

Skin condition associated with intensive use of alcoholic gels for hand disinfection: a combination of biophysical and sensorial data

EVI HOUBEN, KRISTIEN DE PAEPE AND VERA ROGIERS

Department of Toxicology, Dermato-Cosmetology and Pharmacognosy, Vrije Universiteit Brussel (VUB), Brussels, Belgium

Although hand hygiene is an important and inexpensive measure to prevent nosocomial infections in clinical settings, the compliance of healthcare workers remains low. In Europe, alcoholic hand disinfection is first choice, but there exists a limited user acceptability due to estimated adverse effects on skin condition. This study was designed to investigate skin tolerance to alcohol-based disinfecting gels and changes in skin condition depending on humectant concentration, alcohol grades, as well as type of alcohol used. A comparison of 6 alcohol-based gels was made based on a randomized double-blind study under *in use* conditions for 1 day. Skin condition was evaluated by measuring transepidermal water loss (TEWL), stratum corneum hydration, apparent skin pH, redness and degree of scaliness. With respect to user acceptability, all gels were sensorially evaluated using a questionnaire. We saw that none of the alcohol-based gels, applied under *in use* conditions, altered TEWL or caused irritation. All gels hydrated the skin, proportionally to their glycerine content, and decreased skin pH. Elevated ethanol concentrations resulted in increased scaliness. Sensorial assessment revealed less appreciation for isopropanol. From this study, it was concluded that gels containing an elevated glycerine concentration and 70% (v/v) ethanol are preferred.

Key words: alcohol-based hand disinfection, skin pH, stratum corneum hydration, transepidermal water loss, user acceptability. © 2006 The Authors. Journal compilation © 2006 Blackwell Munksgaard.

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Hand hygiene of healthcare workers (HCWs) is of major concern to avoid nosocomial infections (1–4). Therefore, hospitalwide infection control programmes prescribe disinfection of the hands after each patient contact (5, 6). In central Europe, alcohol-based hand rubs are the first choice, because they have been found to achieve a better antimicrobial activity compared with detergent-based antiseptics (7–10). Because no running water is needed, alcoholic rubs – and particularly gelified alcoholic products – are easier to handle, do not require extra hospital infrastructure and their application is less time consuming in comparison with standard handwashing with a detergent-based product (11). Additionally, alcohol-based products seem to be more skin friendly than detergent-containing products (7, 12–14). It was also shown that the usage of an alcoholic gel hand sanitizer can decrease infection rates in healthcare facilities (15). The compliance with alcoholic hand disinfection, however, remains low because of forgetfulness, heavy workload, lack of scientific

information promoting hand hygiene, but mainly because of limited user acceptability (16–18). Indeed, hand hygiene procedures must provide skin comfort in order to be regularly used. Although skin irritation, commonly provoked by detergents, is not present, the short chain alcohols of these products have the reputation to ‘dry out’ the skin – frequently despite the presence of emollients – and are thought to cause a burning skin sensation (19). The present study was designed to objectively measure the changes in a healthy skin condition associated with the usage of alcohol-based disinfecting gels depending on the humectant concentration, the alcohol grade as well as the type of alcohol used. These findings were linked to a sensorial assessment, performed by HCWs. A comparison of 6 disinfecting hand gels (gel A containing 70% (v/v) ethanol and 2% (v/v) glycerine, gel B containing 70% (v/v) ethanol and 5% (v/v) glycerine, gel C 70% (v/v) ethanol and 8% (v/v) of glycerine, gel D 75% (v/v) ethanol and 2% (v/v) glycerine, gel E 80% (v/v) ethanol and 2% (v/v)

glycerine and gel F 70% (v/v) isopropanol and 2% (v/v) glycerine) was made based on a randomized double-blind study using non-invasive bioengineering techniques and a survey containing questions about user acceptability.

Materials and Methods

Study populations

13 female, non-professional volunteers (27 ± 4 years old, age range 21–37) having Fitzpatrick skin type II or III and not suffering from any skin pathology took part in the application study that was biophysically monitored. None of the participants had previous experience of using alcohol-based rubs, and they were instructed to refrain from using skin care products on the skin areas involved in the study (from 1 day before the measurements until after the last measurements).

For the sensorial evaluation of the alcohol-based hand rubs, 21 professional HCWs (18 females, 3 males), not suffering from any skin pathology, were recruited. These participants had a long experience of using alcohol-based rubs due to their employment in clinical settings with a high risk of infection and frequent patient contact.

All participants signed an informed consent after being fully informed about the experimental procedures. An ethical approval for the study was obtained from the Ethics Commission of the Academic Hospital, VUB-Jette (Brussels, BE).

Biophysical measurements

Temperature and relative humidity of the measuring room were controlled and kept within a constant range, i.e. $20.7 \pm 0.4^\circ\text{C}$ and $48.9 \pm 3.2\%$, respectively. The volunteers were resting, prior to the measurements, for 30 min in the climatized room. Skin condition and epidermal barrier function parameters were measured using transepidermal water loss (TEWL) measurements obtained with a Tewameter TM 210[®] (C+K electronic GmbH, Köln, Germany), stratum corneum (SC) hydration values obtained by a Corneometer CM 825[®] (C+K electronic GmbH), apparent skin pH values by a skin pH meter PH 900[®] (C+K electronic GmbH) and the degree of skin erythema by measurement of the a^* parameter of the Chroma Meter CR 300[®] (Minolta, Osaka, Japan). TEWL, SC hydration, skin pH and erythema measurements were always executed in this order to avoid that pressure of the Corneometer probe would interfere with the TEWL measurement and to avoid that the wetness of the skin pH-meter probe would

interfere with the TEWL and hydration measurements.

The degree of the skin's scaliness was determined by squamometry by applying a D-squame[®] with a standardized pressure for 10 seconds, in order to sample the superficial horny layer. After removal of the D-squame[®], it was stained with polychrome multiple stain solution (toluidine blue and basic fuchsin in 30% ethanol), rinsed three times with 10 ml of milliQ water and fixed on a glass slide. To assess the quantity of scales, we performed colorimetric measurements using the chroma C* parameter measurements of the Chroma Meter CR 300[®] (Minolta).

To avoid that squamometric sampling would interfere with the other measurements, we divided each test site into an inner sides for TEWL, SC hydration, skin pH and erythema measurements and an outer side for squamometry (Fig. 1).

The composition of 6 disinfecting alcohol-based hand gels used during the study is given in Table 1.

Experimental design of the application study

The study was conducted over a period of 3 subsequent weeks in autumn. One volar forearm with 6 different test areas of $2 \times 4\text{ cm}^2$ was used for treatment, while the corresponding areas on the other forearm served as untreated control sites (Fig. 1). The application arm and the arm with the control sites were randomized

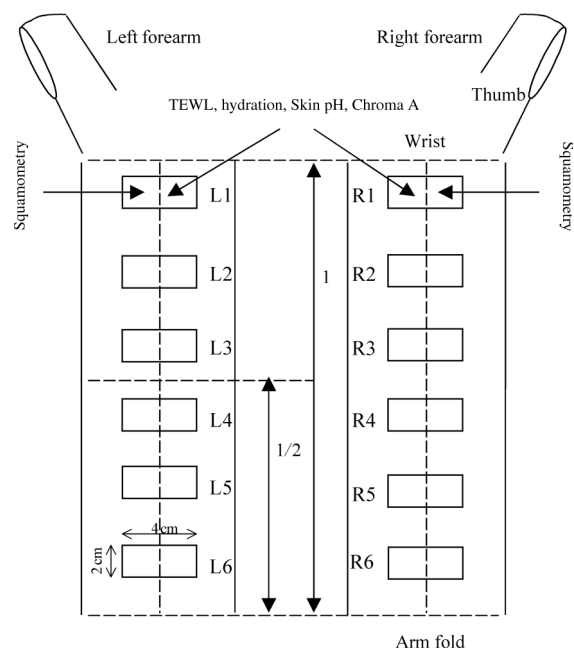


Fig. 1. Schematic representation of the test sites on both volar forearms. One arm (test sites L1 to L6 or R1 to R6) served as application arm, while the corresponding test sites of the other arm served as untreated control sites.

Table 1. Composition of the alcohol-based disinfecting gels used, variations on Gel A are in bold.

Gels	Composition
Gel A	
Ethanol	70.0%
Water	27.6%
Glycerine	2.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%
Gel B	
Ethanol	70.0%
Water	24.6%
Glycerine	5.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%
Gel C	
Ethanol	70.0%
Water	21.6%
Glycerine	8.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%
Gel D	
Ethanol	75.0%
Water	22.6%
Glycerine	2.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%
Gel E	
Ethanol	80.0%
Water	17.6%
Glycerine	2.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%
Gel F	
Isopropanol	70.0%
Water	27.6%
Glycerine	2.0%
Carbomer	0.3%
Tetrahydroxypropyl Ethylenediamine	0.1%

among the participants, as well as the application order for the gels. Randomization was kept blinded for the investigator.

To mimic *in use* conditions, every 20 min 0.03 ml of each gel was rubbed onto the designated test site until dry, and this for 6 consecutive hours. A careful introduction of the application technique to each volunteer was followed by supervision, before allowing them to carry out the procedure on their own. Biophysical measurements were executed on both forearms before product application ($t = 0$ h), 1 h after intensive product usage ($t = 7$ h), found to be necessary for the evaporation of the volatile solvents before TEWL measurement took place, and on the next day ($t = 24$ h).

The relative effect (expressed in percentages) of each gel at $t = 7$ h and $t = 24$ h was counted as follows:

$$\left(\frac{X_t/X_0}{C_t/C_0} \right) \times 100\%,$$

X_0 and X_t are the values measured on the application arm at $t = 0$ h and $t = 7$ h or 24 h, while C_0 and C_t are the values measured on the arm with the untreated control sites at $t = 0$ h and $t = 7$ h or 24 h. Squamometric measurements were only performed at $t = 7$ h on both forearms.

Participants had the opportunity to record any skin reactions like irritation or redness, burning sensations and itchiness, and unspecified comments could also be given.

Evaluation of the user acceptability

To avoid interference with their regular intensive hand disinfection during work, the HCWs could only enroll for the subjective assessment on a day that they were not occupied in their clinical setting.

3 ml of product to disinfect both hands was rubbed in for 30 seconds. Each hand gel was applied once, and only after 1 h, the next product could be tested. All products were blinded, and a randomization scheme was set up between the volunteers.

The participants were asked to evaluate the hand rubs by attributing a score from 1 to 5 with respect to smell (1 = unpleasant, 5 = pleasant), drying speed while rubbing (1 = slow, 5 = fast), emollient effect (1 = drying out the skin, 5 = hydrating the skin) and extent of skin comfort (1 = making the skin rough/scaly, 5 = making the skin smooth/soft) after application. They were asked to record any skin reactions like irritation or redness, burning sensations and itchiness. Also unspecified comments could be given.

Statistical analysis

The data obtained through biophysical measurements fulfilled the conditions for parametric statistical analysis. For each parameter, the $t = 0$ h values were subjected to a one-way analysis of variance to exclude significant differences in baseline measurements. For each individual gel, the measured values (TEWL, SC hydration, skin pH and erythema) on the different time-points were compared with their values before product application by a Paired Student's *t*-test. To discriminate between the gels, we compared the relative effects of the different gels on that particular time-point using the same test. For the scaliness measurements, the chroma C^* value at $t = 7$ h for each gel was compared with its untreated control site, also using a Paired Student's *t*-test.

The data obtained from the sensorial assessment were analysed using a Mann–Whitney test.

Results

Biophysical measurements

No adverse skin reactions with regard to irritation, redness, burning sensation and itchiness were reported.

There was no significant effect on TEWL for any of the gels at $t = 7$ h, nor at $t = 24$ h (data not shown), which made it unnecessary to compare different gels.

Noteworthy is that, in spite of a rigorously standardized application throughout the whole experiment, standard deviations on the mean effects on TEWL are larger than generally seen

by the topical application of other cosmetic preparations, not containing any alcohol. This higher variability is in accordance with other alcohol-based hand disinfectants studies (13, 20) and could be due to potential differences in tolerating alcoholic preparations among the volunteers.

At $t = 7$ h, an increased SC hydration was seen for all gels, and this hydrating effect persisted until $t = 24$ h (data not shown).

A comparison of the relative effects among the gels at $t = 7$ h showed that the higher SC water content is due to the presence of glycerine in all formulations, because the effects were proportional to the glycerine concentration.

At $t = 24$ h, the hydrating relative effects were also more prominent for the gels with an elevated glycerine concentration (Fig. 2).

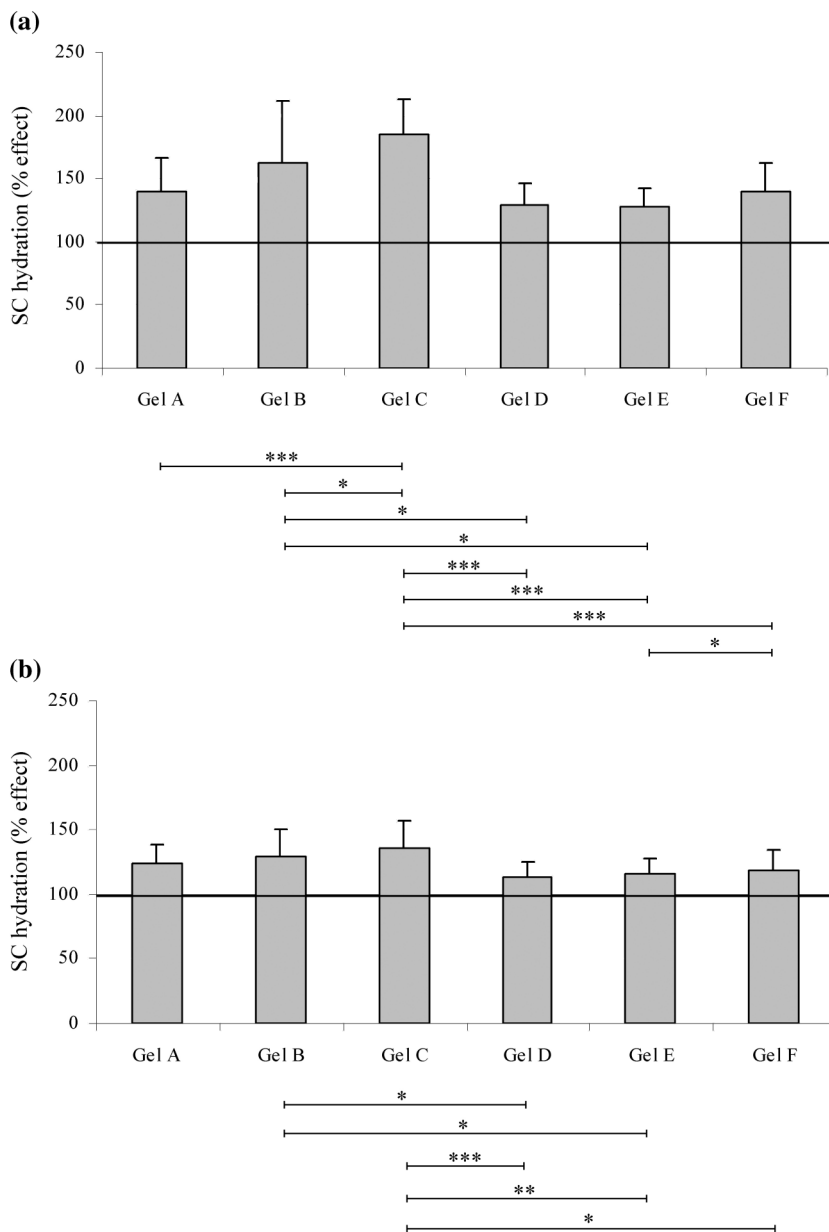


Fig. 2. Comparison of the effects of the tested gels on stratum corneum (SC) hydration at $t = 7$ h (a) and $t = 24$ h (b), expressed as a percentage of the hydration values measured on control skin, which is arbitrarily set at 100%. Mean values $\pm$ SD ($n = 13$). Statistical difference between treatments, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, paired Student's t -test, showing a glycerine-dependent augmentation of the SC hydration.

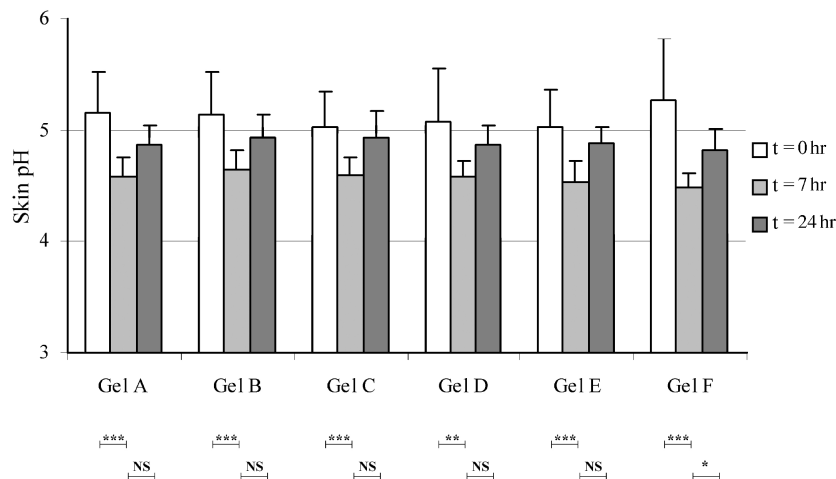


Fig. 3. Representation of the skin pH values at $t = 0$ h (i.e. before product application), $t = 7$ h, and $t = 24$ h. Mean values $\pm$ SD ($n = 13$), $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, paired Student's t -test, demonstrating an acidifying effect for all gels.

All gels caused a significant decrease in apparent skin pH values at $t = 7$ h. However, this effect was completely re-established at $t = 24$ h, with the isopropanol containing gel F as only exception (Fig. 3). When comparing the relative effects on skin pH at $t = 7$ h, the acidifying effect was more significant for gel F in comparison with gels C, D and E (Fig. 4). None of the gels caused a significant alteration in skin redness versus control sites at $t = 7$ h nor at $t = 24$ h (data not shown). This indicates that, under *in use* conditions for 1 day, no erythema occurs.

The Chroma C^* scoring of the D-squames[®] could not discriminate between treated and untreated skin for gels A, B, C and F, but this technique revealed that gels D ($P = 0.020$) and E ($P = 0.009$) gave rise to an increased scaliness, indicating that the higher ethanol concentration is responsible (Table 2). Although this technique was reported earlier to be quite unsuitable for evaluating the moisturizing effects of dermato-cosmetics (21),

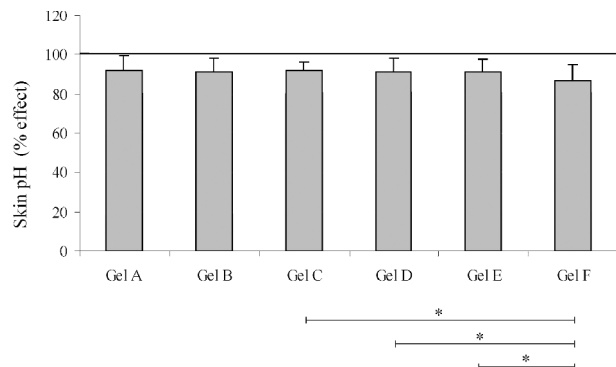


Fig. 4. Comparison of the effects of the tested gels on skin pH at $t = 7$ h expressed as a percentage of the pH values measured on control skin, which is arbitrarily set at 100%. Mean values $\pm$ SD ($n = 13$). Statistical difference between treatments, $*P < 0.05$ (paired Student's t -test), showing an increased and prolonged acidifying effect for the isopropanol-containing gel.

we found it rather useful in this study, where there is expected to be an aggravation of the scaliness.

Sensorial assessment: user acceptability

The outcome of the sensorial assessment is represented in Table 3.

Due to the absence of perfume, none of the gels was scored to smell pleasant. Most of them were found to smell neutral (median = 3), except for gel D and gel F (median = 2). Nevertheless, it was only for the latter, containing 70% (v/v) isopropanol, that the smell was estimated significantly worse than all other gels (gel A versus gel F, $P = 0.001$; gel B versus gel F, $P = 0.0002$; gel C versus gel F, $P = 0.003$, gel D versus gel F, $P = 0.011$, gel E versus gel F, $P = 0.005$).

Gel B and gel C, containing an elevated glycerine concentration, were thought to dry slower than all other gels that contain 2% (v/v) glycerine, although this difference became never significant. The faster drying of gel E, containing 80% (v/v) ethanol, was significantly higher in comparison with the scores for gel A ($P = 0.003$), gel B ($P = 0.016$), gel C ($P = 0.007$) and gel D ($P = 0.010$).

Gel F, containing 70% (v/v) isopropanol, was subjectively found to dry out the skin more in comparison with the effect of gel A ($P = 0.046$), gel B ($P = 0.034$) and gel C ($P = 0.009$).

No differences were revealed between the alcohol gels when considering skin comfort. Medians of 3 and 4 for all gels even implicate that they are thought to rather make the skin smooth and soft than rough and scaly after a single application.

13 skin reactions were reported, of which seven stand for burning sensations that cannot be related to a specific alcohol gel. Redness and/or irritation were only seen for the gels containing a higher concentration of ethanol (two reports for gel D and two reports for gel E). Itchiness was only reported once for gel F. As for the

Table 2. Statistical difference between application sites and corresponding control sites for the scores obtained via chromametry

Gel A	Gel B	Gel C	Gel D	Gel E	Gel F
NS	NS	NS	*	**	NS

NS, not significant.

$n = 13$, * $P < 0.05$, ** $P < 0.01$ (paired Student's t -test).

unspecified comments that could be given by the participants, only an exaggerated stickiness was quoted for gel C, and this 4 times.

Discussion

For the biophysical measurements, the volar forearm was chosen as application zone because of its greater surface and because this zone usually is less exposed to external influences compared with the hands. However, similar effects are expected when using these products on the hands that generally display slightly higher TEWL and hydration baseline values compared with the forearm (22, 23).

The irritation that HCWs complain about in everyday life could be preceded by or could go together with an increase of TEWL. None of our gels either deteriorated or improved the epidermal barrier function of the skin. This confirms the findings of Kramer et al. (20), who have been investigating alcoholic hand sanitizers in a similar study set up. Another TEWL study, investigating the effect on healthy skin of *n*-propanol after a repeated open exposure of 15 min, showed that 60% (v/v) *n*-propanol failed to induce barrier impairment, but a 100% (v/v) *n*-propanol did (24).

Even so, none of the alcoholic gels tested by our group caused erythema. This could be due to the fact that it was only a 1-day study. However, this was neither the case for a repetitive occlusive patch test (24 h) with a hand rub, containing 45% (v/v) isopropanol and 30% (v/v) *n*-propanol, and assessed visually for erythema and oedema (25). On the contrary, the HCWs enrolled for the sensorial assessment obviously experienced more adverse skin reactions in comparison with the volunteers who enrolled for the biophysical measurement part, who underwent much more frequent applications. That this is most likely due to a pre-irritated skin of the HCWs who also use

detergent-based cleansing products was shown by Lubbe et al. (24), and Larson et al. (26) stated that the skin of HCWs' hands is commonly damaged in association with gloving and handwashing practices. Besides in HCWs, skin reactions associated with alcohols are fairly rare.

All gels have an improving effect on SC hydration, clearly due to the presence of glycerine. This is in agreement with a long-term study rubbing twice daily a 85% (v/v) ethanol disinfectant containing glycerine (27) and with the above cited publication of Lubbe et al. (24). Notwithstanding of the perceptive feeling that alcohol-based hand gels dry out the skin, this study demonstrates the opposite. This could arise from the misconception that a rough and scaly skin is dehydrated, which is not always the case (21). Besides the fact that the incorporation of emollients in alcoholic rubs increases the user acceptability (28), the increase of the hydration of the SC as seen in this study confirms their beneficial effect.

A scaly skin is only seen for the higher concentrations of ethanol, suggesting that gels containing 70% (v/v) ethanol or isopropanol are preferable. Watkinson et al. (29) demonstrated that desmosomal degradation, measured as SC chymotryptic enzyme activity, is reduced at low relative humidity. This might explain why volatile alcohols, probably dragging water with them while evaporating, cause a scaly skin.

Surprisingly, all alcohol-based gels used in our study decreased the apparent skin pH, but not in a way that the barrier function of the skin was affected. This discrete pH drop even could be favourable, because it has been shown that an acidic extracellular pH is necessary for the initiation of the epidermal barrier recovery (30) and for a normal SC integrity and cohesion (31, 32). A possible explanation for this phenomenon could be the presence in the epidermis of the enzyme alcohol dehydrogenase, an enzyme that converses ethanol into acetic acid and – to a lesser extent – isopropanol into acetone (33). Nevertheless, this acidifying effect was more prominent for the gel containing isopropanol, suggesting that another mechanism might be responsible.

From this study, it can be concluded that the use of alcohol-based hand disinfecting gels under *in use* conditions does not alter the barrier function of the skin nor causes irritation. The discomfort to the skin caused by these gels seems to be a problem of HCWs exclusively and might have been provoked by other hand hygiene practices. Moreover, the indispensable incorporation of an emollient like glycerine gave these preparations hydrating properties, despite the presence of considerable amounts of alcohol. From a dermatological point

Table 3. Results of the sensorial assessment, $n = 21$ (medians)

	Gel A	Gel B	Gel C	Gel D	Gel E	Gel F
Smell	3	3	3	2	3	2
Drying speed	3	2	2	3	3	3
Emollient effect	4	3	3	3	3	3
Skin comfort	4	3	3	4	4	3

of view, isopropanol 70% (v/v) did not differ from ethanol 70% (v/v), except for a more distinct acidification of the superficial, but the smell of isopropanol is generally not appreciated, and the toxicological profile is less good than that of ethanol.

Finally, this study reveals that the combination of biophysical measurements and sensorial assessments, with appropriate target groups, results in a suitable protocol to discriminate between different formulations of alcohol-based hand disinfectants in a rather fast way. Long-term effects after exposure to these products for consecutive days, however, should be the subject of further investigation.

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Address:

Evi Houben

Department of Toxicology

Dermato-Cosmetology and Pharmacognosy

Vrije Universiteit Brussel

Laarbeeklaan 103

B-1090 Brussels

Belgium

Tel: +32 2 4774596

Fax: +32 2 4774582

e-mail: evi.houben@vub.ac.be