

Regional differences in stratum corneum reactivity to surfactants

Quantitative assessment using the corneofametry bioassay

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The skin does not react similarly to the presence of xenobiotics over all anatomic sites. Distinct regional differences have been described for irritancy and percutaneous absorption. The present study assesses the regional variation of stratum corneum reactivity to surfactants using the corneofametry bioassay. Stratum corneum was harvested from 6 body sites in 20 young adults. Corneofametry was performed using water, 1% SLS and a 5% soap solution. Data show that the best variable to assess regional variability in irritancy is the overall difference in corneofametry (ODC), comparing the effect of a given surfactant with water. The dorsal hand and volar forearm were the least reactive, the neck, forehead, back and dorsal foot the most reactive, sites. It is concluded that the corneofametry bioassay, through the ODC variable, is a practically noninvasive tool for the evaluation of regional variation in irritancy at the level of the stratum corneum.

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The skin response to irritants is subject to anatomic site variation (1-3). Mechanisms determining such variation in biological response are far from being understood. 2 distinct mechanisms presumably modulate the irritant response, corresponding to direct damage to the stratum corneum and to keratinocytes. In a 2nd step, both may activate the biochemical signals initiating the inflammatory reaction (4, 5). Stratum corneum barrier function, as evaluated by measurements of the transepidermal water loss (TEWL), appears to be an important factor in controlling irritation. However, due to the complexity of the biological processes responsible for inflammation, such a simple concept may be inappropriate for some anatomic sites such as the volar forearm. In fact, there is a decrease in TEWL from the wrist to elbow (6), although the severity of irritant reactions increases in the same direction (7).

Percutaneous absorption is also under the influence of the anatomic site and appears to be correlated with the TEWL level (8). Regional variations in TEWL have been documented, with higher levels on the palm, forehead and ankle, as compared to the forearm and upper back (9, 10).

Regional variations in irritancy and percutaneous absorption may appear distinct although probably related as far as the stratum corneum is concerned. Unfortunately, the interpretation of in vivo testing may be difficult due to large interindividual differences (1, 2, 11). In addition, it is impossible to ascribe the part of primary involvement of the stratum corneum function in the data gathered in vivo. Hence, there is a need to develop predictive methods permitting an accurate evaluation of the stratum corneum role in the regional variations underlying irritation and percutaneous absorption. Among the newly introduced methodologies, the corneofametry (CSM) bioassay performed on human stratum corneum quantifies the aggressiveness of surfactants upon corneocytes (5, 12-16). The regular test is performed on cyanoacrylate skin surface strippings (CSSS) harvested from the ventral aspect of the forearms. No information is currently available for other anatomic sites.

The present study compares CSM data at 6 sites to assess the regional variation of response of human stratum corneum to surfactants as model irritants.

Materials and Methods

20 adults aged 27 ± 4 years were enrolled after signing an informed consent. All exhibited discrete signs of chronic dermatitis on dorsal hands and on the forearms. Series of 3 CSSS were harvested from each of 6 sites corresponding to the mid inner forearm, dorsal hand, forehead, neck, back and dorsal foot. Samples were used for CSM testing with either 1% sodium lauryl sulfate (SLS), 5% soap (Ivory[®], Procter and Gamble, Cincinnati, OH) or water. In short, each CSSS was sprayed in excess with 1 test product. After a 2-h contact time at 20°C, samples were rinsed with tap water and stained for 3 min with a toluidine blue-basic fuchsin solution (PMS, Polychrome Multiple Stain, Delasco, Council Bluff, IA). Their color was measured following the $L^* a^* b^*$ system using reflectance colorimetry (Chroma Meter CR200, Minolta) (12).

Data of the assay were calculated from colorimetric variables and expressed by 3 specific CSM variables (Table 1). They have been described previously in detail (5, 13–17). The corneofurfametry index (CSMI) corresponds to the color differential between each surfactant- and the water-treated CSSS. A significant linear negative relationship exists between L^* and Chroma C^* of the samples. The colorimetric index of mildness (CIM) corresponds to the difference between the L^* and Chroma C^* values of each CSSS test sample (15,16). Hence, the irritancy of surfactants is directly correlated with CSMI values while inversely correlated with CIM. The overall difference in corneofurfametry (ODC) values between 2 test products combines the information gained by CSMI and CIM (Fig. 1). In general, ODC is more sensitive than CIM and CSMI to distinguish the severity of corneocyte alteration by surfactants.

Means (M), standard deviation (SD) and coef-

ficients of variation ($V=10^2 \text{ SD.M}^{-1}$) of CSMI and CIM were calculated for each product at each site. The Friedman test was used to compare the stratum corneum reactivity at the anatomic sites. Regression analysis models were applied to evaluate the relationships between paired data. The best model, i.e., linear, logarithmic, exponential or power, was chosen on the basis of the highest coefficient of correlation r . A p -value lower than 0.05 was considered as reaching statistical difference.

Results

Colorimetric index of mildness

CIM values of the 2 surfactant solutions demonstrated that all values were significantly ($p < 0.001$) lower than water-CIM (Fig. 2, 3). For all 3 test

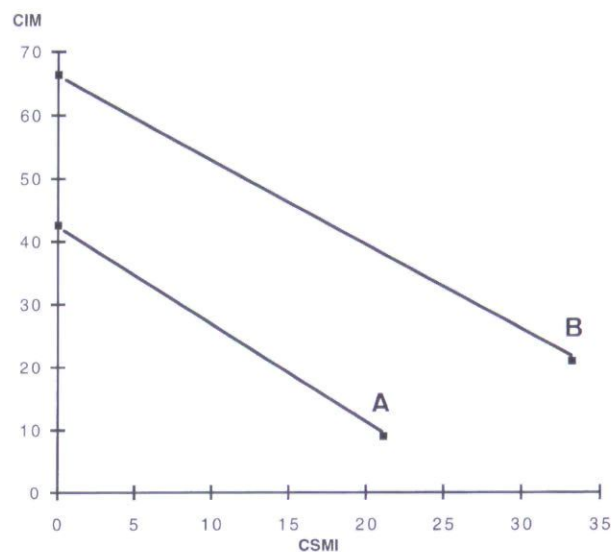


Fig. 1. Schematic representation of 2 ODC (length of the lines A and B) showing different reactivities of the stratum corneum to surfactants. (A) : weak reactivity; (B) strong reactivity.

Table 1. Colorimetric variables used in the corneofurfametry (CSM) bioassay performed on cyanoacrylate skin surface stripings (CSSS)

Basic variables

$$\text{Chroma } C^* = (a^{*2} + b^{*2})^{0.5}$$

$$\text{Luminancy } L^*$$

$$\text{Colour differential } \Delta E^*_{ab} = [(\Delta L^*)^2 + (\Delta C^*)^2]^{0.5}$$

CSM specific parameters

$$\text{CIM} = \text{colorimetric index of mildness for a given sample} \\ = L^* - C^*$$

$$\text{CSMI} = \text{corneofurfametry index between surfactant- and} \\ \text{water-treated CSSS} \\ = \Delta E^*_{ab}$$

$$\text{ODC} = \text{Overall difference in corneofurfametry between 2} \\ \text{products} \\ = [(\Delta \text{CSMI})^2 + (\Delta \text{CIM})^2]^{0.5}$$

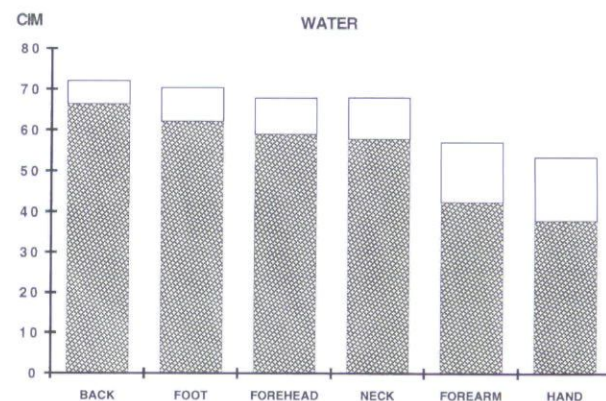


Fig. 2. CIM values (mean $\pm$ SD) for water at different body sites of 20 subjects.

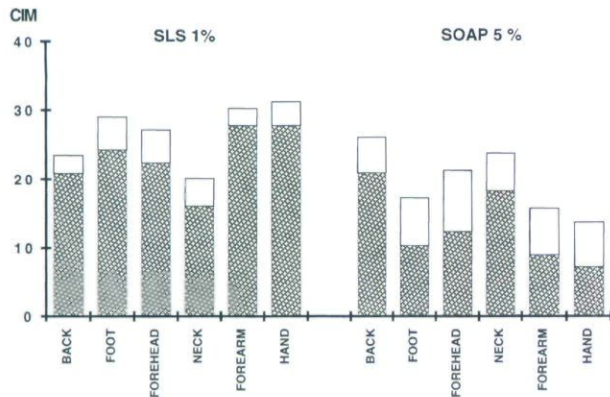


Fig. 3. CIM values (mean $\pm$ SD) for 2 surfactant solutions.

products, the mean values and coefficients of variation of CIM were inversely correlated. The coefficient of variation of water-CIM ranged from 9% on the back to 41% on the dorsal hands. It ranged for 1% SLS from 9% on the volar forearm to 25% on the neck. For the 5% soap solution, it ranged from 24% on the back to 92% on the hands.

Significant differences in water- and surfactant-CIM were observed according to site. However, the ranking of the regional reactivity was not similar for each of the surfactants and water. The dorsal hand and volar forearm yielded a significantly lower water-CIM ($p<0.01$) than the other test sites (Fig. 2). In addition, water-CIM of the forehead and neck were significantly lower ($p<0.05$) than the same variable on the back. Values of 1% SLS-CIM were significantly lower ($p<0.01$) on the neck than on all other sites (Fig. 3). Values on both the dorsal hand and volar forearm were significantly higher than on the dorsal foot ($p<0.05$) and on the other sites ($p<0.01$). Data with the 5% soap-CIM were strikingly different, as values were significantly higher ($p<0.01$) on the neck and back than on the hand, forearm and foot.

Corneofluorescence index

CSMI values of the 2 surfactant solutions evaluated according to the body site are presented in Fig. 4. The coefficients of variation of 1% SLS-CSMI were low and ranged from 6% on the forehead to 13% on the forearm. They were much larger for the 5% soap-CSMI, as they ranged from 15% on the forehead to 41% on the forearm. Similar significant differences in CSMI were yielded for both surfactant solutions according to the body site. Values of CSMI were significantly lower on both the dorsal hand and volar forearm than on both the back and dorsal foot ($p<0.01$) and on the other sites ($p<0.05$).

Overall difference in corneofluorescence

The average ODC values between each surfactant solution and water at each site are presented in Fig. 5. A power relationship ($r=0.78$, $p<0.001$) was noted between all individual values. Coefficients of variation of 1% SLS-ODC ranged from 9% on the back to 25% on the volar forearm. They were higher for the 5% soap-ODC, ranging from 15% on the forehead to 44% on the dorsal hand, between all individual values (Fig. 5). The ODC site reactivity was similar for both surfactants. The SLS-ODC was significantly lower ($p<0.01$) on the dorsal hand and volar forearm than on each other site. The soap-ODC indicated that values for the dorsal hand and volar forearm were significantly lower than for the neck ($p<0.05$) and for the other test sites ($p<0.01$). In addition, the ODC value was significantly lower ($p<0.05$) on the neck than on the foot.

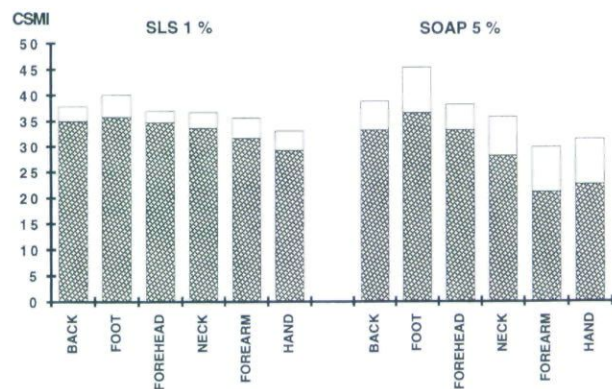


Fig. 4. CSMI values (mean $\pm$ SD) for 2 surfactant solutions.

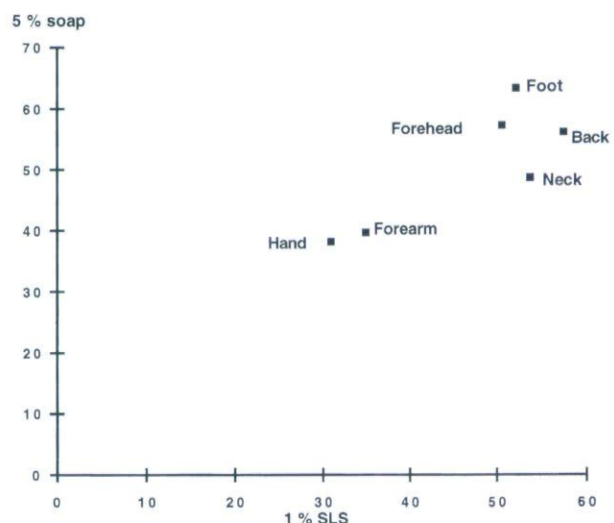


Fig. 5. Scatterplot of the ODC values between water and each of the surfactant solutions.

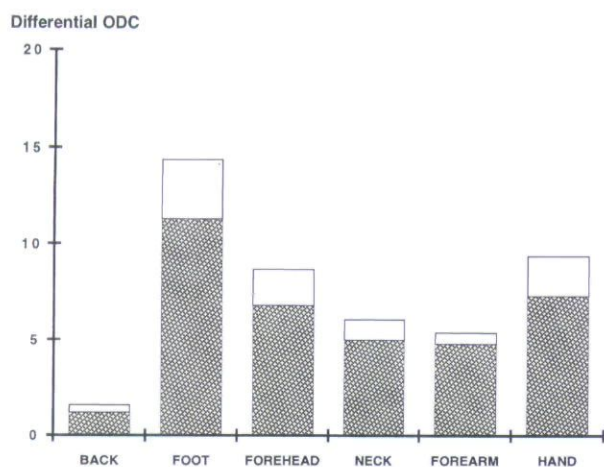


Fig. 6. Difference between the ODC values of 1% SLS and the 5% soap solution.

The inter-surfactant ODC varied according to site (Fig. 6). The back appeared the least discriminant site in differentiating between the surfactant solutions. At the end of the spectrum of reactivity between surfactants and the stratum corneum, the dorsal foot showed the largest difference in ODC between the two test surfactants.

Discussion

Surfactants are among the many chemicals capable of inducing irritant contact dermatitis in man. CSM provides information about the direct damages to the outer portion of the stratum corneum (5, 13–17). The severity of in vivo irritation depends not only on the nature of the chemical agent but also on individual susceptibility and on exposure conditions. In particular, anatomic site influences the proclivity to SLS irritation (3).

The present study using the CSM bioassay shows differences in the reactivity of human stratum corneum to surfactants according to the anatomic site. The test performed with water explores the baseline situation, which reflects both the intrinsic properties of the stratum corneum at a given body site and the effect of previous chemical and/or physical insult to corneocytes. Previous studies conducted on normal stratum corneum harvested from the volar forearm had shown the water-CIM to be about 60 (5, 15, 16). This value is reduced on compromised skin (15–17). In the present study conducted on subjects showing signs of chronic dermatitis, water-CIM was particularly low on the dorsal hand and volar forearm. In fact, the pre-existence of dermatitis almost corresponds to the equivalent of an in vivo CSM. This situation might increase susceptibility to SLS compared to unaffected individuals. This was previously shown

with CSM in sensitive skin and atopic dermatitis (15–17). It was also evidenced in vivo by an increased TEWL in subjects with a positive history of dermatitis after exposure to various concentrations of SLS (18).

The present study shows that, through the ODC values, the stratum corneum response to SLS at different sites predicts the effect of soap exposure at the same sites. This illustrates the validity of drawing general conclusions from ODC corresponding to a single body site. Such a finding contrasts with the higher variability in CIM data and with the inconsistency in severity of irritant reactions at different anatomical regions, as assessed by in vivo measurements of TEWL at patch test sites (2).

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