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Recent Advances in Mild and Moisturizing Cleansers

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ABSTRACT

Mild and moisturizing cleanser technologies, and the science underpinning them, have progressed significantly over the past decade. This includes introduction of amino-acid based milder surfactants into the cleansing arena, a deeper understanding of the roles of stratum corneum lipids and proteins in their interaction with cleanser surfactants, the role of pH in skin cleansing, and the development of improved methodologies for predicting skin irritation and drying potential of cleansers. In this paper, the recent advances in these areas as well as newer technologies are reviewed, and the future directions are outlined.

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INTRODUCTION

Cleansers are designed to remove dirt, sweat, sebum, and other unwanted materials from skin. Normal exfoliation of superficial dead cells is also aided by the cleansing process. Thus, cleansing is the first step in daily skincare.

The cleanser actives, surfactants, are designed to remove oily materials and drive the cleansing process. The challenge is in limiting the interaction of surfactants to just removal of undesirable materials and preventing them from altering the properties of the stratum corneum barrier, leading to skin dryness, irritation, itch, and other undesirable events. It is well-known that cleansers based on alkaline soaps are more irritating to skin than those based on synthetic surfactant actives, commonly referred to as syndets, which function under neutral pH conditions.[1] It has also been established that the harshness of alkaline soaps stems from their harsh cleanser active, the soap molecules, and their high pH.[2,3] Early work on interaction of surfactants with stratum corneum has been reviewed extensively in the literature[4-11] and the importance of milder surfactants underscored.

The emergence of liquid cleansers in the 1990's opened up opportunities for a wider range of surfactants to be explored in the cleansing arena. Synergistic combination of surfactants can lead to improved mildness.[4,7] However, the challenge has been in designing ultra-mild products without compromising on consumer-desired sensory properties such as lather. In fact, dermatologists would acknowledge that compliance even among those with compromised skin is poor for products that have inferior sensory. Recent advances in cleansing surfactant systems have resulted in ultra-mild systems without any compromise on the sensory.[4,12,13]

The liquid format also made it possible to develop technologies that deposit moisturizing and sensory enhancing actives during the wash process. Benefit actives from wash-off systems include humectants such as glycerol, oily materials such as triglyceride oils and petrolatum, sensory enhancers such as silicones, and skin-natural lipids such as fatty acids and sterols.[4,9]

Along with the progress in cleanser technologies, the ability to predict the skin irritation and drying potential of cleansers and assess the skin barrier quality also has advanced significantly.[14]

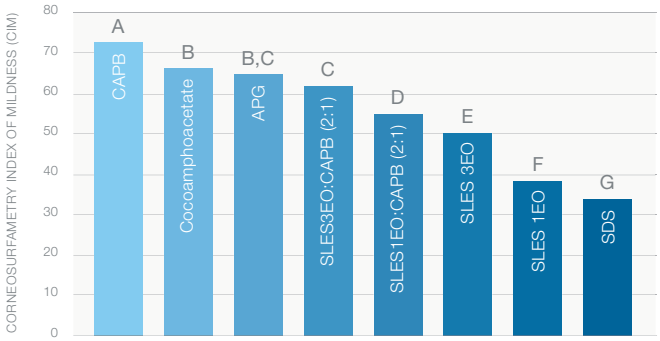
Interaction of Cleanser Surfactants With Stratum Corneum

The human stratum corneum consists of flattened corneocyte cells embedded in a lipid matrix.[15,16] While the corneocytes with their cross-linked keratins and natural moisturizing factors (NMFs) contribute to the mechanical and water holding properties of the stratum corneum (SC), the lipid matrix acts as the main barrier to water loss from the body.[17,18] Recent advances in our understanding of the stratum corneum have shown that it is not only a physical barrier, but also an immunological and a microbial barrier.[19, 20] Thus, any damage to the stratum corneum from use of harsh cleansing products can impact its multiple barrier functions.

Interactions of Surfactants With SC Proteins and Relevance to Skin Irritation

The early work on interaction of common cleanser surfactants with skin showed that in vivo irritation potential of surfactants correlated with the ability of surfactants to denature proteins such as BSA or Zein, and/or swell cross linked proteins such as collagen.[4,7] Over the years, there have been attempts to use stratum corneum itself as a substrate for in vitro irritation studies.[5,6,14, 21] Skin irritation potential of some of the common

FIGURE 1. Corneosurfametry index of mildness (CIM) values for individual surfactants. Bars having the same letter are not significantly different from each other. Results showed CAPB was the mildest and SDS was the harshest and also showed SLES 1 EO to be milder than SLES 3EO and SLES 1 EO and 3EO blends with Betaine were milder than the corresponding SLESs. SDS: sodium dodecyl sulfate, SLES xEO: sodium lauryl ether sulfate with x number of ethylene oxide groups, CAPB: cocoamidopropyl betaine, APG: Alkyl polyglucoside



cleanser surfactants assessed in a modified ex vivo corneosurfametry assay is given in Figure 1.

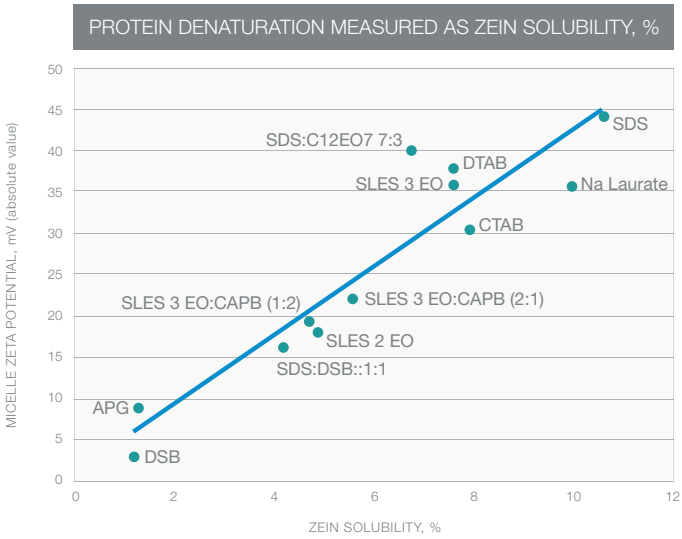
The results in Figure 1 show that anionic surfactants are harsher than amphoteric and nonionic surfactants and addition of amphoteric surfactants to anionics make them milder. This assay has been previously validated for its correlation with in vivo evaluation of formulation mildness and irritancy potential.[14]

It is evident from the past work that the charge of the surfactant plays a role in their irritation potential. Further research along these lines has led to the development of a quantitative relationship between the charge density of surfactant micelles (self-assembled surfactant aggregates in solution) in the cleanser system and their skin irritation potential (see Figure 2).[22] Such quantitative structure–function relationships will help formulators assess the relative irritation potential of technologies prior to expensive clinical studies.

The reason SC swelling by surfactants correlates with skin irritation is because, upon swelling, the permeability of the structure increases, significantly leading to penetration of foreign materials into deeper layers causing a biochemical reaction that manifests as irritation, inflammation, and itch.

The inherent irritation potential of surfactants and other chemicals to skin can be determined from keratinocyte cell culture studies or living skin equivalent (LSE) models studies in which irritation can be related to the release of inflammatory biomarkers such as IL1 alpha (interleukin 1α (IL1-α) and IL1-Ra).[23,24] Since these systems do not have a fully developed corneum barrier, they may not predict the irritation potential under normal use conditions. However, such testing may be appropriate for testing products intended for compromised skin situations such as those in sensitive, atopic, and infant skin.

FIGURE 2. Correlation between protein denaturation measured as zein solubility in 5% surfactant solutions and the charge density of micelles estimated from micelle zeta potential measured at 1% surfactant level. Protein denaturation potential scales linearly with the micellar charge/potential. Correlation appears to hold good for a wide range of surfactants including anionic, zwitterionic, nonionic, and even cationic surfactants and surfactant mixtures. This provides a quantitative ruler for mildness assessment of surfactants and surfactant mixtures toward proteins. SDS: sodium dodecyl sulfate, SLES xEO: sodium lauryl ether sulfate with x number of ethylene oxide groups, APG: alkyl polyglucoside, DSB: dodecyl sulfobetaine



Surfactant Interactions With Skin Lipids

Surfactants are designed to interact with fatty materials such as sebum and skin lipids. While removal of sebum is important during cleansing, interaction with SC bilayer lipids is not desirable as the latter constitutes the main barrier to water transport through skin. Cleanser surfactants can intercalate into the bilayer and increase its permeability by altering the bilayer structure.[4,25] It can also extract the "more extractable" lipids such as medium chain fatty acids (eg, palmitic or stearic acid) and cholesterol and affect the skin permeability.[4,25-28] A quantitative determination of the amount of SC bilayer lipids during cleansing has been a challenge because of their complexity in terms of chain length and the absolute amounts involved.[28] Superficial effects of surfactants on skin lipids may not immediately lead to skin irritation, but may manifest as skin dryness.[4, 27] With continued damage, such a situation can progressively result in scaling, flaking, and disruption of barrier.

Several in vitro methods exist to estimate the tendency of surfactants to damage SC lipids.[4, 25-29] This includes simple assays

to determine the solubility of SC lipids such as fatty acids, cholesterol and ceramides in surfactant solutions, destruction of model bilayer membranes in the form of vesicles, removal of lipids from isolated SC, or changes in bilayer structure of isolated SC by vibrational spectroscopy. Such studies have also shown that the tendency of surfactants to damage lipids may not be the same as that for damaging SC proteins.[4] For example, certain nonionic surfactants such as alkyl polyglucosides and amphoteric surfactants such as cocoamidopropyl betaine (CAPB) have minimal tendency to interact with proteins, but show higher tendency to interact with lipids. Mild cleansing requires mildness towards both proteins and lipids and therefore choosing surfactants that are mild towards both is important. A combination of anionic surfactant with amphoteric and/or nonionic surfactants can lead to such optimal conditions.

The past work also showed that an amino acid surfactant, cocoyl glycinate, is as mild as the well-known syndet surfactant, cocoyl isethionate, commonly used in neutral pH syndet cleansing bars. These findings created the pathway for the introduction of an amino acid surfactant-based body wash by a major brand several years ago[13] and the potential for other amino-acid surfactants in the future.

Role of pH in Skin and Skin Cleansing

It is well established that alkaline soaps are harsher than neutral pH syndet surfactant based cleansing bars.[1-4] It is also well-known that the natural pH of SC is around 4.5 to 5.0.[30] Korting et al have shown that use of alkaline soaps lead to a transient increase in pH of the order of almost 2 units and it returns to normal skin pH values with time.[30] However, continued use of alkaline soaps can lead to a change in the steady state pH of skin and accompanying changes in the skin microflora.

An elevation in the steady state pH has been observed also for abnormal different skin conditions. For example, it has been shown that extremely dry and atopic skin generally have higher than normal pH values, eg, around 5.5 to 6.0 or even higher.[31] In such cases, it is not clear if skin pH change is the cause or the effect of skin conditions.

Elias and team have shown that hyper acidification of SC can lead to improved SC cohesion, increased lipid synthesis, and enhanced antibacterial activity.[32, 33] Subsequent work by several researchers has shown that intentionally lowering the pH of skincare lotions to values below the SC pH can lead to improved rates of recovery of tape stripped skin or even elderly dry skin.[34, 35] Thus, there may be a case for lowering the pH of lotions and creams for improved skin benefits. More work is needed to validate the generality of these findings.

In the cleansing arena, there have been attempts to make implied skin benefit claims by formulating skin cleansers under skin pH or even lower than skin pH conditions.[10,36] In such cases, the claims have been based on just the pH of the product alone, rather than any experimental evidence of skin benefits for low pH cleansers.

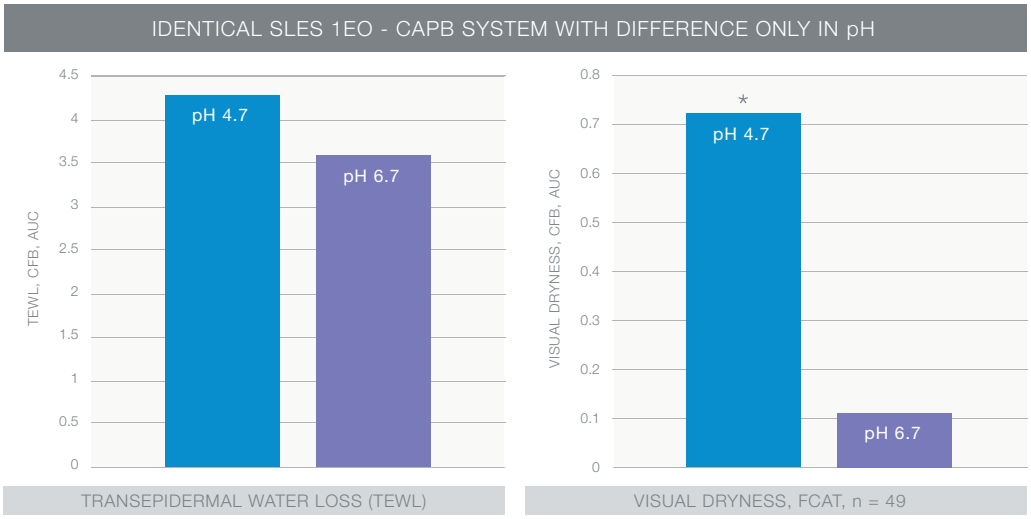
In order to test the effect of pH on skin cleansing systems, two identical syndet bar formulations, one under neutral pH conditions and the other under low pH conditions, were tested for their relative mildness in a typical forearm controlled application test (FCAT), which is commonly used to rank relative disruption to the skin's barrier following exaggerated use conditions.[10,37] The results showed that the neutral pH cleansing syndet bar was milder by lower transepidermal water loss (TEWL) and clinical visual dryness.[10] Results of similar studies carried out with a typical SLES (sodium lauryl ether sulfate, 1 EO) and CAPB systems are shown in Figure 3.[38] These results also show that the lower pH cleanser is harsher than the neutral pH cleanser in TEWL and visual dryness.

The above study results suggest that neutral pH is better for mild cleansing. These are contradictory to the leave-on results mentioned earlier and can be explained as follows. The isoelectric point of keratin is around pH 5.[39] The results for the zeta potential of human stratum corneum given in Figure 4 also shows that the IEP is around 5. Therefore, skin proteins have a net negative charge under neutral pH conditions. As the pH is lowered from neutral to acidic values, skin will have more positively charged sites than under neutral pH conditions and this in turn should promote increased binding of anionic surfactants to skin.[10,11] Significant reduction in the zeta potential of SC in the presence of an anionic surfactant, SLES, is evident from the results given in Figure 5 and this is brought about by the binding of surfactants to the SC. Thus, in systems with predominantly anionic surfactants, there can be more residual surfactants left on skin under low pH conditions than under neutral pH conditions leading to more damage.

The other question that arises when comparing neutral pH cleansing vs acidic pH cleansing is whether long-term use of a neutral pH cleanser elevates the pH of SC from its normal value. Previous reports show that transient pH change immediately after cleansing with a neutral vs a mild low pH cleanser is about the same and the skin pH values return to normal in less than an hour in both cases. Furthermore, even water wash is known to lead to a transient increase in pH that returns to normal values in less than one hour.[38] Thus, unlike alkaline pH cleansing, neutral pH cleansing itself does not pose any harm to the SC.

Note that the above arguments do not imply that it is not possible to create a low pH cleanser that is very mild. The current observation simply implies that conventional anionic surfactant rich-cleansers can be more irritating under low pH conditions.

FIGURE 3. FCAT (Forearm controlled application test) study results for SLES 1 EO-CAPB based regular body wash formulations differing only in pH. Results show that the lower pH formulation at pH 4.7 is more drying to skin than the one at pH 6.7. Bars represent change from base line (CFB) of area under the curve for TEWL (trans-epidermal water loss) and dryness over the test period. SLES 1EO: sodium lauryl ether sulfate with 1 ethylene oxide group, CAPB: Cocoamidopropyl betaine



Role of Fatty Acids in Skin Mildness

An approach to minimizing the tendency of surfactants to cause delipidization and the consequent skin dryness has been the incorporation of fatty acids in the formulation.[12,28,40] This stems from the hypothesis that fatty acids and cholesterol are the surfactant-extractable lipids in the SC and, between the two, fatty acids are more extractable. Incorporation of fatty acids can prevent extraction of medium chain fatty acids from skin as well as replenish fatty acids that are likely to be removed during the cleansing process.[28,40] Figure 5 reproduced from reference 12 shows how addition of stearic and palmitic acids improves the relative reduction of TEWL and visual dryness in an FCAT clinical study even in a relatively mild isethionate surfactant system.[12] In addition to modulating the harshness of cleanser surfactants, fatty acids may also provide other skin benefits and this aspect will be examined in a later section.

Moisturization from Cleansers

Moisturizing cleansers are designed to provide positive skin benefits beyond simple mild cleansing. Typically, these are measured as increased hydration levels and reduced visible skin dryness and transepidermal water loss in comparison to starting conditions. These are typically achieved by depositing "oily" materials such as petrolatum or triglyceride oils often in combination with humectants such as glycerol[4,9,41] and such deposition provides an immediate visual dryness reduction benefit.

There are products in the marketplace that emphasize both mildness and moisturization and others that emphasize more on just moisturization. The rationale behind the use of a strong moisturization system with less regard for the mildness of the cleanser base is that the former can overcome the negatives of the harsh base while maintaining its overall sensory properties. Our hypothesis, based on previously published research on cleanser mildness, is that both of these elements are critical for superior skincare from cleansing systems.[42] It has also been shown that it is possible to create ultra-mild systems without any compromise on sensory properties.[12,13]

FIGURE 4. Stratum corneum zeta potential as a function of pH. Sonicated pieces of corneum dispersed in water and treated with 0.01% SLES. Isoelectric point of SC appears to be around 4.5. In the presence of SLES, the SC corneum charge becomes significantly more negative because of anionic surfactant binding. As the pH is lowered from neutral to lower values, more surfactant binding can be expected.

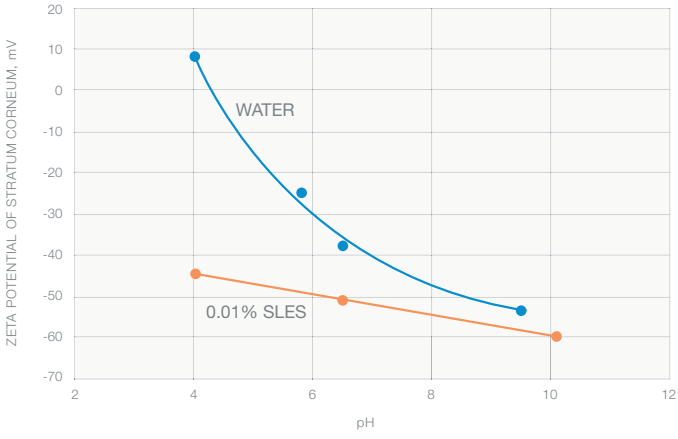
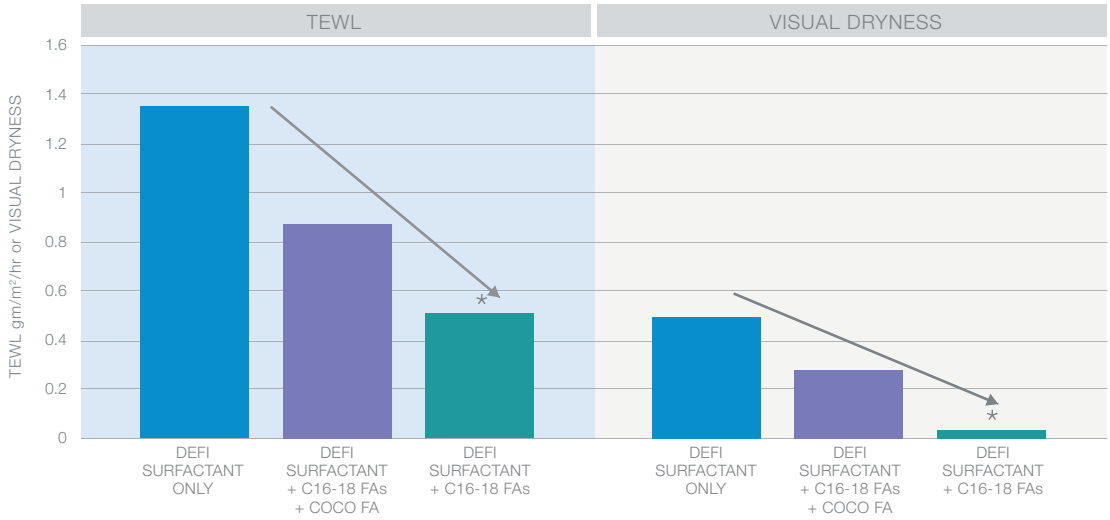


FIGURE 5. The effect of fatty acid addition to a prototype body wash formulation with DEFI surfactant (directly esterified isethionate) on in vivo TEWL and visual dryness in a standard FCAT study. No emollients present in the BW. DEFI is directly esterified fatty isethionate surfactant. In systems with fatty acids, total fatty acid level is 7.3%, in system with both coco and longer chain fatty acids, coco fatty acid level is 2.8%. *Indicates statistically significant from the surfactant only system. Visual dryness scale 0 to 6.



Rebuilding the Skin Barrier With Advanced Skincare Benefit Technologies

Beyond the immediate visual dryness reduction and improved skin hydration benefits, moisturization technologies are progressing towards improving damaged skin barrier from wash-off and leave-on formats. As discussed earlier, ensuring minimal changes to skin pH is the first step towards skin barrier repair.

Another approach to barrier repair is the use of complex lipid mixtures consisting of ceramides, fatty acids, and cholesterol that can form SC bilayer-like film on the skin surface.[43,44] Such films can be expected to reduce the water loss and help repair the barrier. This can be considered as an "outside-in" approach as the barrier reinforcement is essentially coming from the outside. This is similar to the use of an occlusive such as petrolatum. However, because of the differences in the composition of the film, their performance can be different from that of petrolatum.

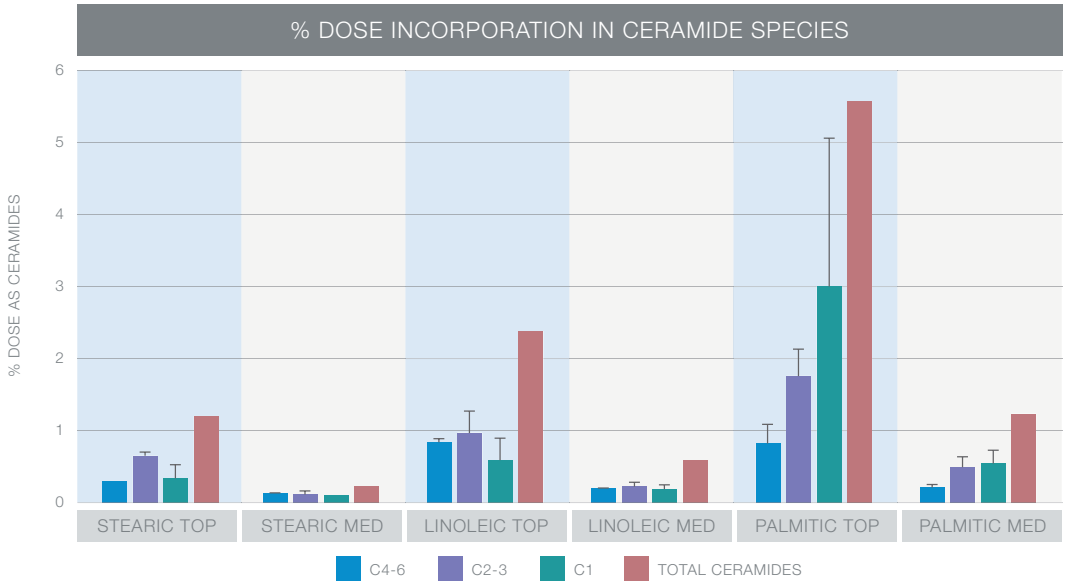
Pro-lipid technologies aim to supply ingredients that the skin can utilize to rebuild the barrier from within. The early work by Rawlings et al involving the use of triglyceride oils as a source of essential fatty acids that skin can utilize to increase the synthesis of ceramides is noteworthy.[45] Subsequent work by Harding et al in living skin equivalent (LSE) models showed that fatty acids, especially palmitic acid, can be utilized by skin to increase synthesis of ceramides in skin.[46] In these studies, radiolabeled palmitic acid and stearic acid were applied to LSE topically as well as in the culture medium. Analysis of SC lipids after 24 hours of incubation showed the presence of radiolabeled ceramides in them indicating the incorporation of the fatty acids into the building of ceramides (see Figure 6). In this regard, recent work by Bouwstra and team is also noteworthy.[47] The latter group showed that addition of deuterated palmitic acid to their cultured skin model resulted in elongation of the fatty acid to longer chain fatty acids such as C22 and C24 fatty acids. This shows another route by which palmitic acids can be taken up by skin to build SC bilayer lipids. Note that in vivo leave-on and wash-off study results with products containing fatty acids such as palmitic and stearic acids have clearly shown that they do penetrate into deeper layers of skin.[9,28] In vivo demonstration of conversion of fatty acids, ideally using deuterated fatty acids, may be a logical next step in this research.

Similar to the case of fatty acids, externally applied ceramides from leave-on formats in LSE-type models have also been suggested to be taken up by skin in the creation of ceramides.[48] Noting that the skin barrier in the case of LSE models is relatively weak compared to a healthy corneum, penetration of ceramides into deeper layers for incorporation is yet to be validated. In fact, some of the recent studies using Raman imaging and microscopy suggests that externally applied ceramides tend to get trapped in skin's furrows and valleys rather than penetrating deeper into skin.[49] Given the two-tailed structure of ceramides, its high molecular weight and its low solubility in typical cleansing and leave-on systems, its lack of penetration into skin is not surprising.

Cleansing Technologies

Based on the above discussion, a strategy for developing cleanser technologies to meet the various market needs is outlined in Figure 7. Current market trends for various cleansing applications is shown in Figure 8. For a specific type of cleanser

FIGURE 6. Fatty acids applied either topically or into the medium in a radiolabeled form to a living skin equivalent model skin shows conversion of fatty acids into different forms of ceramides after 24 hours of incubation. Palmitic acid shows more conversion than other forms. *Reproduced from Harding C and Alexis J*[54]



system, one approach to increasing the overall mildness is by reducing the level of the surfactant in the formulation. This is commonly practiced in the liquids area and the recent launch of micellar water is an example of this approach. In the bars area, there have been attempts to make the bars milder by reducing the total fatty matter (TFM), ie, the surfactant active in the bar. Addition of polyols and other mildness enhancers can further improve their mildness.

Cleansing Technologies for Vulnerable Skin Conditions

Cleansing technologies for sensitive skin and other vulnerable skin conditions such as infant skin and atopic skin generally differ from the typical adult cleansing systems. Even in adult cleansing, "gentler" technologies are thought to be ideal for facial cleansing.

Infant Skin Cleansing

Infant skin at the time of birth is not as fully developed as the adult skin and it takes as much as a couple of years before it is fully matured.[50] Recognizing that the infant skin barrier is relatively weak, extra care should be exercised in the development of baby cleansers. In addition, some of the recent findings suggests that early skincare, particularly during the first year of birth, can help prevent such conditions as atopic dermatitis and other allergies in the future.[51] Noting that skincare starts with skin cleansing, the importance of mild cleansing for infants cannot be overemphasized.

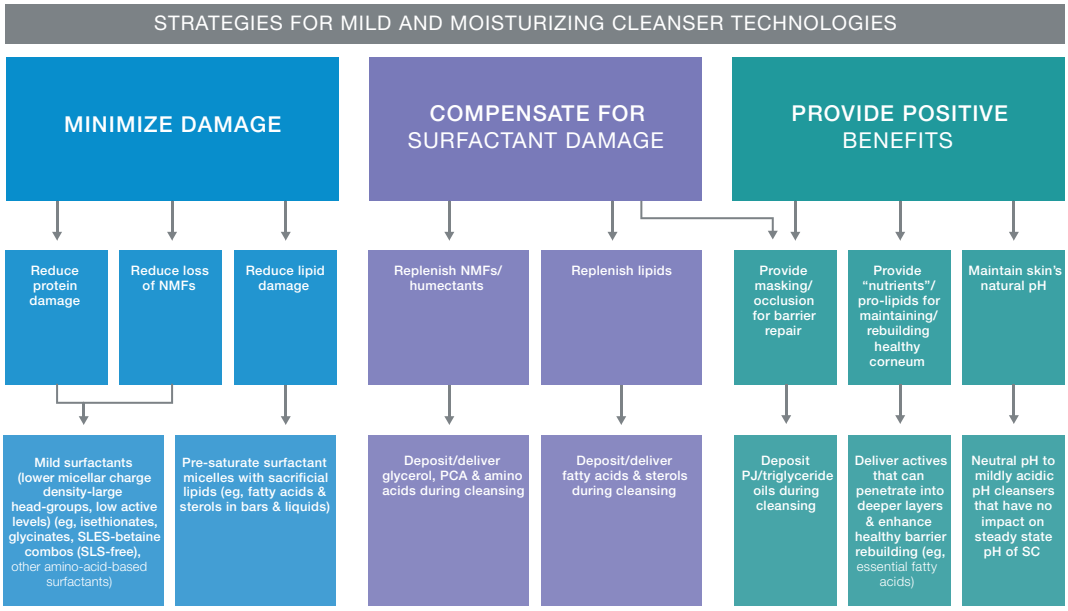
Currently available baby cleansers include both bar and liquid formats. It is well established that the neutral pH syndet cleansing bars are milder than the alkaline pH soap bars.[1,10] With regard to weakly acidic pH skin cleansing, as discussed in an earlier section, typical anionic surfactant rich bars under acidic pH conditions have a higher skin drying potential than the neutral pH syndet bars.[10] Thus, neutral pH bars may be preferable for infant cleansing.

In the liquid cleansing area, there are several options for milder surfactant combinations and additives that enhance the mildness of surfactants. Typically, the baby cleansing products have lower level of surfactants than that in adult formulations. They also tend to have higher ratios of amphoteric and/or nonionic surfactants to anionic surfactants. A balanced formula that takes into account both protein and lipid damage potential of surfactants, as discussed in the earlier section, is more appropriate for baby cleansing. In this regard, formulations containing skin lipids such as fatty acids that can mitigate some of the lipid damaging tendencies of surfactants are more appropriate for infant cleansing.

Cleansers for Sensitive Skin

Even though the percentage of self-perceived sensitive skin population has been increasing steadily in the recent past, the reasons for sensitive skin are still poorly understood.[52] A weaker skin barrier is thought to be one of the factors that results in sensitive skin in at least part of the sensitive skin subjects.[53] Therefore, the general approach has been to limit or avoid the type of ingredients that have an inherent tendency to penetrate deeper into skin and cause irritation. Specifically, this includes avoidance of harsh surfactants and fragrance and limiting pre-

FIGURE 7. Technology routes to mild cleansing and moisturizing cleanser technologies.



servatives in cleansing technologies. This area is likely to get increased attention from researchers in the coming years for a better understanding of the skin condition and for technologies specifically developed for them.

Facial Cleansing

A detailed discussion of facial cleansing is beyond the scope of this paper. Briefly, the type of products for facial cleansing vary from almost water-like non-foaming cleansers to foaming cleansers that leaves the skin with a well-stripped taught feel. Cleansers also vary significantly in their pH values all the way from highly alkaline soap like cleansers to highly acidic anti-acne cleansers. Another newer entry into the anti-acne area includes a technology using natural actives such as thymol and terpineol that has shown efficacy in clinical studies.[54] In general, unlike in body wash, "oily" emollients are not ideal for facial cleansing. Instead, humectants such as glycerol and light moisturizers are preferred.

FIGURE 8. Market trends in cleanser technologies.

	REGULAR	MILD	VERY MILD	ULTRA MILD
BARS	Soap bars (alkaline)	Low TFM bars, glycerol/polyol bars	Syndet bars with fatty acids	
REGULAR BODY WASH	SLES-betaine based	Milder surfactant base (eg, isethionate/glycinate/ other milder surfactants (SLS-free))	Milder surfactant base + fatty acid/lipid enriched cleanser with mild surfactants	
MOISTURIZING BODY WASH	SLES-betaine base, moisturizers	Milder surfactant base, moisturizers, humectants	Milder surfactant base + fatty acids/lipids, moisturizers, humectants	
FACIAL CLEANSERS	Alkaline soap bars and SLES-betaine liquids	Milder surfactant base, humectants, light emollients	Milder surfactant base, lipids, humectants, light emollients	Low surfactant/ low foaming/non-foaming humectants, light emollients (eg, micellar water)
INFANT CLEANSING	Alkaline soap bars, SLES-betaine based liquids	SLS–free, milder foaming cleanser	Amphoteric surfactant rich, fatty acids/lipids, humectants, moisturizers and emollients	Low surfactant/ low foaming humectants, light emollients, moisturizers
SENSITIVE SKIN		Milder surfactant base, fragrance-free	Milder surfactant base, humectants, fatty acids/lipids, emollients, moisturizers, fragrance-free	Low surfactant/ non-foaming, humectants, moisturizers, emollients, fragrance-free

The idea of low-active, water-like, low/non-foaming cleansers is highlighted by the recent growth of "micellar water" in the market place. The fact is that all conventional cleansers have "micelles" or molecular surfactant aggregates in them under conditions of cleansing and they play a significant role in the cleansing process. Micellar water is created by relatively mild, nonionic, or ultra-mild surfactants at low levels, along with low levels of solvents such as short-chain alcohols that aid in the removal of make-up and other oily materials on skin. They may also contain light moisturizers and humectants.

SUMMARY AND CONCLUSIONS

Significant advances have been made in mild and moisturizing cleanser technologies over the past 10-15 years. This includes a deeper understanding of the relative roles of SC proteins and lipids in the interaction of SC with cleanser surfactants leading to skin dryness, irritation, and erythema, and the role of co-surfactants and lipids such as stearic and palmitic acids in mitigating their effect. Typical moisturizing technologies from wash-off systems involve deposition of triglyceride oils or petrolatum during the rinse phase. The importance of cleanser base mildness even in high emollient containing moisturizing cleanser systems is now clearly established. Recent work also shows that the moisturizing technologies can move further in the direction of helping skin build better barrier by supplying actives such as fatty acids and other pro-lipids that skin can utilize in its repair process. Future trends in the cleansing area include increased use of sustainable and greener ingredients, better understanding of the skincare needs of the very elderly, and unraveling the role of skin microbiome in the context of daily skincare.

DISCLOSURE

At the time of most of this work, KP Ananthapadmanabhan was an employee of Unilever. KP Ananthapadmanabhan and JJ Leyden are consultants for Unilever. S Hawkins is an employee of Unilever.

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