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Soap and syndets: differences and analogies, sources of great confusion

L. COIFFARD, C. COUTEAU

Université de Nantes, Nantes Atlantique Universités, Faculty of Pharmacy, Nantes, France

Abstract. – OBJECTIVE: Soap has been used by humankind since ancient times and was probably already known to the Sumerians. It is a fatty acid salt obtained from the reaction of a strong base with a fatty substance of animal (tallow) or plant origin (oil). This reaction is called saponification. Syndets, on the other hand, are much more recent and have been in use for about a century. In the case of liquid syndets, they are mainly alkyl sulphates and their derivatives alkyl ether sulphates while isethionates and sarcosinates are more commonly found in solid syndets. Synthetic soaps and detergents are surfactants and, as such, they have detergent properties. The way soap works accounts for its antimicrobial properties. Thanks to its amphiphilic structure, it is able to interact with the lipid membranes of microorganisms (viruses, bacteria, etc.) and inactivate them.

In this coronavirus pandemic period, health authorities worldwide recommend hand washing with soap and water. We therefore wanted to provide a summary of the chemical characteristics and applications of soaps, on the one hand, and synthetic detergents, on the other. Soap is not the only product used for hand hygiene and, given the current situation, alternatives are complex and varied.

Key Words:
Soap, Syndet, Chemistry, Properties, Barrier gestures.

Introduction

Although it is likely that the Babylonians and even the Sumerians were familiar with soap[1], it is the Greeks and the Romans who have given us more explicit references. Physicians and poets of antiquity provide us with valuable insights on its cosmetic and medicinal uses[2-6]. We must believe in Pliny the Elder and disregard the legend by which the first saponification took place on Mount Sapo, a site close to Rome where animals were sacrificed. Animal fat was mixed with the plant ash and the addition of rainwater formed a soapy mixture. It would therefore be more accurate to attribute the invention of soap to the Gauls. This substance, prepared from tallow and beech wood ash, was used by the inhabitants of Gaul to dye their hair red and to treat a variety of skin conditions[7,8].

Still considered a medicinal product in the 19th century, it was the Act of 1975[9], and then Directive 76/768/EEC[10] that made it a cosmetic. Syndet (synthetic detergent) cleansing bars have a much shorter history, and their relatively recent use corresponds to a need in certain circumstances to have a hygiene product without the adverse effects of soap.

During this period of the COVID-19 pandemic, thorough and frequent handwashing is at the core of the contamination prevention strategy and is one of the main protective measures.

We hereby propose to clarify the situation by highlighting the differences that exist between soap and syndet cleansing bars.

Soap, a Very Ancient Product with Multiple Uses

A Review of Soap Chemistry

Soap is a salt of fatty acid, obtained through the reaction of a strong base with fat of animal or vegetable origin. This reaction is known as saponification[11,12] and occurs as shown in Figure 1. The strong base in question can be soda or potash, and the choice between the two will influence the nature of the resulting soap at room temperature: soaps from soda are solid, whereas soaps from potash are liquid. In the latter case we speak of "black soaps" as opposed to those obtained from soda, which are known as "white soaps".

The fat of animal origin, which is still used today, is tallow, a substance composed mainly of saturated fatty acids (palmitic and stearic acids) and an unsaturated fatty acid (oleic acid)[13]. A va-

Corresponding Author: Laurence JM Coiffard, MD; e-mail: laurence.coiffard@univ-nantes.fr

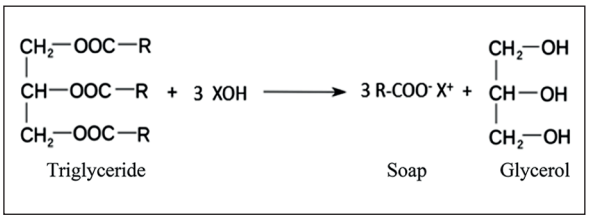


Figure 1. Saponification reaction. Where X = Na or K and R is a hydrocarbon chain of 10 to 18 carbon atoms.

riety of oils can be used, including palm oil, palm kernel oil, coconut oil or olive oil, to name only the most common[14]. With regard to olive oil, it was in 1688 that Louis XIV laid out specific rules of manufacture, through the Edict of Colbert, that defined Marseille soap. It is made by cooking in large boilers and is based strictly on olive oil. It still does not carry a PDO (Protected Denomination of Origin) label, with the sole importance being the method of manufacture; therefore, a soap labeled "Marseille" can be produced anywhere in France.

In all cases, the result of saponification is the production of a detergent, emulsifying and foaming substance.

Uses and Properties of Soaps

One of the main uses of soap in antiquity was clearly medical. For example, the physician Asclepiades of Bithynia, in his treatise on colds, provided ten soap-based (saponon) formulas for "clearing the head", including one intended for "drawing out phlegm"[5]. Galen makes reference to soap very often. The indications are extremely broad since they cover calluses as well as elephantiasis[5]. The African Cassius Félix in the 5th century proposed a recipe for soap to be used "in a burning bath" to treat itching, which serves here as an excipient. In the 6th century, the Gaul Marcellus reported the use of various soaps to treat tinea, nail suppuration or to facilitate the healing of burn scars[5]. In the 17th century, soap was still used for medical purposes, as shown in the guidance of Louise Bourgeois, the appointed midwife of Queen Marie de Médicis, who advised using "a small piece of white soap as a small, strong suppository, and rubbed with fresh butter" to promote expulsion of meconium[15,16]. It is to Michel-Eugène Chevreul that one owes, in 1823, the rationalization of the saponification process which he approaches in scientific[17]. This will allow the industrialization of soap production. In the 19th century, two uses for soap were clearly identified: firstly, cosmetic use, which used dyed and perfumed toilet soaps, and secondly, medical use, for which there were "medicinal soaps". Soap served as an excipient in these latter preparations, to which additions were made of camphor, to treat frostbite; tannin, to combat excessive sweating of the feet; or carbolic acid (the former name for phenol), to be used if an individual was in contact with someone with a contagious disease, which is reminiscent of its current use. Tar soap and salicylic acid soap were used to treat "skin eruptions". These are only a few examples of the many soap formulas. In the first half of the 20th century, medicinal soap was still recommended in some disorders such as scabies[18]. Without specific regulations, the distinction between different types of soaps was therefore based solely on the composition of the products. In some cases, medicinal active principles were present; in others, nothing at all was added, as in the case of Marseille soap, or only organoleptic additives consisting of dyes and fragrances. Some could be manufactured extemporaneously at the pharmacy per medical prescription, and others produced industrially. Because of the separate respective definitions of medicines and cosmetics, it is no longer possible for a product that belongs to the category of cosmetics to claim any therapeutic action. The current definition of a cosmetic product, which differs very little from the original definition, is that set out in Article 2 of Regulation (EC) No. 1223/2009, which took effect in July 2013[19]. As a result, a cosmetic may only claim properties relating to hygiene, perfuming, changes in appearance and skin protection, as well as control of body odors. There can be no question of claiming curative or preventive properties with regard to human diseases, properties that would otherwise make it a medicine or possibly a medical device. Furthermore, based on Annex II to Regulation (EC) No. 1223/2009, which establishes the list of substances prohibited in cosmetics, it has become impossible, for example, to produce phenol soaps as in the past. The last soaps to have been marketed that could qualify as medicinal were sulfur soaps, which were recommended for daily cleansing in patients with acne or oily skin, before its distribution was completely stopped once it was found to be comedogenic[20].

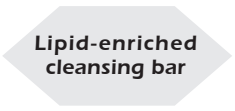
Outside the time of a pandemic, soap today is a basic hygiene cosmetic product that is used for daily cleansing. Its other uses are domestic, with the washing of laundry and surfaces, although these have become rather marginal.

The different types of soaps currently on the market are compiled in Table I. We find toilet soap, for example, which includes several sodium salts of fatty acids based on tallow (sodium tallowate) or a vegetable oil (sodium cocoate, sodium palmate, sodium palm kernelate, etc.). A soap is said to be lipid-enriched when excess fat is added relative to the base and its component triglycerides are therefore not saponified. Finally, liquid soap, as stated previously, is made with potash. This type of soap therefore consists of a molecule like potassium cocoate.

A category of products that remains on the market is known as "antiseptic soaps", which are intended for the disinfection of hands and avoidance of hand-transmitted contamination. They must meet the clearly defined criteria of bactericidal, fungicidal and/or viricidal efficacy described in the corresponding standards: Standards NF EN 1040, 13727, 1500, 1275, 1650, 13624 and/or NF EN 14476, respectively. Labelling them as soap is a misnomer since in reality, they are liquid syndets with an added antiseptic agent, e.g., chlorhexidine digluconate. They have a status as "medical devices", which is logical because of their function and that they are intended for hand disinfection of health workers, particularly in hospital settings. Such procedures have been in place since the end of the 19th century, as demonstrated by the conference delivered at Saumur in 1890 by Dr. Péton[21] at the inauguration of the Société de l'Union des Femmes de France [Society of the Union of French Women]. It concerned only soap, as syndets had not yet been invented. The current situation in the industry is that products that differ greatly in their composition and their status exist side by side, and yet all are usually referred to as 'soap'.

In this context and in the present circumstances of the COVID-19 pandemic, the French Ministry of Solidarity and Health provides a summary on its website of the protective measures applicable to all persons and essential for blocking the spread of the coronavirus. The first stated

Table I. Different types of soap available.

Name	Pharmaceutical form	Characteristic(s)	Standard formula
Marseille soap		One or more sodium salts of fatty acids No additives	Sodium tallowate, aqua (water), sodium cocoate, glycerin, sodium chloride, sodium hydroxide
Toilet soap		One or more sodium salts of fatty acids Additives present (dyes, fragrances, etc.)	Sodium palmate, sodium tallowate, sodium palm kernelate, aqua (water), glycerin, lauric acid, fragrance, sodium chloride, pentasodium pentetate, pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate, benzyl salicylate, butylphenyl methylpropional, citronellol, coumarin, limonene, linalool, CI77891, CI 47005, CI 61570
Lipid-enriched cleansing bar		One or more sodium salts of fatty acids Excess fat relative to the base	Sodium tallowate, sodium cocoate, sodium palm kernelate, Aqua (Water), lanolin, glycerin, Prunus dulcis, Prunus persica, fragrance, coconut acid, pentasodium pentetate, sodium chloride.
Liquid soap		One or more potassium salts of fatty acids	Water, potassium cocoate, glycerin, Cocos nucifera oil, Olea europaea fruit oil, caprylyl glycol, disodium phosphate, polysorbate 20, potassium olivate, polysorbate 60, hydroxyethylcellulose, disodium EDTA, sodium phosphate, BHT, fragrance, alpha-isomethyl ionone, limonene, linalool

measure is very regular handwashing. It is noted that "hands must be systematically washed with soap (preferably liquid) and water, or alternatively with hand sanitizer (hydroalcoholic solution) 1) before caring for a baby, preparing meals, serving meals or eating; and 2) after nose blowing, having coughed or sneezed, visiting a sick person, caring for a baby, after each outing, after having taken public transport when arriving at work or home, or having used the toilet."[22]. Soap is thus considered preferable to hand sanitizer, which has the status of a "medical device". This then raises the question of what the status of soap should be. In the context we are concern with here, soap implicitly (at the very least!) has the status of a medical device because of the function it has been assigned. The efficacy of handwashing with soap and water has been documented with regard to viruses such as the H1N1 virus[23] but also in the prevention of diarrhea of microbial origin[24-26]. It is difficult to know, however, what various authors mean by the term "soap" since we have seen that it does not necessarily involve fatty acid salt. And yet, the empirical use by health workers, like the renowned Florence Nightingale, a pioneer in nursing care at the end of the 19th century, leads us to think that it really involves just soap[27]. It is readily apparent that soap makers are not ready to accept the status of medical device for the product they manufacture and the procedure for obtaining the CE marking associated with it. This therefore means that no mention of any antiseptic effect is made on the packaging and only the authorities can communicate the value of using such a product during an epidemic.

Soaps are classified as anionic surfactants since they are capable of ionizing in aqueous solution; the largest ion generated is an anion. As surfactants, they are emulsifiers, i.e., key substances in the creation and stability of emulsions. Indeed, these amphiphilic molecules are capable of interacting with both water and fats[28]. Stearate creams, which are also foaming agents[29,30], have been attracting interest for some time. Lastly, they are detergents. Detergency is the ability of a substance to remove dirt from solid surfaces, such as the skin (in the case of soap), or any other surfaces, such as textiles (in the case of laundry soap), and then to enable its elimination by rinsing[30]. The simple fact of handwashing with soap and water considerably reduces the hands' microbial load[31]. The characteristics of soaps explain their antimicrobial properties. Indeed, owing to their amphiphilic structure, they are capable of interacting with lipid membranes of microorganisms, thereby inactivating them[32]. A number of studies have tended to show that soap is more effective than alcohol-based disinfectants, which are unable to eliminate all types of germs, whether these are viruses like noroviruses or the H1N1 type virus, or bacteria such as *Clostridioides difficile*[33-35]. Soap thus constitutes a protective measure that is easy to implement, accessible to most people, and economical.

Adverse Effects of Soaps

As we have seen, soaps are detergents, which contributes to their cleaning effect. Their second property, which is a source of skin discomfort, is their alkaline pH[36,37]. A pH between 11.0 and 12.0 can very easily be reached, and this results in a transient increase in skin pH. Normally, the pH of the skin is acid (mean pH close to 5.5) because of the physiological buffering systems present on it. After using soap, it will return to its normal value within a variable time period. These two elements combined, detergency and alkaline pH, are responsible for what is commonly referred to as a "soap effect", which corresponds to an alteration in the skin barrier[38,39].

Regulatory Issues Concerning Soaps

In Europe, soaps are cosmetic products. They fall within the definition of Article 2 of Regulation (EC) No. 1223/2009. To comply with this definition, there can be no claim of any curative or even preventive property with regard to human or animal diseases, properties that themselves fall within the definition of a medicinal product. This has resulted in some regulatory uncertainty relative to soap use during the coronavirus pandemic.

Synthetic Detergents: Century-Old Substances That Also Have Multiple Uses

Historical Aspects

The history of synthetic detergents is much more recent than that of soaps, beginning only in 1916[40]. It was following World War II, at the end of the 1940s[41], that their development took off to gradually gain major importance in the areas of personal hygiene, as well as laundry products. They currently account for 60% of the global production of surfactants[42] and are of considerable industrial importance since they are the basis of formulation for both personal care products and laundry products.

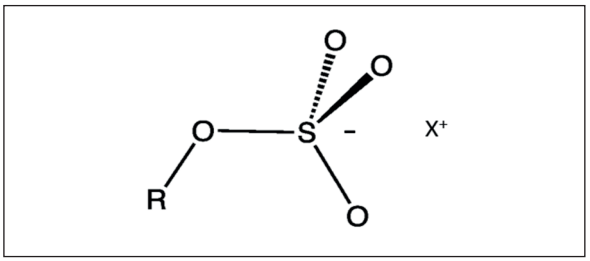


Figure 2. Chemical structure of an alkyl sulfate. R = hydrocarbon chain including 12 to 18 carbon atoms; X = Na, K or NH_4.

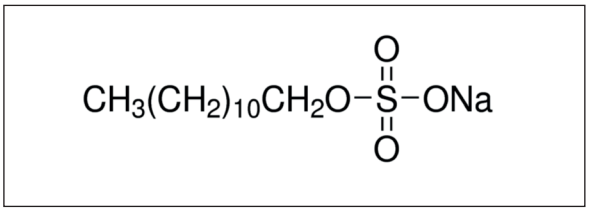


Figure 3. Chemical structure of sodium lauryl sulfate.

A review of Chemistry

The synthetic detergents of interest to us here are mainly alkyl sulfates (Figure 2) and their derivatives, often improperly referred to in the field of marketing as "sulfates".

Leading this family of alkyl sulfates is sodium lauryl sulfate (or dodecyl sulfate) (Figure 3), a molecule that includes 12 carbon atoms that is synthesized from lauryl alcohol and sulfur trioxide[43].

Because of their irritant potential, which will be discussed below, alkyl sulfates have now been nearly abandoned (with the exception of a few organic shampoos in which they are still found) in favor of alkyl ether sulfate homologues. These alkyl ether sulfate products are obtained through ethoxylation (or polyoxyethylenation) of their corresponding alkyl sulfates. In this reaction, ethyl oxide radicals are grafted, as seen in Figure 4.

Ethoxylation decreases the irritant nature of alkyl sulfates without, however, eliminating it. The procedure of ethoxylation is not authorized under charters for organic products, so alkyl ether sulfates cannot be used in this brand products of this type.

Isethionates and sarcosinates are now generally used, almost exclusively in shampoos and shower products, for the formulation of soap-free cleansers, syndets or cleansing bars (Table II). In the family of isethionates, the most common compounds are alkyl chains (C12-18) derived from coconut oil, such as sodium cocoyl isethionate. They are obtained through condensation of a fatty acid with sodium isethionate ($HO\text{-}(CH_2)_2\text{-}SO_3Na$) in the presence of a catalyst and at a temperature from 180 to 200°C[44]. In addition to their value in the formulation of syndet cleansing bars, they are used for the manufacture of solid shampoos (which, in fact, are cleansing bars), and which are currently having some success.

N-acetyl sarcosinates are derivatives of an amino acid, sarcosine (or N-methylglycine) and a fatty acid. They are obtained via the Schotten-Baumann reaction between an acid chloride (R-COCl) and sodium sarcosinate ($CH_3\text{-}NH\text{-}(CH_2)_2COONa$)[44].

Properties of Synthetic Detergents

As with soaps, syndets are anionic surfactants since they also act as amphiphilic molecules[45]. And like them, they are wetting agents[46], emulsifiers, detergents (hence their name) and foaming agents.

Adverse Effects of Synthetic Detergents

Since these are condensation reactions, their production does not involve a strong base, and as a result synthetic detergents are not capable of altering skin pH as soaps do. However, like soaps, their detergency can disrupt the skin's barrier function[47,48].

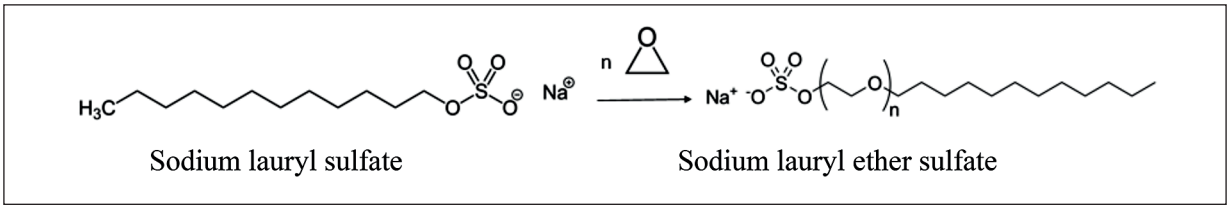
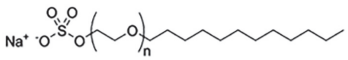
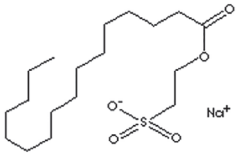
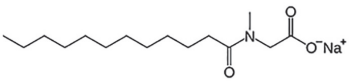
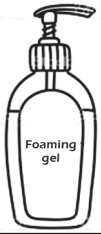


Figure 4. Ethoxylation reaction.

Table II. Different anionic surfactants families.

Chemical family	Chemical structure	Pharmaceutical form	Standard formula
Alkyl ether sulfates	 Sodium lauryl ether sulfate		Aqua (water), sodium laureth sulfate, glycerin, cocamidopropyl betaine, PEG-7 glyceryl cocoate, cocamide MEA, sodium salicylate, sodium benzoate, fragrance, citric acid, tetrasodium EDTA, limonene, CI 19140, CI 17200.
Isethionates	 Sodium cocoyl isethionate	Cleansing ba	Sodium cocoyl isethionate, cetearyl alcohol, glyceryl stearate, paraffin, aqua (water), cocamidopropyl betaine, citric acid, PEG-150, sodium chloride, octyldodecanol
Sarcosinates	 Sodium lauroyl sarcosinate		Aqua (water), sodium lauroyl sarcosinate, acrylates/ steareth-20 methacrylate copolymer, lauryl glucoside, glycerin, phenoxyethanol, tetrasodium EDTA, citric acid, potassium sorbate, sodium benzoate

Their irritant potential varies according to which substance is considered. It is very significant and has been long known for alkyl sulfates[49]. Sodium lauryl sulfate is an irritant agent, capable of inducing serious eye damage that can lead to blindness through contact with the eyes. The irritant effect is seen through skin contact at concentrations over 2%[43]. This makes it the reference molecule for modeling irritation *in vivo* by means of patches[49,50]. This irritant effect is determined by the concentration of lauryl sulfate applied and the contact time[49,51]. In the field of cosmetics, in certain organic shampoo formulations, only ammonium lauryl sulfate remains, which is just as irritant as the sodium salt or even more so[52].

Lauryl sulfate appears to enhance the antimicrobial effect of a number of substances, hence its incorporation in foaming solutions in the past (Table III).

Regulatory Issues Concerning Foaming Solutions

The vast majority of foaming solutions have a status of cosmetic products and therefore, like soaps, meet the requirements of (EC) Regulation No. 1223/2009 and, above all, the definition it gives. A few of them, however, once had a status as medicinal products (Table III) but are no longer commercially available.

Conclusions

Products that can be used for hand hygiene are therefore highly diverse both from a chemical viewpoint and in their pharmaceutical forms. It is therefore always important to know what is being referred to and to be able to accurately identify what, for example, will benefit a patient.

Table III. Examples of foaming solutions with antimicrobial properties.

Active substance(s)	Brand names	Status	Remarks
Mercurobutol	Mercryl lauryle	Medicinal product	Marketing discontinuation
Oxyquinol, salicylic acid	Dermacide	Medicinal product	Marketing discontinuation

Conflict of Interest
The Authors declare that they have no conflict of interests.

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