, Li Y, Kan Q, Li S: **Preparation and evaluation of a novel anticancer drug delivery carrier for 5-Fluorouracil using synthetic bola-amphiphile based on lysine as polar heads**. *Mater Sci Eng C* 2017, **75**:637–645, https://doi.org/10.1016/J.MSEC.2017.02.106.

76. Gonçalves Lopes RCF, Silvestre OF, Faria AR, do Vale MLC, Marques EF, Nieder JB: **Surface charge tunable catanionic vesicles based on serine-derived surfactants as efficient nanocarriers for the delivery of the anticancer drug doxorubicin**. *Nanoscale* 2019, **11**:5932–5941, https://doi.org/10.1039/C8NR06346J.

77. Wolf JD, Kurpiers M, Baus RA, Götz RX, Griesser J, Matuszczak B, Bernkop-Schnürch A: **Characterization of an amino acid based biodegradable surfactant facilitating the incorporation of DNA into lipophilic delivery systems**. *J Colloid Interface Sci* 2020, **566**:234–241, https://doi.org/10.1016/j.jcis.2020.01.088.

78. Oliveira IS, Silva JPN, Araújo MJ, Gomes AC, Marques EF: **Biocompatible thermosensitive nanostructures and hydrogels of an amino acid-derived surfactant and hydroxyethyl cellulose polymers**. *J Mol Liq* 2021, **322**, 114540, https://doi.org/10.1016/J.MOLLIQ.2020.114540.

79. Hermet M, Espinosa YR, Fait ME, Zulueta Díaz YdlM, Morcelle S, Bakás LS, Ariel Alvarez HA, Fanani ML: **Arginine-based surfactants alter the rheological and in-plane structural properties of stratum corneum model membranes**. *J Colloid Interface Sci* 2023, **631**:224–238, https://doi.org/10.1016/J.JCIS.2022.10.118.

80. Patra A, Taner HA, Bordes R, Holmberg K, Larsson A-C: **Selective flotation of calcium minerals using double-headed collectors**. *J Dispersion Sci Technol* 2019, **40**:1205–1216, https://doi.org/10.1080/01932691.2018.1503547.

81. Arkhipov VP, V Arkhipov R, Filippov A: **Dynamic and molecular association in premicellar aqueous solutions of dicarboxylate amino acid-based surfactant as studied by 1H NMR**. *Magn Reson Chem* 2022, **60**:359–368, https://doi.org/10.1002/mrc.5222.

82. Wang L, Wang G, Ge P, Sun W, Tang H, Hu W: **Activation mechanisms of quartz flotation with calcium ions and cationic/anionic mixed collectors under alkalescent conditions**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2022, **632**, 127771, https://doi.org/10.1016/J.COLSURFA.2021.127771.

83. Guo W, Han Y, Zhu Y, Li Y, Tang Z: **Effect of amide group on the flotation performance of lauric acid**. *Appl Surf Sci* 2020, **505**, 144627, https://doi.org/10.1016/J.APSUSC.2019.144627.

84. Li J, Nie G, Li J, Zhu Z, Wang Z: **Flotation separation of quartz and dolomite from collophane using sodium N-dodecyl-β-amino propionate and its adsorption mechanism**. *Colloids Surfaces A Physicochem. Eng. Asp.* 2022, **641**, 128586, https://doi.org/10.1016/J.COLSURFA.2022.128586.

85. Cao Q, Zou H, Chen X, Wen S: **Flotation selectivity of N-hexadecanoylglycine in the fluorapatite–dolomite system**. *Miner Eng* 2019, **131**:353–362, https://doi.org/10.1016/J.MINENG.2018.11.033.

86. Peng Z, Sun L, Cao Y, Fan X, Sun W, Wang Q: **Sodium lauroyl glutamate as a collector in cassiterite flotation**. *Minerals* 2023, **13**, https://doi.org/10.3390/min13010061.

87. Sun H, Ma X, Fei L, Cao Z, Zhong H, Wang S: **Amide group enhanced self-assembly and adsorption of dicarboxylic amino acid surfactants on a rhodochrosite surface through intermolecular weak interaction**. *Sep Purif Technol* 2023, **309**, 122905, https://doi.org/10.1016/J.SEPPUR.2022.122905.

88. Fei L, Sun Q, Wang S, Cao Z, Sun H, Zhong H, Ma X: **Inter-/intramolecular synergism improve self-assembly behavior of hydroxamate-modified amino acid surfactant for flocculation of micro-fine particles**. *Chem Eng Sci* 2023, **282**, 119345, https://doi.org/10.1016/J.CES.2023.119345.

89. Fei L, Ma X, Sun H, Wang S, Cao Z, Zhong H, Deng L: **Understanding adsorption mechanism of a novel "Y" structure carboxylate-hydroxamate surfactant towards rhodochrosite**. *Miner Eng* 2023, **203**, 108310, https://doi.org/10.1016/J.MINENG.2023.108310.