REVIEW ARTICLE

Surfactants, skin cleansing protagonists

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Abstract

The correct choice of cosmetic products and cleansers is very important to improve skin hydration, to provide moisturizing benefits and to minimize cutaneous damage caused by surfactants. In fact, surfactants may damage protein structures and solubilize lipids. Soaps, defined as the alkali salts of fatty acids, are the oldest surfactants and are quite aggressive. Syndets (synthetic detergents) vary in composition and surfactant types (anionic, cationic, amphotheric, non-ionic). These new skin cleansing products also contain preservatives, fragrances, and sometimes emollients, humectants and skin nutrients. We present a revision of the literature and discuss recent findings regarding skin cleansers.

Keywords cutaneous cleansers, irritation, occlusive patch test, open test, surfactants, syndet

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Introduction

It is only recently that dermatologists focused their attention on skin cleansing, regarding it as an essential part of skin care. Cleansers have the indispensable role to remove dirt, sebum, sweat, microorganisms and exfoliated corneum cells from the skin, but they may cause repeated and subclinical insults to the cutaneous barrier.[1,2] These

damaging effects include: protein denaturation, delipidation and inflammatory processes with keratinocyte-derived cytokine release.[3,4]

Cosmetic companies market a wide variety of detergents, proposing them as very mild products. Nevertheless, there is no international agreement about the criteria to establish mildness of cleansers, and actually several products for sensitive skin have considerable irritant effects.[5,6] On the other hand, physicians and even dermatologists often have no sufficient chemical knowledge for critical examination of detergent composition. As even soaps recommended for 'sensitive' skin sometimes may contain aggressive components, the physician needs to understand their properties for proper product recommendation to the patients.

Cleansing and skin cleansers

Cleansers include the common soaps and the 'syndets' (synthetic detergents) first introduced as bars and later as liquid detergents (moisturizing body wash/shower gel).[3] Soaps, chemically defined as the alkali salt of fatty acids (of animal or vegetable origin), are the most commonly used and usually have a simpler composition than complex formulations of syndets, comprising moisturizers, emollients, preservatives, fragrances, lather enhancers, chelating agents (i.e. EDTA).[7–9] The real protagonists of these cleansing agents are surface-active substances (briefly, surfactants), that lower the surface tension on the skin and remove dirt in an emulsified form.[7,10] While in the simplest way of cleansing (affinity cleansing), hydrophilic dirt can be removed only by water, and fat-soluble lipophilic dirt only by oils, surfactant-based cleansers (traditional soaps and modern syndets) allow elimination of dirt by solubilizing it in micelles successively removed by water.

Surfactants

Surfactants are usually organic compounds that are amphipathic, that is they contain both non-polar or hydrophobic groups (their 'tails'), typically a long alkyl chain, and polar or hydrophilic groups (their 'heads'). Therefore, they are soluble in both organic solvents and water. Surfactants reduce the surface tension of water by adsorbing at the liquid-gas interface and also lower the interfacial tension between oil and water by adsorbing at the liquid–liquid interface.[2,10]

Surfactants can also assemble, into the solution, the aggregates known as micelles. In these aggregates, the lipophilic ends of the surfactant molecules dissolve in the oil, while the hydrophilic-charged ends remain outside, shielding the rest of the hydrophobic micelle.[10]

Surfactants can be categorized according to the charge present in the hydrophilic head (after dissociation in aqueous solution) into four primary groups: anionic, cationic, amphoteric (dual charge) and nonionic. The first three are charged molecules.[9,10]

Anionic surfactants

Anionic agents possess a negative charge of their hydrophilic head. The members of this group have the highest cleansing power, good wetting properties, excellent lather characteristics, but moderate disinfectant properties, and they are commonly used as primary surfactants in cleansers, because their moderate the final product cost. Anionic agents are considered potent irritants to skin.[2,10]

Typical anionic agents used in detergents include soaps containing carboxylate ions and synthetic surfactants, mostly alkyl sulphate, alkyl ethoxy sulphate, acylglutamates, alkyl taurates and alkyl sulfosuccinates (40% to 50% surfactant content) in European formulations.[3,9,10]

A well-known alkyl sulphate, widely used in personal care products, is sodium lauryl sulphate (SLS), anionic surfactant, wetting agent and detergent. This anionic agent has been proven as a potent primary irritant to skin, causing large alterations in barrier properties.[10–12]

The corresponding ethoxylate (sodium laureth sulphate, SLES) is the favourite primary surfactant in body wash/shower gel and shampoo, because of its good cleansing power and its low cost, even if it has some irritant potential.[13]

Actually, new mild cleansers are marketed and they are based on other surfactants, such as sodium cocoyl isethionate.

According to recent studies, alkyl sulphates and alkyl sulfosuccinates have the highest cleansing power, followed by very expensive acyl glutamate and triethanolamine soaps.[9]

Cationic surfactants

Cationic agents, positively charged, have lower detergent properties than anionic surfactants. On the contrary, because of their considerable bactericidal activity against a wide range of microorganisms, they may be used as antimicrobial preservatives rather than as surfactants. Cationic surfactants prove to be at least equally irritating, but more cytotoxic than anionics.[2,10,11] They are common conditioner ingredients (hair-conditioning agents) and anti-static agents in shampoo.[10]

The most common cationic surfactants are amine salts and quaternary ammonium salts (cetrimide and benzalkonium chloride). Cetrimide solutions (0.1% to 1%) may be used for cleaning wounds and burns on the skin, for disinfection of medical instruments and as hair-conditioning agent in shampoo. Benzalkonium chloride (0.5% to 2%) is also used as a preservative for ophthalmic products.[10]

Amphoteric surfactants

Amphoteric surfactants exhibit the properties of anionics or those of cationics, according to the pH of the solution.[9,10]

The members of this group are reputedly less aggressive than anionic surfactants and, therefore, they are used in combination to enhance mildness.[3]

Final cost of amphoteric agents is not negligible, but they are extensively used in liquid cleansers, moisturizing body wash, shower gel, shaving products, shampoo, toothpastes, contact lens detergents. The reasons for this wide utilzation of amphoterics are their good cleansing power and lather characteristics, a moderate antimicrobial activity, the lack of toxicity and compatibility with different pHs.[2,10]

Commonly used amphoteric surfactants include cocamidopropyl betaine, cocoamphoacetate and cocoamphodiacetate.[3]

In particular, one of the most common agents among this group is cocamidopropyl betaine. It is increasingly used in shampoos and liquid cleansers since its introduction in the 1970s, because of its moderate irritancy potential. This surfactant is also considered as a viscosity builder and foam booster.[12] Cocamidopropyl betaine is responsible for increasing cases of allergic contact dermatitis (ACD) from shampoos and detergents. Nevertheless, according to the latest studies, the real sensitizers in these cases seem to be impurities, such as the parent compound dimethylaminopropylamine, that may be present in some sources of the surfactant.[11,14–16]

As regards amphoacetates, they are used in cosmetics as gentle surfactants with low irritancy potential (at concentrations of 0.1% to 50%).[16,17]

Nonionic surfactants

Nonionic agents have no electric charge in its head.[9] Their cleansing power and lather characteristics are quite weak. Furthermore, the members of this group have a relatively low potential toxicity and they are considered the most gentle surfactants, but they are also the most expensive.[8,10]

As in detergents, the nonionic surfactants are also used as thickeners for shampoos, as emulsifiers and suspending agents in cosmetics, pharmaceutical products and foods.[10] Commonly, nonionic agents are considered the lowest irritants to skin among the different types of surfactants.[10] Nevertheless, some authors noticed that nonionic surfactants alter the cutaneous lipid layer more than anionics, because they can solubilize fatty acids and cholesterol in skin.[3]

Among the compounds belonging to this group are alkyl polyglucosides, such as coco glucoside, lauryl glucoside, decyl glucoside.[3]

Another common nonionic agent is cocamide DEA (coconut diethanolamide), widely used in personal care products for its thickener property and foam booster, and in metalworking fluids as a corrosion inhibitor.[18,19]

In addition, this class of surfactants includes fatty acid esters of fatty alcohols, sorbitan esters, sucrose and cholesterol derivatives used like emulsifiers.[10]

Critical micelle concentration: an interesting surfactants property

An important characteristic of surfactants is the critical micelle concentration (CMC) defined as the concentration of surfactants above which micelles are spontaneously formed.

At low concentrations, surfactants added to water will arrange on the surface, with their hydrophobic tail (the non-polar part) projected outside. As the surface becomes crowded with more surfactants added, their molecules start to form agglomerates (known as micelles) in the liquid. Upon reaching CMC, any further addition of surfactants will just increase the number of micelles.[3,20,21]

The surfactant amount not involved in micelle arrangement is called a monomer. It is the monomer that allows the washing effect; beyond CMC, there is no increase of the washing effect. On the other hand, if the CMC value is elevated, there is also a high concentration of monomer that interacts with, and damages, the skin. For this reason, surfactants characterized by elevated CMC value (as lauryl sulphates) has proven to be primary irritants to the skin.[21]

CMC is influenced by the charge degree of hydrophilic component; usually, anionic and cationic surfactants have a higher CMC than nonionic agents, and thus become more aggressive.

CMC reduction can result from a combination in syndets of different surfactants types such as lauryl sulphates and amphoteric or nonionic agents (with low CMC). Therefore, irritant power is decreased.

On the characteristics of surfactants' lipophilic tails, long alkyl chains reduce CMC that is instead increased by double bonds. Therefore, middle-long chain saturated fatty acids (e,g, palmitic and stearic acids from palm and coconut oils) are less aggressive than the short chain fatty acids and unsaturated fatty acids from olive oil.[2,20] The last one contains oleic acid (mono-unsaturated) and linoleic acid (poly-unsaturated) that eventually can become rancid.

Effects of the surfactants

‘Surface active’ molecules or surfactants, because of their amphipathy (that is the presence of hydrophilic and hydrophobic components in the molecules), lowers the surface tension, disrupting the cohesive energy at the surface of the water and remove the debris in an emulsified form.[11]

In particular, surfactants have the following effects:[7,10]

- Cleansing, to remove dirt from skin and hair
- Foaming, to enhance lather in bath foam and shampoo. Some surfactants types have greater foaming power
- Wetting, to increase the contact between the product and the substrate (dirt)
- Emulsifying, to arrange itself at interface between two immiscible liquids. This permits emulsions preparation
- Solubilizing, to introduce insoluble substances in preparations where it needs to preserve the clearness.

Although cosmetic companies have been marketing a wide variety of new products recently with low potential of injurious effects, surfactants may induce some negative effects on the skin.[4,5,22]

The damaging effects of surfactants on the skin are the following:

- Alkalization, a rather remarkable property found in traditional soap bars (with a pH of 9.5–13). Alkaline pH is an intrinsic feature of these common soaps and it is not modifiable by cosmetic technologies. Synthetic detergents vary in pH-adding acids (i.e. citric acid) or alkalis (i.e. sodium hydroxide)[2,3,9]
- Delipidation, the ability of surfactants to solubilize lipid membranes (prevalently ceramides)
- Skin proteins damage, the interaction with keratins and their denaturation
- Swelling of cell membranes and collagen fibres, resulting from damaging effects for skin proteins. Under wash conditions, there is a transient swelling due to interactions between surfactants and these proteins, leading to hyper-hydration. This is usually followed by de-swelling after the water evaporation, with dryness, roughness, tightness and scaling as late consequences.[3,21] Swelling of cell membranes from anionic surfactants is related to their irritant potential, whereas the cationic agents do not seem to promote this swelling effect. Stratum corneum (SC) hydration is defined capacitance and is measured with a corneometer[23]

- Cytotoxicity expressed with cellular lysis when skin barrier damage and its permeability alterations become irreparable. Cytotoxic effects must be distinguished from those irritants; in fact, there are some differences between cytotoxic and irritant potential in different types of surfactants.[10] Some authors tried to rank experimentally the cytotoxicity of different classes of surfactants as follows (according to decreasing cytotoxicity):

  Cationic = amphoteric > anionic > nonionic

In fact, benzalkonium chloride and cetrimide seem to be more cytotoxic than sodium lauryl sulphate (SLS). Also, cocamidopropyl betaine proved to be highly cytotoxic compared with other surfactants.[10,24]

- Irritation related to time exposure of cleansing agent on the skin, to its concentration and to its frequent use. Surfactants are known to be irritants to the skin, leading to irritant contact dermatitis (ICD) that become chronic after frequent and prolonged exposures. Barrier damage and keratinocyte-derived cytokine release can elicit skin irritation, erythema and itching. Generally, anionic surfactants are potent irritant for human and animal skin. In particular, SLS is an acute and cumulative irritant, and thus, an important model of experimental ICD.[12] Cationic surfactants have at least the same irritant effect as that ofanionics, besides they are more cytotoxic. Instead the irritation potential of amphoteric agents is considered lower, and nonionics are regarded as the least irritant:[10,24]

  Cationic ≈ anionic > amphoteric > nonionic

- Sensitizing potential, possible but generally unusual for surfactants. In fact, besides the possibility to reveal an allergic contact dermatitis (ACD), surfactant ability to induce ACD is still under discussion. Sensitizing power is well known for cocamidopropyl betaine.[11,15,16] However, considering the very large use of this surfactant in shampoos, bodywashes and syndet bars, ACD seems to be very rare.

Methods to evaluate cytotoxic and irritant potential of surfactants

At present, different *in vivo* and *in vitro* tests are available to predict and quantify cytotoxic and the irritant potential of a given compound.

Generally, irritancy and cytotoxic power are determined by *in vivo* assays, while tests *in vitro* are used to evaluate cytotoxicity.

In vitro tests

Several *in vitro* assays to examine toxic effects on keratinocytes and other cell cultures, the so-called ‘skin equivalents’, have been developed.[10]

Bovine red blood cell hemolysis, pH rise of bovine serum albumin, collagen swelling are useful *in vitro* tests for evaluation of surfactants.[25]

Another method to estimate the effects of surfactants on human stratum corneum is corneosurfametry.[26] This test requires taking skin surface biopsies with a microscopic slide and cyanoacrylate glue, the incubation of these biopsies with aqueous solutions of tested surfactants, their stain with basic fuchsin-toluidine blue dye solution and the evaluation of their colour changes with a tristimulus chromameter. Finally, an index of irritation is calculated with this reproducible *in vitro* assay. Such index of irritation seems to well correlate with results of *in vivo* tests, in contrast to *in vitro* assays that do not always correlate with *in vivo* observations.[25,26]

In vivo tests

Although numerous *in vitro* alternative assays are available to evaluate irritation potential, exposure methods (patch and use tests) to assay suspected compounds on human volunteers are decisive and necessary screening techniques.[10]

Before *in vivo* testing, preventive analyses of toxicological data are necessary to conform to ethical standards.[27]

In actual practice, because most cosmetic products are very low irritant, many cosmetic companies evaluate their products' cutaneous compatibility rather than their irritation power.

This cutaneous compatibility estimation of cosmetics is taken into great consideration by Colipa working group. Colipa is the European Trade Association representing more than 2000 cosmetic companies, ranging from major international firms to small family-run organizations.[28]

The aim of cutaneous compatibility tests is to estimate near-use conditions; this leads to the analysis of use safety, but not to the definition of the intrinsic irritant potential of the tested substances.[28]

Use and wash testing

In the literature, there are different use-test protocols involving clinical and instrumental assessment that may be helpful in establishing the skin compatibility of a new product, conceived for repeated or frequent use. These normal-use tests are:

- Controlled use test undertaken in normal exposure conditions or in slight overexposure in the laboratory under supervision. The suspected material is applied in open skin, once or twice daily for 1 to 3 weeks. Hand immersion test and half-head test are some examples of use assays.[28]

- Uncontrolled in-home use test (in uncontrolled exposure conditions), a product assay in usual exposure conditions, at home. The test lasts 4 to 6 weeks, with a changeable frequency of applications. Volunteers are selected to represent peculiar skin types or different consumers.[28]

Moreover, several wash-and-rinse test protocols, involving different levels of exaggerated washing, have been proposed to evaluate rinse-off products. Several variations of these tests are used, such as exaggerated arm wash, flex wash or hand wash tests and forearm-controlled application technique (FCAT). In all these standardized washing procedures, products are applied repeatedly and for more time than in normal use. Exaggerated hand or arm immersion tests have been also described for liquid cleansers testing. However, there are disadvantages to the test in that repeated wash or immersion is time-consuming, difficult to perform on several products, and influenced by environmental and individual factors.[25,29–31]

Patch testing

- Single application open epicutaneous test: indicated for new compounds and mainly for very irritant products. The substances are applied undiluted to the arm or the forearm for exposure times of 15 to 30 min. The test may be read immediately upon the effect's first time occurrence, after the last application, then after 24 and 48 h.[28]

- Repeated application open epicutaneous test: the substances are applied to the volar aspect of forearm, under standard conditions with regards to time of exposure, quantity and solution concentration. Application frequency differs, but generally, it is twice daily at most for a week until a reaction is noted..[16,28]

- Single application occlusive or semi-occlusive patch test (overexposure in contrast to normal-use condition): indicated for known basic elements or for new preparations that are proven safe in open patch test. Chambers filled with 0.07 to 0.1 mL of the testing diluted or undiluted substances are applied on the upper back or on the arm in occlusion or semi-occlusion, and fixed by hypo-allergenic tape. Exposure time can be up to 48 h and readings are at 30 min/1 h after patch test removal, then at 24 and 48 h.[28]

- Repeated application occlusive or semi-occlusive patch test (overexposure to estimate irritation thresholds or use restrictions): useful to assay products that are low irritant but for frequent and repeated use, such as those with surfactants. Repeated applications of diluted substances are made in occlusion or semi-occlusion; exposure is for 24 h on the first day and for 6 h daily on the next four consecutive days.[28,32]

Reactions of these tests are assessed visually, elaborating scores not only for eythema, scaling and fissures, but also for objective measurements that have been performed. One of these is TEWL (transepidermal water loss), that measures the integrity of stratum corneum barrier function. Another is quantification of erythema by skin colour

reflectance measurements with colorimeter.[23] Other non-invasive bioengineering measurement methods are evaluation of electrical conductance and Doppler velocimetry to quantify the effects on the skin not apparent to the eye.[25]

With regards to rinse-off products, diagnostic patch tests are performed with their dilution of 0.5% to 4% in water.[6,12,16,23]

In relation to the choice of test to evaluate rinse-off agents or their components, repeated open test and use test allow an adequate evaluation of products containing surfactants for frequent and repeated use (i.e. for professional use). In these cases, skin recovery time is not enough among the different applications, causing a cumulative effect. Repeated occlusive patch tests are useful to estimate cutaneous compatibility of the preparation, assuming that prolonged or repeated contact can cause skin damage (i.e. stratum corneum lipid removal by solvents and surfactants).[16,28]

Moreover, it is necessary to consider that irritant cutaneous effect of a detergent can be expressed differently by various exposure methods. One-time occlusive tests can cause mainly erythema, while repeated tests promotes scaling and roughness.[33]

Conclusions

Repeated and prolonged use of soaps and detergents, both at work and for skin care, can cause irritant as well allergic contact dermatitis, although rarely.

Thus, the physician needs to understand well these properties of the most common cleansers.

In the literature, comparative studies about the irritant and sensitizing potential of different surfactants are very heterogeneous and still inconclusive for indicating unequivocally the best molecules to use.

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