Formulation technology as a key component in improving hand hygiene practices

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Proper hand hygiene has long been recognized as a primary tool in reducing transmission of health care-acquired infections. Compliance with recommended practices and an increase in the frequency of hand hygiene can have a negative impact on skin condition. Poor skin condition can result in reduced compliance with hand hygiene guidelines. In addition to reduced compliance with proper hand hygiene, deterioration in skin condition leads to reduced barrier function of the skin, changes in skin microflora, and increased shedding of skin squames. Thus, poor skin condition can increase the risk of infection, increase costs to the facility, and reduce the quality of life for the health care worker. To address the problem of skin irritation and its link to low compliance to hand hygiene practices, the Centers for Disease Control and Prevention (CDC) Guideline for Hand Hygiene for Health Care Settings recommends that hand hygiene agents should be well accepted, well tolerated, and formulated to minimize irritancy. Sophisticated formulation technologies and the proper selection of ingredients can provide products that encourage hand hygiene compliance through pleasing aesthetic properties and by overcoming the damaging effects of hand hygiene practices. (Am J Infect Control 2006;34:S82-97.)

Proper hand hygiene has long been recognized as a primary tool in reducing transmission of health care-acquired infections.[1-4] This tool had traditionally consisted of handwashing with plain or antiseptic soaps and in more recent years has expanded to include the use of alcohol handrubs.[5] Ironically, compliance with recommended practices and the commensurate increase in the frequency of hand hygiene can have a negative impact on skin condition and a resultant decrease in compliance. As compliance decreases, educational programs are instituted to spark improvements in hand hygiene frequency.[6-13] As compliance increases, the damaging effects of many of the products used as part of these infection control programs lead to damaged skin, manifested as dryness, redness, cracking, and scaling.[4] This sets up the unfortunate cycle involving increases in hand hygiene compliance (frequency), health care worker skin damage, and reduced compliance, which then requires new educational intervention.[1,3,14-18] In addition to reduced compliance with proper hand hygiene, deterioration in skin condition leads to reduced barrier function, changes in skin flora,[19] and increased bacterial shedding. Thus, poor skin condition can increase the risk of infection,[20,21] increase costs to the facility,[21-23] and reduce the quality of life for the health care worker.[24-26] Effective hand hygiene practices using hand hygiene agents that do not negatively impact skin condition will maintain an adequate skin barrier, sustain compliance obtained through education and training, and, thus, reduce the overall cost of health care.[27]

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THE IMPORTANCE OF SKIN CONDITION

Skin is the primary care interface, acting as a vital boundary between the health care worker and the environment and the patient. Skin performs an important protective function. The architecture of this protective layer is multifaceted and serves as a physical barrier between the body and the external environment. This barrier regulates temperature, maintains moisture, and prevents microbial entry. The outermost layer, the stratum corneum (SC), is in constant interaction with the environment. As the regulator of water flow between the skin and environment, the healthy maintenance of the SC is critical. The removal of fats and oils (defatting) and other protective components from the skin and constant exposure to irritating materials can trigger a cascade effect. These effects may not be apparent immediately but can have long-term consequences on both moisturization and inherent barrier properties of the skin.[15] This damage can further lead to contact dermatitis and other skin diseases.[28]

Hand health and hand hygiene compliance are inescapably interrelated. If, through education programs and vigilance with infection control practices, hand

hygiene compliance increases,[12,29] the use of hand hygiene products also increases. If the skin becomes dry and irritated through interaction of those products with health care workers' skin, then compliance with hand hygiene practices may decrease.[3,14,30] Thus, those who comply will be less likely to comply in the future, ie, compliance can lead to noncompliance. As a result, sustained compliance becomes difficult to achieve.

To address this complex problem of skin irritation—low compliance to handwashing—and the negative impact of hand hygiene agents, the Centers for Disease Control and Prevention (CDC) recommended in the Guideline for Hand Hygiene for Health Care Settings that hand hygiene agents should be well accepted, well tolerated, and formulated to minimize irritancy.[31] A thorough understanding of skin physiology and the interaction of various ingredients with the skin is therefore important to assess adequately the product contribution to overall skin health.

The skin is a complex organ made up of many different physical and chemical components that fit well together to protect the body from environmental insult.[28,32] The nature of that matrix represents a physical barrier. Poor skin condition can result in aberrant architecture, which in turn is more readily penetrated by outside insults, including microorganisms.[15,28,33] The microbiologic makeup of the resident flora on skin also serves as an impediment to carriage of other organisms.[34-36] In addition to the physical character of the barrier being affected, when skin is damaged, important chemicals can be more readily leeched from within the skin matrix. This can cause a shift in both skin lipids and pH of the skin[37-39] and thus a shift in the environment that is balanced to support a specific resident flora.[33,38] This damage to skin can result in a change in both the numbers and types of bacteria present. Skin damaged by high-frequency handwashing has been shown to harbor increased levels of organisms.[19,35,40-43] Flora can shift from gram-positive bacteria to higher levels of gram-negative bacteria.[44] Along with this shift toward increased levels of gram-negative bacteria, greater antibiotic resistance of the remaining gram-positive organisms has also been demonstrated.[19,44]

As well as reduced barrier properties, a shift in the skin's ecologic environment, and changes in the numbers and types of bacteria, an increase in skin shedding usually accompanies diminishing skin condition.[43,45-51] These skin squames can contain large numbers of microorganisms, thus dispersing organisms into the health care environment as the skin sheds.[44,49-53]

FACTORS INFLUENCING SKIN CONDITION

The skin condition of the health care worker is a complicated subject and is influenced by many factors[4,47] (Fig 1). These factors include frequency and types of products utilized, glove usage (eg, occlusion, latex, and powder), ingredients in products used, age, season and location (climate). A number of these factors cannot be controlled (such as age, season, and location), and, therefore, it is essential to mitigate and control those variables that can be controlled, to break the cycle of reduced compliance.[4,17]

The use of gloves has significantly increased with the adoption of universal precautions. Gloves can impact skin condition in a number of ways, both physically and chemically.[54,55] Friction injury because of interaction of the glove with the skin surface can result in physical damage to the SC. The reaction of a health care worker to the ingredients that make up the glove (latex, nitrile, or powder within the glove) can result in substantial irritation and/or allergic reaction. Ingredients under occlusion can also engender greater irritation response.[15,56] The use of gloves and the occlusion of the skin can also result in swelling of the horny layer, which can in turn release water-soluble inflammatory substances normally found within this layer, triggering a downward spiral toward dermatitis.[57] Thus, the impact of poor skin condition is magnified with increased glove use.[26]

Hand hygiene practices (frequency of use and product type used) are in good part driven by the condition of the skin of the person using them.[30,58] However, skin condition is derived from the product choices made.[5,59-61] There are 3 main types of products used as part of a hand hygiene regimen: cleansers, alcohol hand sanitizers, and lotions.[62,63] The composition of these products and the frequency of their use will have significant impact on the skin condition of the health care worker.[30,64-68] The CDC makes recommendations in the Guideline for Hand Hygiene for Health Care Settings[31] that include indications for the use of all 3 of these product types. Numerous studies have demonstrated that the use of product regimens is more effective and better tolerated by the skin than soap and water alone.[20,30,52,69,70] The appropriate choice and use of all of these products (mild cleansing agents, moisturizing alcohol hand sanitizers, and moisturizing lotions[62,71-74]) can result in significant mitigation of negative impacts on skin condition.[26,75] It is important to understand that product formulation of hand hygiene agents utilized as part of any skin care regimen can have significant effects on skin. It is not just the active ingredients that impact skin condition but the inactive ingredients as well. Therefore, for informed product choices to be made, the evaluation of the total formulation (product) on human skin is necessary to assess properly the acceptability for use in the health care environment.

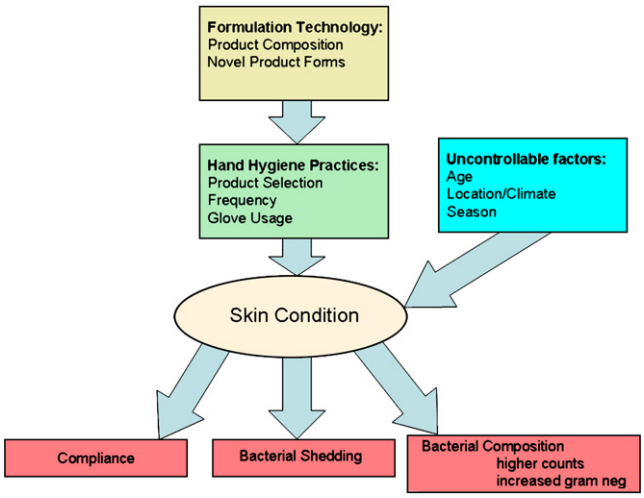

Fig 1. Factors influencing skin condition.

MEASUREMENTS OF SKIN CONDITION

In the same way that compliance with hand hygiene practices should be monitored to assure that proper procedures are followed and to measure their effectiveness at reducing infection, hand hygiene products should be evaluated for proper ingredient inclusion and to measure their effectiveness at maintaining skin health. To assess accurately the impact of various products on skin health, a variety of test methodologies are used. These test methods use a number of instrumental and visual assessment techniques to quantify parameters important for good skin health, including both visual markers and physical properties. These can include measurement of moisture levels, barrier function, skin redness, dryness, and swelling.

METHODS

Inherent irritation or sensitization potential is typically assessed using either animal or human subjects and a method involving products or ingredients left in contact with the skin surface for extended periods of time. The skin is assessed for a physical reaction in the form of redness or swelling. These include tests for primary skin irritation, sensitization, and hypoallergenicity.

The Forearm Controlled Application Test (FCAT) has been used primarily for assessing drying (and conversely moisturization) potential of skin care products. It involves the application of products in the manner in which they would be used and utilizes the volar forearm of a subject. The surface area and relative flatness of this surface allows for multiple products to be evaluated side by side on the same subject.[76] This type of study also has the benefit of the subject's skin serving as its own control. Products are then compared either with each other and/or with untreated or control sites (where only water has been applied) using measurements generated utilizing various instrumentation and/or visual evaluation.[77] Later discussion within this article utilized data generated using this testing technique to emphasize various points in an evidence-based manner. To aid in evaluation of those specific studies presented in this review, a generalized procedure follows. Subject numbers and applications techniques will be outlined in the Figure legends accompanying the graphs within the appropriate sections.

Subjects

The subjects were volunteers, male and female, ages 18 to 65 years. All subjects completed a 5-day conditioning period utilizing a marketed bar soap product in place of their normal cleansing product. All subjects were to avoid the use of creams, lotions, ointments, and powders on the forearms. All subjects were only accepted into the study with dryness scores of <3 prior to the first treatment for washing studies and ≤ 2 for leave-on application studies. No subject could be currently participating in another study or have participated in another study within the previous 4 weeks. Other exclusion criteria were insulin-dependant diabetes; obvious skin pathology; and use of corticosteroid, antihistamine, or antiinflammatory medications. No subject with allergies to article components, soaps, latex, or fragrances was allowed to participate.

Procedure

For the testing of cleansing products, the treatment phase consisted of 2 washing sessions of 2 washes each, daily for 4 days with a morning session on the fifth day. Washing was done on 3 test sites per volar forearm, 3 cm in diameter. Assignment of test sites was done utilizing a Latin square design randomization. Each site was wet with running water (34°C-39°C), and the requisite product was applied volumetrically. The bar soap was applied by stroking a masslinn towel across the bar for 6 seconds and transferring the lather to the test site with the towel. Test sites were washed for 10 seconds, the lather allowed to sit for 90 seconds and rinsed for 15 seconds, then blotted dry. Visual observations were made prior to each morning (including initial baselines prior to the first wash) session, with visual and instrumental analysis made 3 hours after the final wash on day 5.

For the testing of leave-on products (lotions, alcohol rubs), the treatment phase consisted of a washing session of 1 wash of Ivory soap (Proctor and Gamble, Cincinnati, OH), 30 minutes prior to the application of test articles to dry out the skin. Each site was wet

with running water (98°F ± 5°F) for 5 seconds, the bar lathered for 10 seconds, and the forearms washed for 20 seconds. The forearms were then rinsed for 20 seconds and gently dried with a disposable towel. After a 30-minute waiting period, baseline evaluations were conducted. After baseline evaluations, the test article was applied volumetrically to a 3-cm-diameter test site (foam products were applied first to weight boat on a balance, weighed, and then applied). Assignment of test sites was randomized utilizing a complete block design. Test sites were rubbed for 60 seconds. The instrumental evaluation for moisture levels in the skin was measured at baseline (just prior to application of test articles) and at varying times after application utilizing the instrumentation noted in the figure legends. Readings were taken in a room maintained at 70°F (±2°F) and 30% to 50% relative humidity following a 30-minute equilibration period. Three replicates of each reading were taken.

Statistical analysis

Data used for statistical analysis were changes from baseline. Within-treatment analysis was conducted using Wilcox signed rank test. Instrumental data were analyzed using the Student *t* test for paired data. The significance level of .05 was employed.

ASSESSMENTS

Clinical studies can also involve the use of the products in an actual health care environment. Assessments are made on subjects using the products as part of their everyday activities under actual in-use situations.

Technology enables clinicians to measure the impact of a given formulation/product on skin health. The variety of tools currently available offers a multidimensional approach to understanding subtle, often invisible changes that can impact the skin's function. A variety of parameters, such as hydration and barrier function, and visual assessment of dryness and redness, can be done on the same test site.

A trained evaluator assesses the skin surface using magnification of at least ×3. The dryness and erythema scores usually range from 0 to 6. Zero is considered normal with no observable scale or irritation. A score of 6 indicates extensive cracking of skin surface and widespread reddening of the skin. Assessments can also be made with the aid of high-resolution photography, by which the increased image resolution allows for the ability to differentiate between normal and damaged skin at a very low level.

Transepidermal water loss (TEWL) reflects the integrity of the SC water barrier and can be an indicator of skin damage.[78] It is the classic technique used to determine the disruption to the skin barrier by soap and surfactants, alcohols, or other various treatments.[79] TEWL is measured with an evaporimeter. This instrument can detect changes in the skin integrity before they become visually apparent.[80] It utilizes a humidity sensor to record the rate of water loss from the skin. Relative increases in TEWL values are indicative of skin barrier damage.

Various instruments have been designed to measure moisture content of the SC. The electrical conductance, capacitance, or impedance of the skin surface is measured by these types of instruments.[81-86] The measurements of these ''moisture meters'' have been demonstrated to correlate to water content in the SC.[87-89] The values decrease as the skin dries out because of moisture loss and increase as moisture content in the SC increases. Therefore, undesirable negative changes in the water content of the SC results in a lower or diminishing reading. The selection of instruments is usually made based on the range of moisture content (ie, dry vs very moist skin).[90] A variety of other physical and chemical properties of skin can also be quantified, including elasticity, topography, and measurement of chemical compounds typically found within the skin matrix, such as natural moisturizing factors.

Impact of formulation on skin condition

To be able to maintain healthy skin under the stress conditions (listed earlier) that exist in a health care environment, the products used must be designed to both work well for the intended function (cleansing, antimicrobial efficacy, moisturization) and to be kind to the skin. As health care workers comply with appropriate guidelines and utilize infection control products, it is important to encourage their continued use through acceptable aesthetics and positive impact on skin health.[91] If skin becomes dry and irritated, compliance with appropriate infection control guidelines will decrease.[4,58] Therefore, the products used as part of a comprehensive infection control program must contain ingredients with characteristics that make them appropriate choices for a given formulation, and they must function well together.[92] Thus, evaluation of any product formulation should include review of the individual ingredients as well as data generated on testing of the total formulation.[77] Milder surfactants and antimicrobials, as well as the use of skin conditioning agents that redeposit moisture and/or refat the skin, can have an influence on skin condition and significantly mitigate the drying effects of cleansers[93] and alcohol.

The use of formulation technologies offers the opportunity to break the cycle of noncompliance by controlling the types and amounts of ingredients that

are used on the skin. Formulation technology can help provide products with pleasing aesthetic properties (also recognized as an important factor in encouraging proper hand hygiene) that do not negatively impact skin condition and novel product forms that provide innovative strategies for encouraging hand hygiene.

Ingredients

Antiseptic agents. Antimicrobial-containing products are used in situations in which increased reductions of organisms on the skin (compared with plain soap and water cleansing) are desired.[94] Antimicrobial agents can cause irritation, either directly or through the choice of other ancillary ingredients (eg, a defatting or irritating surfactant) that are mandated by compatibility issues with the antimicrobial agent. Certain antimicrobial agents can also cause sensitization in some users. Although active ingredients can cause irritation or sensitization in some instances, it is important to understand that it is the formulation as a whole that impacts skin health. In many cases, the antimicrobial ingredient plays little or no part in the irritation or dryness experienced when using hand hygiene products. It is the ''inactive'' ingredients in a formulation, such as cleansing agents or the lack of moisturizing agents, as much as any active ingredient, that can have the greatest impact.

Iodophors were initially developed to provide a ''tamed'' form of iodine, a well-established antiseptic agent. However, no matter how ''tamed'' the form of iodine is, this active still functions through oxidizing chemistry, so the list of ingredients that are compatible with this chemistry are narrow. This limits the surfactants and skin-conditioning agents that can be used in combination with iodophor compounds. Unfortunately, this compromise produces an antimicrobial with reduced clinical efficacy in combination with less aesthetically pleasing and relatively irritating overall formulations that still possess sensitization potential.[45,95-97] These characteristics, as well as staining issues, have limited iodophor use to primarily surgical scrub and prep applications.[98]

Chlorhexidine gluconate (CHG) is a cationic molecule with good substantivity to skin.[99] This skin substantivity makes CHG-based products exceptionally good at providing the cumulative and persistent activity that is a required or desirable attribute for specific health care applications.[99,100] CHG is inherently mild to the skin, based on available data.[101] This combination of substantivity and mildness has made CHG a popular choice as an antimicrobial agent used in health care environments. However, the cationic nature of CHG that makes the skin-binding characteristic possible also limits the cleansing formulations that utilize it as an active ingredient because it can only be formulated with a relatively small list of compatible surfactants that do not generally foam well.[99] As a result, some formulations of CHG cleansers have included higher concentrations of surfactants to generate foam, a desirable attribute for skin cleansers.[100] These higher levels of surfactants tend to defat the skin with frequent use. Other approaches have used surfactants that have higher intrinsic foam but are less mild. As a result, CHG cleansing formulations have historically not been able to realize fully the fundamental potential of CHG-based cleansers to deliver the best skin compatibility. CHG can also be a sensitizer to a small portion of the population.[96,102,103]

Alcohols can defat the skin,[104,105] an effect even more pronounced when used in rinse-off applications. However, data indicate that alcohols applied to the skin in a leave-on application produce little irritation when properly formulated.[5,106] This is presumably due to the fact that lipids momentarily solubilized by alcohol are immediately redeposited to the skin as the alcohol evaporates. This evaporative property of alcohol also limits its persistence.[31,107,108] However, some formulations overcome this limitation though the inclusion of evaporation retardants and other agents that can extend and enhance activity.[109] Alcohols can also enhance the penetration of skin-conditioning agents and other antiseptic agents. There have been suggestions that alcohol types vary in their skin compatibility properties, but there is little evidence to substantiate those views.[110] When formulation effects are taken into account, there seems to be little difference in skin compatibility among alcohols.[111,112]

Triclosan is widely used as an antiseptic agent in professional health care and household products.[70,113,114] Triclosan has low inherent irritation potential and is not known to produce sensitizing effects.[70,113] In fact, studies suggest that triclosan exhibits antiinflammatory properties in human tissue.[70,73,113,115] This active ingredient is substantive to the skin as a result of binding to epidermal lipid components. These properties make triclosan a preferred choice for antiseptic cleansing formulations and provide good user acceptance. However, the antiseptic efficacy of triclosan can be dramatically affected by formulation properties because it can be trapped by surfactant micelles.[70] Optimizing activity, while maintaining low irritation and positive aesthetic properties, presents a significant formulation challenge.

A variety of other less common antiseptic agents are also used in health care settings around the world.[31] Although these agents vary in inherent mildness, in almost every case, the observed irritation potential and acceptability of specific products are highly formulation specific.

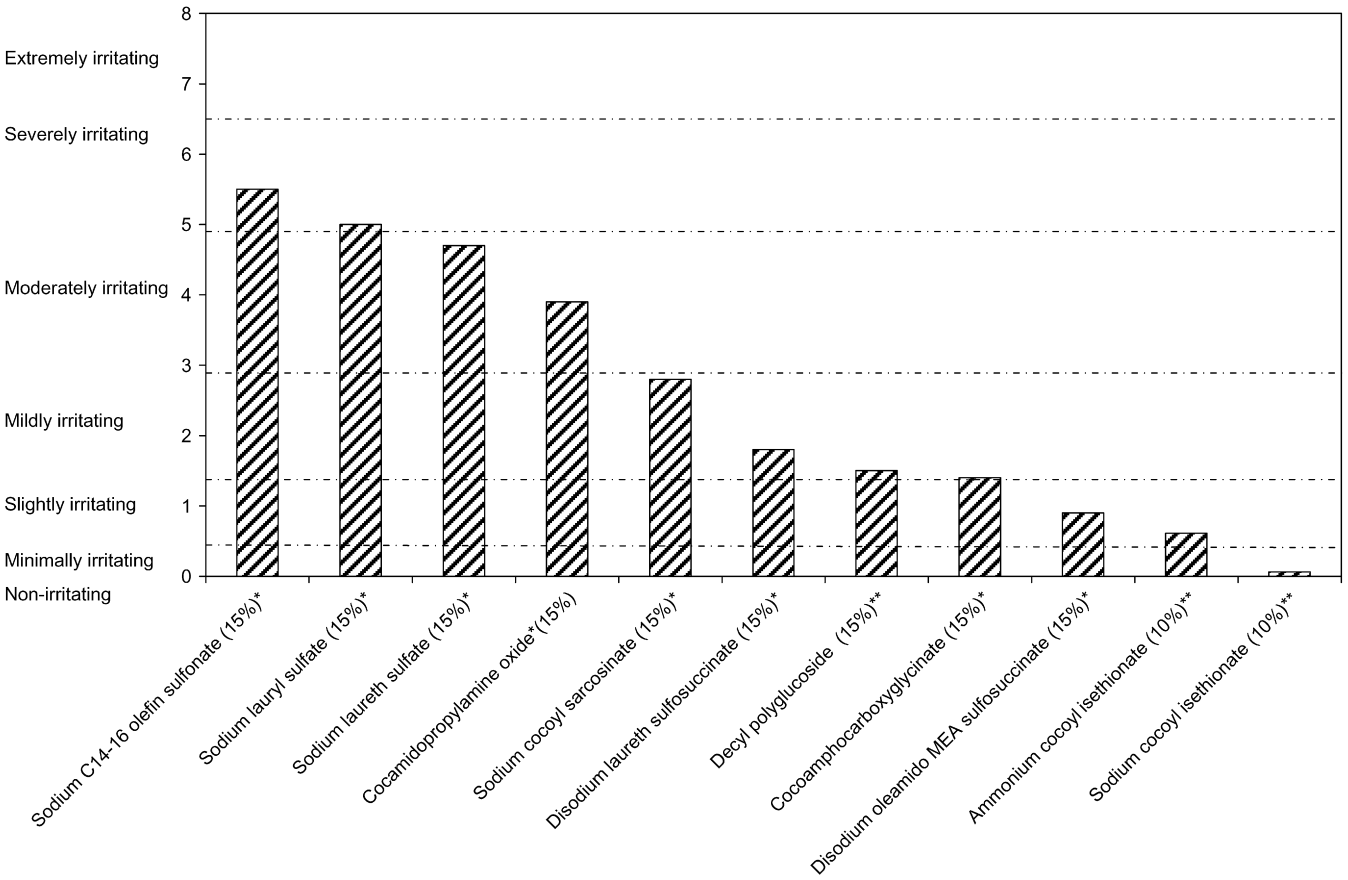

Fig 2. Mean primary irritation (PII) score for commonly used surfactants. *Data adapted from Schoenberg T. Formulating mild foaming bath products, Cosmetics and Toiletries. Vol. 100, No. 5, page 53. **Individual surfactant supplier literature, "Jordaopon Cocoyl Isethionates," printed in the USA January 1995 by PPG Specialty Chemicals, Gurnee, Illinois.

Surfactants. Surfactants (surface-active agents) are multifunctional ingredients that have the ability to reduce surface or interfacial tension. They perform this function by lining up at an interface. They can act as wetting agents by reducing the surface tension of water (lowering the tendency to "bead up" and allowing "spread" on a surface). They can act as cleansing agents by emulsifying or solubilizing soils and exhibiting lathering properties. They can perform as emulsifiers to create and maintain dispersed droplets of one liquid in another (lotions, creams). They can also serve as hydrotropes (increasing the solubility of other less water-soluble surfactants) and soil-suspending agents.

The very nature of cleansing products can make them irritating to the skin.[73,116-119] The act of removing soil from the skin surface seems in conflict with maintaining adequate moisture and lipid levels. However, the choice of ingredients is critical to being able to walk the fine line between soil and organism removal and skin irritation and dryness. The damaging effects of high-frequency handwashing results from both the inherent irritation characteristics and stripping (defatting) properties of the product used and the damaging effects of water.[120,121] By solubilizing or disrupting the lipids that help maintain healthy water content and normal skin physiology, negative impact on skin condition can result. In cleansing products, the ingredients performing soil removal are surfactants. The right choice of surfactants, as well as the inclusion of proper moisturizing agents, can prevent or dramatically lessen the dryness and irritation associated with the act of washing.[93] This is accomplished by using surfactants that are mild, that are not defatting, and that rinse well from the skin surface.[5]

There are many surfactants that are well-known to be irritating to skin.[118,122,123] These tend to be prevalent in consumer products because they foam and clean well and are inexpensive for the manufacturing company.[69] In a consumer home setting, the limited numbers of times these products are used during a day makes the negative properties of these surfactants less apparent

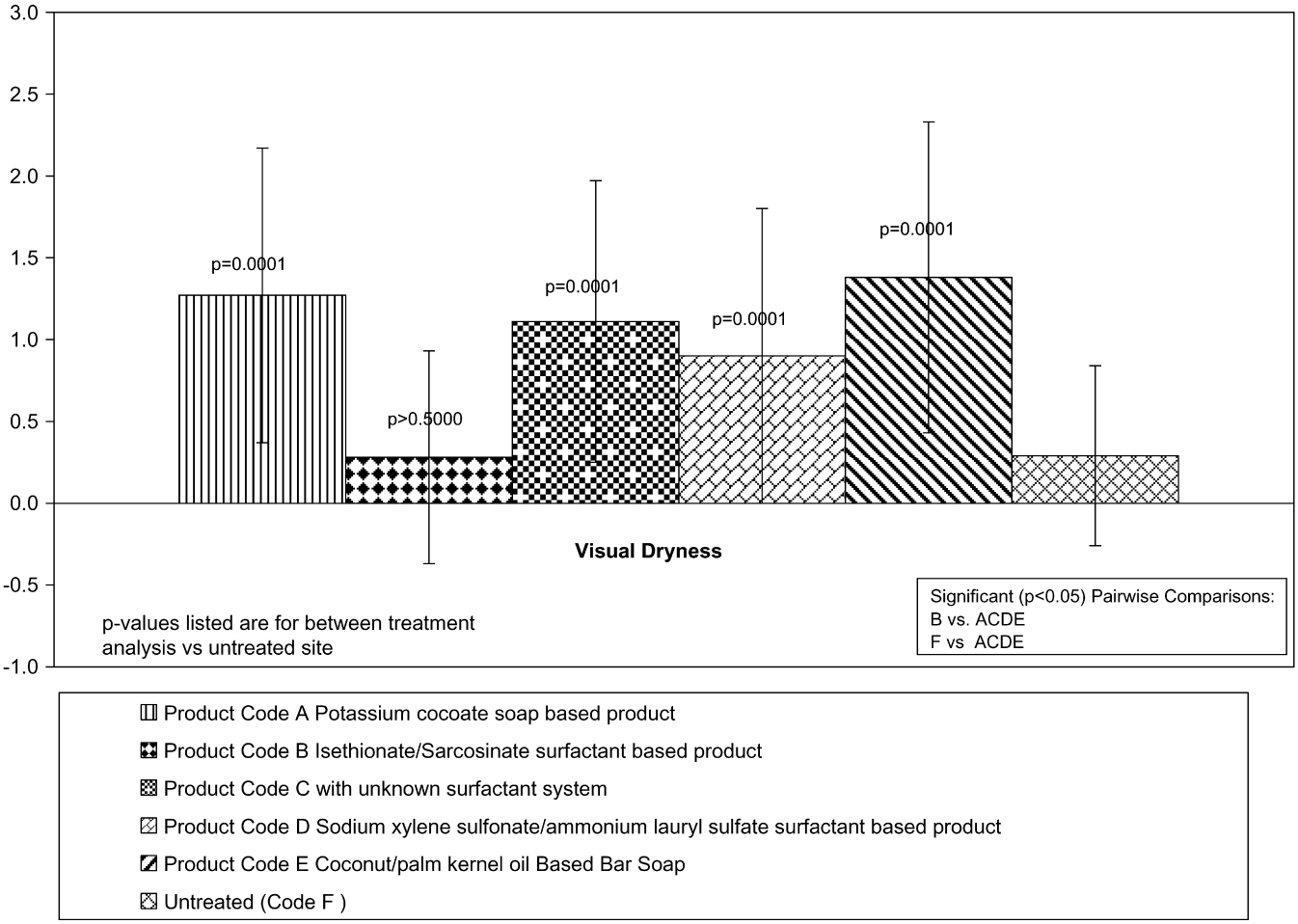

Fig 3. Comparison of skin dryness because of frequent handwashing using foamed soaps in a Forearm Controlled Application Test (FCAT). Forty-eight subjects used the products 18 times over 5 days. Each site utilized test product volumes of 0.2 mL on day 1 and 0.3 mL on days 2 to 5. Visual evaluation was done by trained panel. Study was conducted by Hill Top Research, Inc. (236 Osborne Street, Winnepeg, MB R3L 2W2) Study ID 04-123162-114.

Table 1. Visual evaluation scale for dryness

Grade	Dryness
0	None
1	Patches of slight powderiness and occasional patches of small scales may be seen. Distribution generalized.
2	Generalized slight powderiness. Early cracking or occasional small lifting scales may be present.
3	Generalized moderate powderiness and/or heavy cracking and lifting scales.
4	Generalized heavy powderiness and/or heavy cracking and lifting scales.
5	Generalized high cracking and lifting scales. Powderiness may be present but not prominent. May see bleeding cracks.
6	Generalized severe cracking. Bleeding cracks may be present. Scales large, may be beginning to disappear.

Scale adapted from HTR reference No. 04-123162-114, Hill Top Research, Inc.

and of less significance than in a health care setting. However, based on their inherent skin binding, irritation, and/or defatting characteristics,[5,122,124,125] these surfactants are not generally appropriate to be used as the primary surfactants in products used for the health care environment in which caregivers can wash their hands upward of 50 times per day.

Defatting cleansers can remove lipids from the skin during washing.[37,93,122] Surfactants can solubilize or disrupt the lipids that help maintain healthy water content and normal skin physiology. Disruption of the lipid layer of the skin can result in excessive water evaporation and removal of the skin's natural moisturizing factors and can lead to dry and irritated hands. This is the case for both nonantimicrobial and antimicrobial cleansing products. The drying and irritation effects seen with the use of some skin antiseptics can be attributed to the use of defatting surfactants rather than the antimicrobial agent itself.

Even in those instances when the fatty acid level in the skin is maintained, some surfactants bind to the skin surface more readily and possess greater irritation

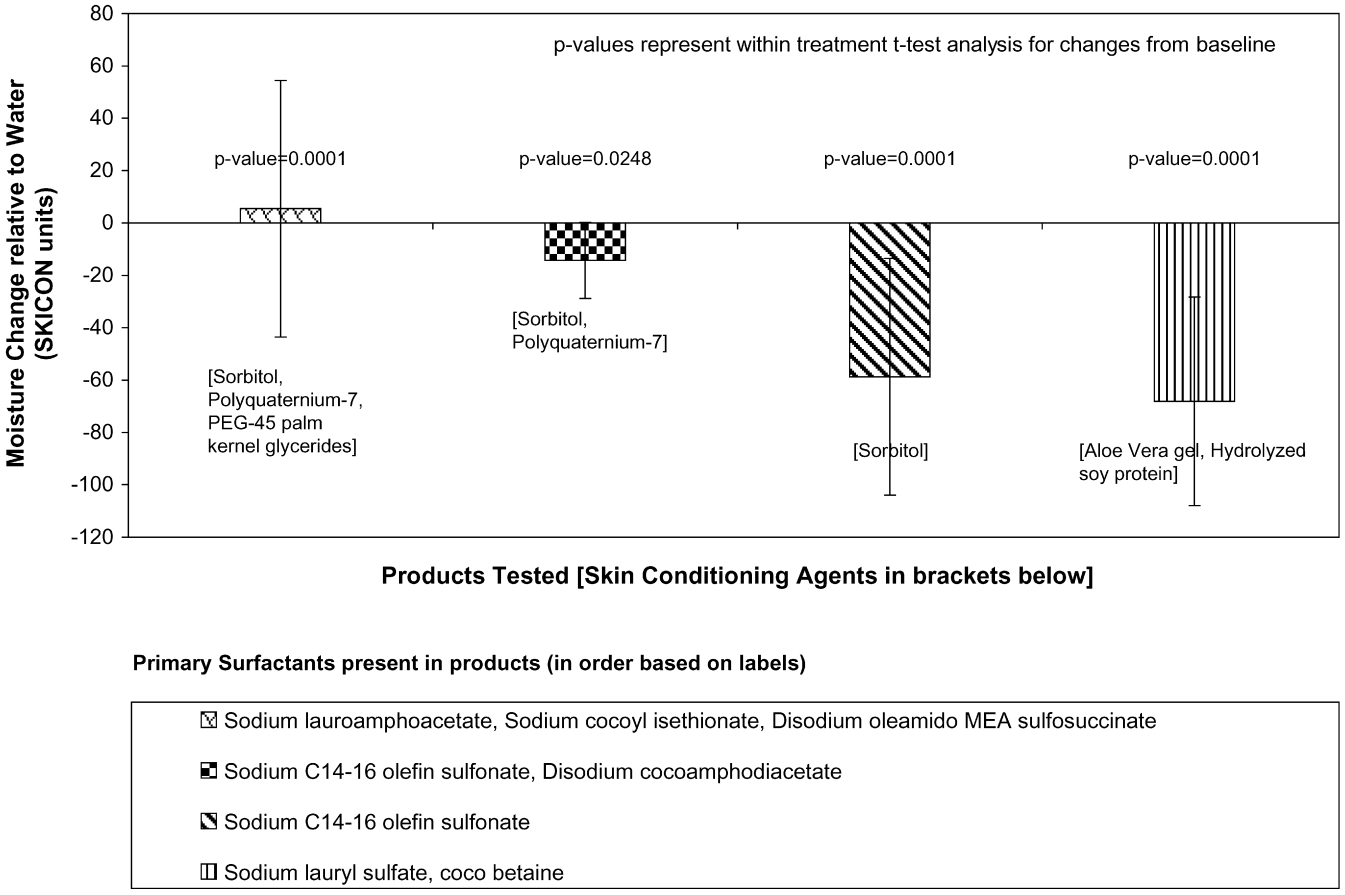

Fig 4. Comparison of skin surface hydration change because of frequent washing using skin cleansers in a Forearm Controlled Application Test (FCAT). Forty-three subjects used the products (0.25 mL) 18 times over 5 days. Untreated skin utilized water alone for washing and rinsing. Moisture level was assessed utilizing a Skicon-200 (I.B.S. Co, Ltd., Shizuoka-ken, Japan) moisture meter. Clinical evaluation March 20, 2000, to March 24, 2000. Study ID 105098-70. Data on file.

potential.[124,126,127] Surfactants such as amphoacetates, amphodiacetates, sulfoscuccinates, and isethionates are significantly milder and a more appropriate choice for use as primary surfactants in health care products.

One can learn which surfactants have inherent mildness characteristics by comparing the primary irritation index for individual components (Fig 2). This index compares the irritation reaction (a combination of swelling and redness) for ingredients in contact with the skin for an extended period of time. Each score is both an addition of multiple evaluations and an average over multiple test subjects. Thus, the higher the irritation score, the more inherently irritating is the surfactant. Therefore, the amount of ingredients in a formulation with high primary irritation index scores should be minimized or eliminated. Blending of milder surfactants with those that are inherently more irritating can also provide increased mildness.

In vivo testing of cleansing products is also an important part of defining mildness of a given formulation.[116,121] Although inherent irritation potential (based on mildness of individual ingredients used) is a good starting point, a product containing ingredients with low irritation potential can still be defatting and, therefore, drying to the skin. Combinations of ingredients can also have different effects than individual ingredients. A test mimicking the actual use (ie, cleansing of skin) is thus important to define which products have the least negative impact on skin condition (Fig 3; Table 1). The FCAT testing shown in Fig 3 utilizes the visual assessment of skin cleansed with a variety of products to demonstrate the effect of surfactant systems on skin dryness. Within the test represented in Fig 3, sites washed with product code B were similar to those that were untreated and significantly less dry than other articles tested. Product code D was also significantly less drying than product codes A and C. The milder surfactant-based systems resulted in less drying of the skin over the test treatment of 18 washes.

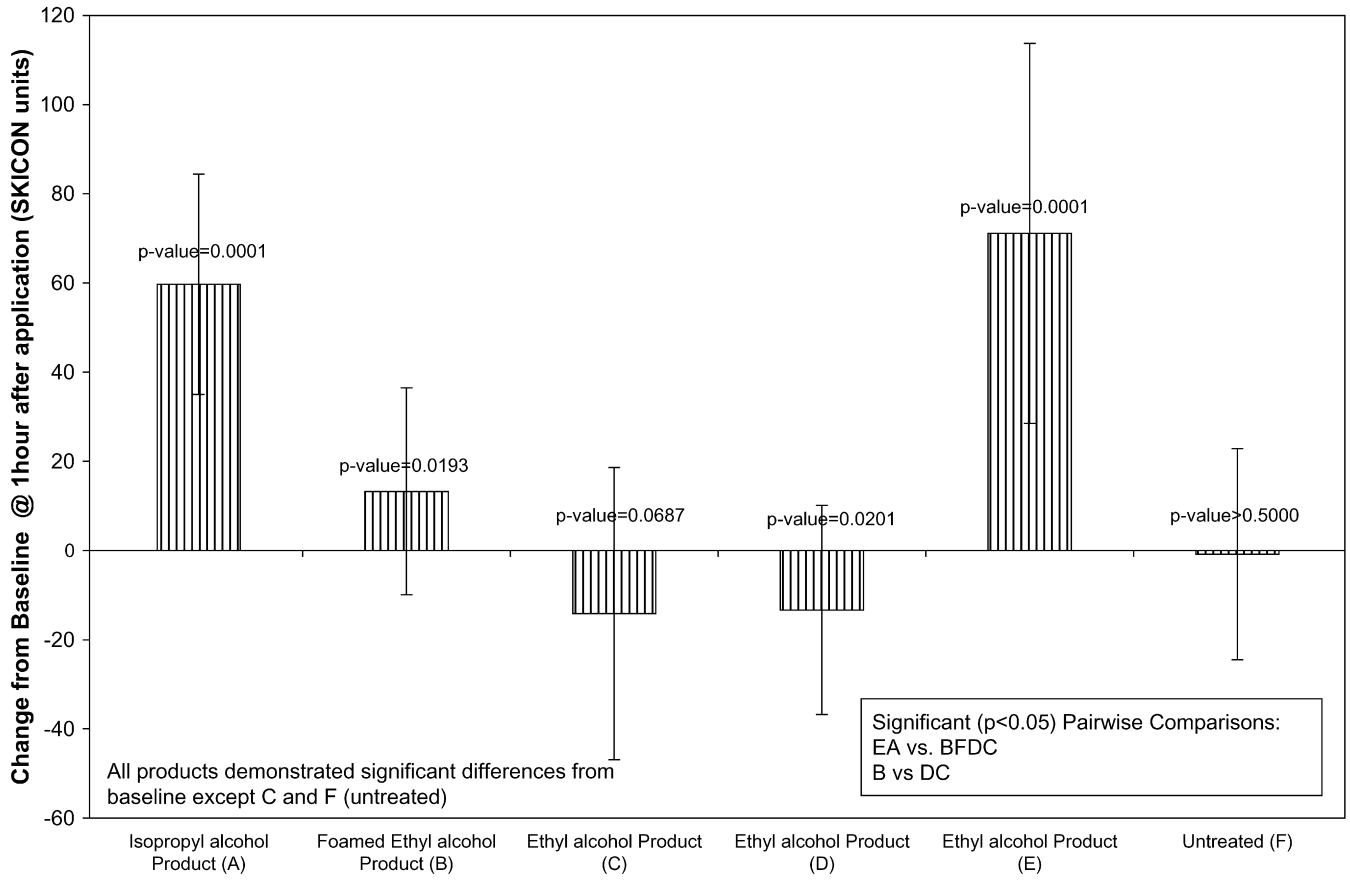

Fig 5. Comparison of moisture levels in skin 1 hour after single application of alcohol product in a modified Forearm Controlled Application Test (FCAT). Moisture level was assessed utilizing a Skicon-200 moisture meter with an MT-8C probe (I.B.S. Co, Ltd.) in 20 subjects. A single application of the test article (0.05 mL) was applied. One test site remained untreated. Triplicate readings were taken. Clinical evaluation June 3, 2004, to June 4, 2004. Study ID 04-123124-112. Data on file.

Skin-conditioning agents. Skin-conditioning agents are important across a wide variety of product types and forms. The addition of skin-conditioning and -moisturizing agents to a formulation can have a significant impact on the overall drying potential of a product by either replacing or helping to prevent further loss of moisture and by refatting the skin.[70,128-131]

There are different types of skin-conditioning agents, which are distinguished by their effects. Emollients (such as PEG-45 palm kernel glycerides or isopropyl myristate) smooth the skin surface and improve the appearance of skin by reducing flaking and improving pliability. Humectants (such as glycerin or methylpropanediol) increase moisture in the upper skin layers by binding water. Occlusive agents (such as mineral oil or dimethicone) retard the evaporation of water from the skin by forming a layer on the skin that moisture does not penetrate well. Other miscellaneous agents (such as behentrimonium methosulfate or polyquaternium-7) can enhance appearance by adhering to the skin surface. Different types of moisturizing agents make sense for different product application, and combinations of agents are usually best to maximize effectiveness. Skin-conditioning agents can also grant lubricity to cleansing products, improving the aesthetic appeal while washing and providing a soft after feel, once hands are rinsed and dried.

In cleansing products, the use of mild surfactant combinations to ameliorate drying effects can be further enhanced by the addition of skin-conditioning agents. Although moisturizing agents have a great benefit, they cannot overcome the inherent binding or irritation potential of poor surfactant selection. Surfactants and moisturizing agents must work together to minimize the drying effects of washing with water. The combination of mild surfactants and appropriate skin-conditioning agents can result in products that exhibit minimal change to the skin moisture levels with frequent use. Figure 4 graphically represents the ability of mild surfactants (amphoacetate, isethionate, and

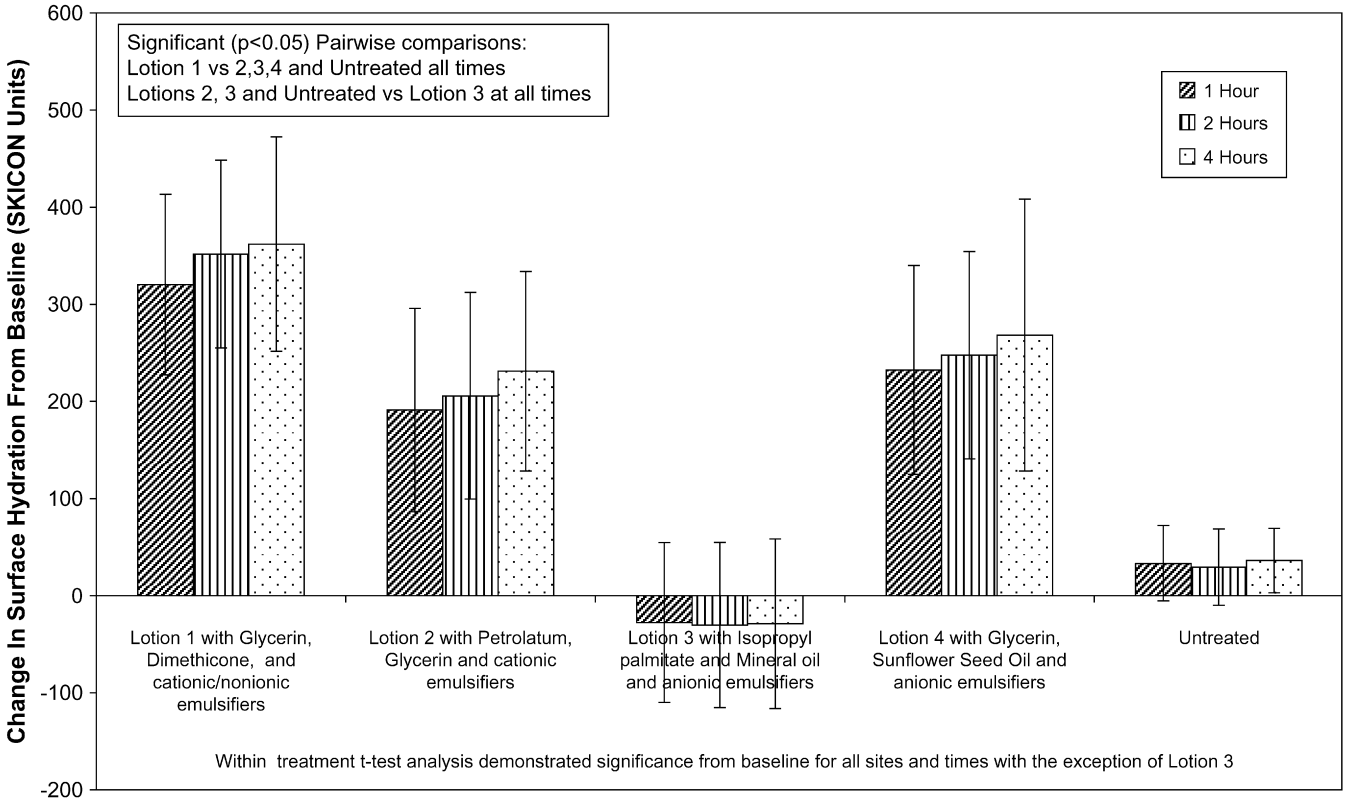

Fig 6. Comparison of moisture levels in the skin after application of lotion products in a modified Forearm Controlled Application Test (FCAT). Moisture level was assessed utilizing a Skicon-200 (I.B.S. Co, Ltd.) moisture meter with an MT-8C probe in 20 subjects. Two applications of the test article (0.05 mL) were applied 30 minutes apart. Clinical evaluation August 18, 2004, to August 19, 2005. Study ID 04-12004-112. Data on file.

sulfosuccinate) combined with moisturizing ingredients to improve the moisture levels seen in the skin when compared with washing with water alone. The FCAT testing and moisture meter assessment demonstrated that sites washed with the product containing sodium lauroamphoacetate as the main surfactant and sorbitol, polyquaternium-7, and PEG-45 palm kernel glycerides as emollients demonstrated a slight increase in moisture over the untreated site. Even in the cases in which the emollients utilized were similar (3 of the products tested utilized sorbitol as a moisturizing agent and 2 of the products utilized both sorbitol and polyquaternium-7 as emollients), it appears that it is the utilization of both mild surfactants and the proper skin-condition ing agents that makes the greatest difference to skin hydration. Only the product with a combination of a mild surfactant (sodium lauroamphoacetate) and multiple skin-conditioning agents demonstrated a positive effect (increase) on skin hydration in this test. All others varied in the level of moisture loss as compared with untreated skin. There were, however, significant differences in moisture content lost from the skin among the other products tested, depending on which surfactants were used and how much skin-conditioning agent(s) was present.

Skin-conditioning agents must be included in alcohol-based hand antiseptic product formulations, or alcohol will have a drying effect with repeated use. The trend toward increased use of alcohol products has been, in part, driven by the need to counteract the decreased compliance resulting from frequent handwashing with irritating and defatting skin cleansers.[132] The benefit of this movement toward the use of these leave-on products, which do not require the use of water, could be offset by the drying effects of alcohol. Therefore, it is important to include skin-conditioning agents in alcohol-based products to increase and maintain compliance with recommended use patterns. The use of appropriate thickeners and emollients can also increase the antimicrobial efficacy of these products by increasing contact of the alcohol antimicrobial ingredient with microorganisms on the skin surface.[133]

Figure 5 represents a modified FCAT test in which products were applied and left on the skin (instead of

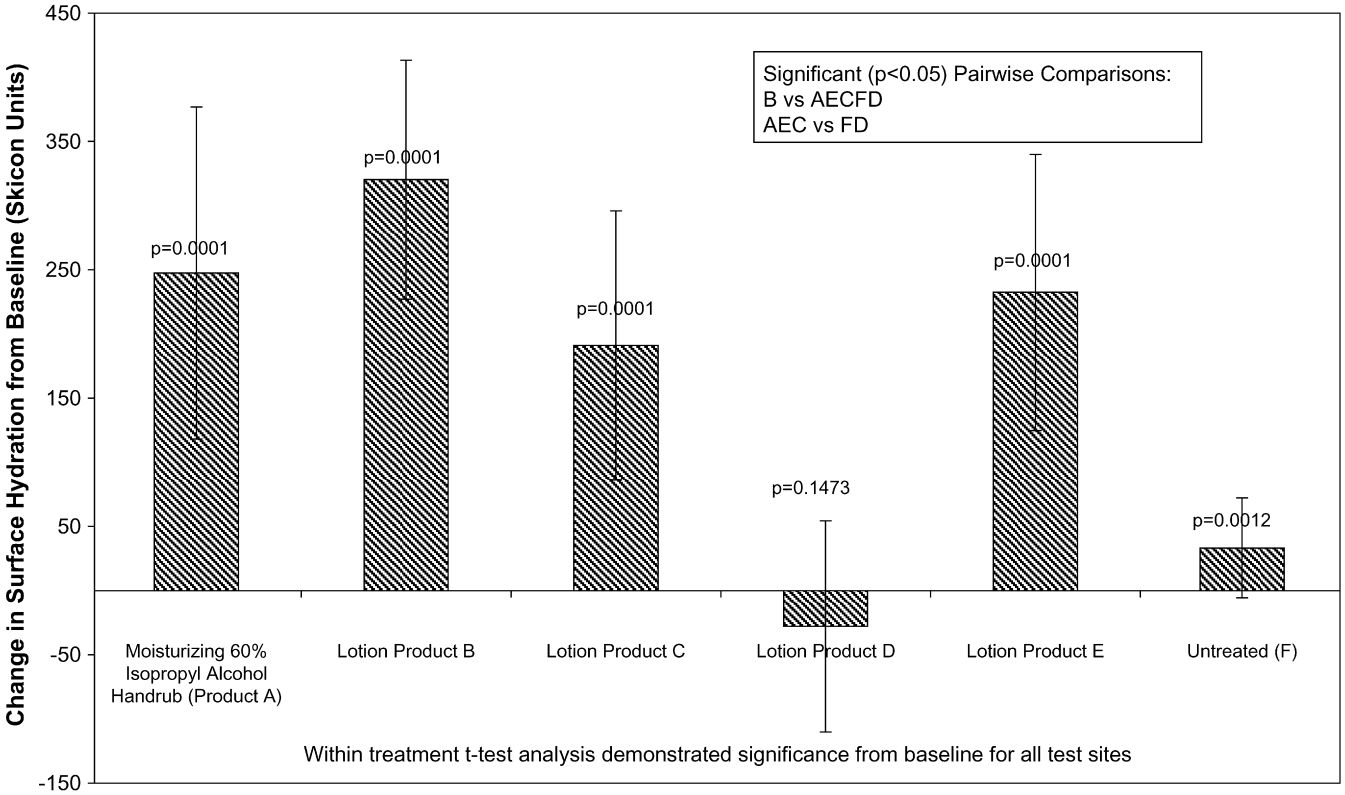

Fig 7. Comparison of moisture levels in the skin 1 hour after 2 applications of alcohol or lotion product in a modified Forearm Controlled Application Test (FCAT). Moisture level was assessed utilizing a Skicon-200 (I.B.S. Co, Ltd.) moisture meter in 20 subjects. Only the site for product B was significantly more moisturized than that of site for alcohol product (A) in pairwise comparisons. Clinical evaluation August 18, 2004, to August 19, 2005. Study ID 04-12004-112. Data on file.

being rinsed off). The products tested all contain approximately the same concentration (61%-63% vol/vol) of alcohol, although the types of alcohol and the form (liquid, gel, or foam) varied. When hydration levels were measured, 2 of the products reduced the level of moisture in the skin over baseline 1 hour after application. Two of the 3 other products tested had a significant positive impact on the moisture level in the skin. All of the products demonstrated significant differences from baseline with the exception of product C. All of the products claim to be moisturizing. Because the alcohol levels were all very similar, it is obvious that other formulation excipients (including thickening and skin-conditioning agents) can demonstrate dramatic effects on the moisturization capabilities of alcohol-based hand hygiene agents. Testing on human skin and resultant data generated can make a substantial difference in the ability to evaluate claims made in regard to moisturization and thus allow informed decision making and a truly positive impact on moisture levels and skin condition.

Lotion products are an important part of any skin care regimen targeting good skin condition.[71,72,134,135] Their function is the transfer of moisture to the skin surface. The routine use of lotions can help to maintain skin health through the replacement of moisture lost by washing or by soothing skin irritated by frequent glove use.[136,137] Not all moisturizing agents work in the same way, and the same moisturizing ingredient in 2 different formulas may demonstrate less effectiveness in one than the other.[138] It is therefore important to gather data that demonstrate the moisturizing efficacy of a product, rather than just an ingredient's presence in a formulation.

A modified FCAT was conducted in which lotions were applied to the skin. The levels of hydration were measured 1 hour postapplication. Figure 6 demonstrated that the 3 different products containing glycerin had different moisturization efficacy profiles. One of the lotions demonstrated 35% better moisturization than the other 2 after 4 hours. The lotion that did not contain glycerin actually exhibited a negative number (loss of moisture) in the testing as compared with both initial values and the untreated control. Based on this information, it becomes clear how very important it is to evaluate a final formulation for skin effects

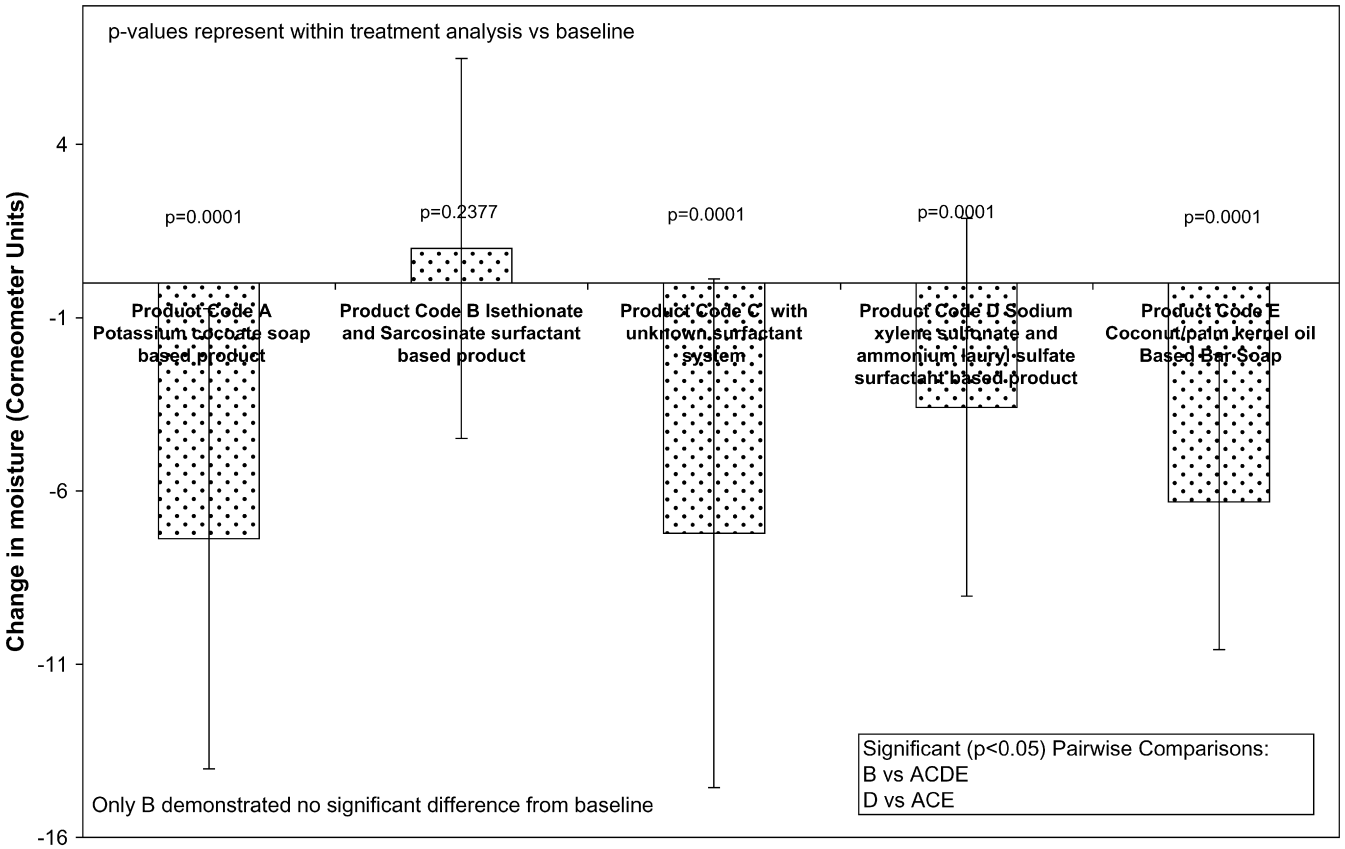

Fig 8. Comparison of moisture loss because of frequent handwashing using foamed soaps in a Forearm Controlled Application Test (FCAT). Forty-eight subjects used the products 18 times over 5 days. Skin surface hydration level was assessed utilizing a Corneometer CM 820 (Courage-Khazaka, Kohl, Germany). Clinical evaluation February 2, 2004, to February 6, 2004. Study ID 04-12316-114. Data on file.

and not to rely only on a listing of label ingredients when making product choices for use as part of an overall skin care regimen.

Other ingredients. There are a large number of other ingredients that can have an influence on user acceptance of a product. These include thickening agents, fragrance, color, and preservative. An ingredient's impact on aesthetic appeal of product is an important factor in ingredient selection. Inappropriately high fragrance levels or inclusion of an unacceptable fragrance can negatively impact use patterns, for example, as can a product that stains fabric or skin. A product must also be adequately preserved to be acceptable.

Novel product forms

When alcohol-based hand sanitizers were first introduced widely in the United States in the early 1980s as a replacement for handwashing, the drying effects of alcohol did little to encourage their use.[31] Currently, alcohol-based hand sanitizers intended exclusively for the health care market incorporate emollients and moisturizers in an effort to overcome this inherent drying effect.[132] This has been successful to varying degrees and is extremely formula dependent. The use of alcohol-based products as a substitute for handwashing is appropriate in many cases because the hands of caregivers can often be contaminated with pathogens without being visibly soiled. In fact, the CDC guidelines suggest that, when used in this manner, these products help improve overall skin condition.[31] Because the intent behind the use of these products is (at least in part) to reduce the negative impact of handwashing, incorporation of moisturizing agents into these products is no longer optional. Newer formulations provide skin-conditioning agents that moisturize similarly to many hand lotions[139] (Fig 7). Thus, the inclusion of appropriate skin-conditioning agents enables the use of alcohol-based hand sanitizers that provide both time savings and opportunity to reduce the frequency of washing with traditional cleansers and water.

Figure 7 represents an evaluation and comparison of an alcohol product containing highly effective

moisturizing agents to lotions in a modified FCAT study. Within this test, the alcohol product moisturized statistically as well as 2 lotions and statistically better than a third lotion. The alcohol product was directionally more moisturizing than all but 1 of the 4 lotions tested. It is possible to get great moisturization characteristics utilizing the proper ingredients, even in a product containing high levels of alcohol. It is false to assume that, because a product is a lotion, it is therefore moisturizing. Not all lotions, nor all alcohols, are moisturizing. Data to support the claims, in the form of data generated on human subjects, are necessary to prove value.

Brushless surgical scrubs have become popular offerings because of formulations that help penetrate and can act on nail beds and cracks and crevices of the hand surface without brushes.[140] Brush usage can result in physical damage, which is an additional insult to the dryness, irritation, and skin damage listed above. Although hand hygiene compliance in the surgical scrub area is not a major issue, other negative consequences of skin damage, such as barrier disruption and increased skin shedding, may be addressed through the use of this relatively new technology.

Another important recent development is the advent of disposable pathway delivery systems that dispense foam soap. These systems utilize mechanical methods to induce foam, making the products more aesthetically pleasing to use. Although some formulations are based on the need to provide less expensive alternatives to liquid soap products, the more important opportunity exists in the ability to utilize milder surfactants that inherently do not foam well and to incorporate increased levels and improved combinations of skin-conditioning agents. In more conventional liquid soaps, these combinations could inhibit foam formation during washing. Thus, it is possible through the use of this foaming technology to formulate cleansing products that do not have a significant or measurable negative impact on skin condition. Figure 8 compares the differences in moisture levels in skin after human subjects washed multiple times over a 5-day period (FCAT study) with a variety of foamed soaps intended for use in the health care environment.

Visual assessment of the skin (Fig 8) demonstrated that sites washed with product code B were similar to those that were untreated and significantly less dry than other articles tested. Product code D was also significantly less drying than product codes A and C. The milder surfactant-based systems resulted in less drying of the skin over the test treatment of 18 washes.

At least 1 of the products (product code A), containing milder surfactants and significantly increased levels of skin-conditioning agents, demonstrated no negative impact on moisture levels in the skin as compared with the baseline levels of moisture present in the skin at study initiation. All other products tested, including 1 for which ingredients were unavailable, demonstrated statistically significant loss of moisture from the skin (as measured using a corneometer). Although all of the products tested are intended for use in cleansing hands, there are dramatic differences in the amount of moisture left in the skin after testing is completed.

CONCLUSION

The problem of sustaining compliance with hand hygiene practices is one that has been addressed from many different directions. Understanding how the condition of the health care worker's skin affects compliance and taking steps to improve skin health is an important angle that must not be overlooked. The CDC Guidelines for Hand Hygiene in Health Care Settings includes recommendations for improving skin condition and increasing compliance by using well-accepted products, with low irritancy potential, as part of infection control hand hygiene programs. It is possible to develop and select skin cleansers, alcohol handrubs, and lotions that work together to provide a positive impact on skin health and consequently help to sustain compliance with hand hygiene guidelines. Sophisticated formulation technologies and the proper selection of ingredients can provide new products and product forms. These technologies offer the opportunity to change the established paradigm that increased hand hygiene will result in increased skin damage and offer the promise of breaking the troublesome cycle of skin damage and reduced compliance.

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