



Dermal tolerance and effect on skin hydration of a new ethanol-based hand gel

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Summary: We studied the dermal tolerance (repetitive occlusive patch test; ROPT) and the skin hydrating properties of a new ethanol-based gel [85% (w/w)], Sterillium[®] Gel. For the ROPT, 53 participants were studied. Gel was applied to one site on the back under an occlusive patch during an induction phase (nine applications over three weeks) and two weeks later to a virgin site on the back during a challenge phase (one application). Twenty-four hours after the removal of the patches (induction phase and challenge phase), then 48 and 72 h later (challenge phase) sites were graded for skin reactions using a standardized scale. In the induction phase none of the 53 participants had a skin reaction. In the challenge phase one participant had a barely perceptible skin reaction, and one had mild erythema at one time point. To evaluate skin hydrating properties of the gel, treated skin of 21 participants was compared to untreated skin. The gel was applied twice a day to the forearm for 14 days. Control corneometer values were taken before application of the gel (mean: 32.7 ± 5.0) and after one (36.3 ± 4.4) and two weeks (36.1 ± 5.4). Relative skin hydration on treated skin in comparison with an untreated control field was significantly higher after one week by 6.85% ($P=0.0031$; paired *t*-test for dependent samples) and after two weeks by 4.47% ($P=0.0153$). Sterillium Gel did not demonstrate a clinically relevant potential for dermal irritation or sensitization, and significantly increased skin hydration after repetitive use, and so could enhance compliance with hand hygiene among healthcare workers.

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Keywords: Dermal tolerance; skin hydration; ethanol-based hand gel; Sterillium Gel.

Introduction

Hand hygiene is currently undergoing a renaissance in many countries. In the USA, for example, the national recommendation has been revised with emphasis on alcohol-based hand rubs.^{1,2} This is probably because of the increasing evidence supporting the benefit of alcohols in comparison with non-medicated soap or antiseptic soaps.^{3–6} Sterillium was one of the first commercially available alcohol-based

hand rubs in Europe. Recently alcohol-based hand gels became available, however the antimicrobial activity of these has been demonstrated to be significantly lower than liquid hand rubs.^{7,8} We have developed an alcohol-based hand gel with an equal antimicrobial activity to the liquid hand rubs. This new hand gel contains 85% ethanol (w/w), which is higher than other gels, and is the first to fulfil the requirement of EN 1500 within 30 s.

Compliance with hand hygiene is a key factor for reducing the hospital-acquired infection rate.¹⁰ Factors influencing compliance include dermal tolerance^{11,12} and skin care properties.¹³ The aim of this investigation was to study the dermal tolerance (potential for irritation and sensitization) of the new gel in a repetitive occlusive patch test as well as its effect on skin hydration.

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Material and methods

Hand gel

Sterillium Gel contains ethanol [85% (w/w)] as the active ingredient, together with water, a thickening system (e.g., glycerol), skin care components and a fragrance.

Repetitive occlusive patch test

Participants between the ages of 20 and 70 years were recruited. Individuals were excluded if they had a history of acute or chronic dermatological, medical and/or physical conditions that could interfere with dermal scoring, or treatment with sympathomimetics, antihistamines, non-steroidal anti-inflammatory agents, and/or corticosteroids in the week before the study began.

In order to remove sebum, dead skin cells or any traces of cosmetic or toiletry products the test area was gently wiped using one or two wipes of alcohol-soaked cotton (70% isopropyl alcohol). This was done only prior to the first induction patch application and the challenge patch application as the participants were instructed not to use any products on the test sites during the study. The test material (0.2 mL) was allowed to volatilize and was applied under an occlusive patch (occlusive strip with Flexcon, TruMed Technologies Inc., Burnsville, MN, USA) to the upper back between the scapulae. The test material was allowed to remain in direct skin contact for 24 h.

Patches were applied to the same site on Mondays, Wednesdays and Fridays for three weeks (nine applications). Patches were removed by the participants on Tuesdays, Thursdays and Saturdays. The sites were graded by a nurse or scientist trained to score for degrees of erythema and oedema under the supervision of a dermatologist. Grading was done immediately prior to the next product application which was either 24 h after Tuesday's and Thursday's patch removal or 48 h after Saturday's patch removal.

After two weeks rest the challenge patches were applied to previously untreated test sites on the back. After 24 h the test patches were removed by a technician. The test sites were evaluated for dermal reactions immediately after removal of the patches then 48 and 72 h later. The sites were graded according to the following scoring system:

- 0 No visible skin reaction
- ± Barely perceptible erythema (minimal)

- 1+ Mild erythema (diffuse)
- 2+ Well defined erythema
- 3+ Erythema and oedema
- 4+ Erythema and oedema with vesiculation

Skin hydration study

Female participants of phototypes I to IV and between the ages of 18 and 70 years were included. Males were excluded because measurement of skin hydration is impaired by hair. Other exclusions included systemic illness, acute skin diseases (e.g., atopic eczema), excess hair, warts, scabs or tattoos on the investigation sites, or if pregnant, breast feeding, diabetic, human immunodeficiency virus (HIV) positive, an alcohol or drug addict or participation in other studies on the forearms two weeks prior to study initiation.

About $3 \mu\text{L}/\text{cm}^2$ of gel was applied twice a day for 14 days by the volunteers at home according to a protocol from study diary, containing information on times of applications (day, date, morning or evening). Volunteers were instructed to record all product applications. Practical instruction on using the product and the procedures of application was given after the baseline examination. Immediately after the baseline measurements, a product application was performed by volunteers under supervision of the investigator. The investigator checked that the quantity of the applied product, the localization of the application sites, the distribution and the utilization of the product was according to the study protocol. In addition, participants were provided with printed information concerning the dates for examinations in the Institute and instructions regarding behavior during the study.

The application and investigation sites were on the volar surface of the forearms. For at least seven days before and throughout the study all treatment with leave-on products or use of oily skin cleansing products on the forearms was prohibited. The product was homogeneously spread over an investigation site of about $7 \times 7 \text{ cm}^2$ in a quantity of about $150 \mu\text{L}$. The application of the product started immediately after the initial investigation as a controlled application in the institute. In the morning of the second (day 8; t_1) and third day (day 15; t_2) of measurements, the investigation sites were left untreated. Treatment had been performed on these days as a controlled application in the Institute. Before starting the measurements, the investigation sites were exposed to the indoor climate of the Institute (21.5°C ; 50%

relative humidity) for at least 20 min. Skin hydration was measured with the corneometer CM 825 (Courage & Khazaka, Cologne, Germany), by placing the probe with low pressure, vertically on to the skin surface. For each application site, six measurements were performed. Data were directly transferred into the computerized study file, classified by study code, code of the volunteer, day of the study and code of the investigation site.

The analysis was performed by relating the original data of the product treated investigation sites to the untreated situation and the corresponding starting value. The mean and standard deviation were calculated. Normal distribution of the paired differences was assessed with the Kolmogorov–Smirnov test. Statistical significance was determined using a *t*-test for dependent samples.¹⁴ A difference was accepted to be statistically significant when the *P*-value was <0.05.

Results

Repetitive occlusive patch test

Fifty-six participants were enrolled and 53 finished the study; three discontinued for reasons unrelated to the test preparation. Eight of the 53 participants were male (15.1%), 45 were female (84.9%). The mean age was 44.2 ± 13.5 years. None of the 53 had any reaction at any time after the nine induction applications. Fifty-one (96.2%) had no visible skin reaction 24, 48 or 72 h after the challenge application. One participant had a '±' reaction after 48 and 72 h, and another had a '1+' reaction after 48 h and a '±' reaction after 72 h.

Skin hydration study

Twenty-two female participants were recruited. One dropped out for personal reasons. The mean age of the remaining 21 was 45.2 ± 15.2 years. The mean skin hydration values before the application of Sterillium Gel were 32.7 ± 3.7 (treated site) and 32.7 ± 5.0 (untreated site). Untreated skin areas revealed after one week a mean skin hydration value of 36.3 ± 4.4 and after two weeks a mean value of 36.1 ± 5.4 . The treated skin areas were found to have a mean skin hydration value of 38.8 ± 4.7 after one week and 37.7 ± 2.8 after two weeks. All pair differences were found to be normally distributed after one and two weeks ($P > 0.2$; Kolmogorov–Smirnov test). Differences in skin hydration after relating the data between the treated and untreated test fields (set at

Table I Mean skin hydration values with standard deviation of 21 volunteers after one and two weeks of twice a day use of Sterillium Gel on the forearm and the corresponding untreated control fields

	Control	Sterillium Gel	Relative difference (%)	<i>P</i> -value
Baseline	32.7 ± 5.0	32.7 ± 3.9	0	not applicable
One week	36.3 ± 4.4	38.8 ± 4.7	+ 6.85	0.0031
Two weeks	36.1 ± 5.4	37.7 ± 2.8	+ 4.47	0.0153

Comparison of relative differences with the paired *t*-test for dependent probes.

100%) were significant after one week with an increase of 6.85% ($P = 0.0031$; paired *t*-test for dependant samples) and after two weeks with an increase of 4.47% ($P = 0.0153$; Table I).

Discussion

Chronic, irritative dermatitis of the healthcare worker is an important issue in occupational dermatology. Up to 70% of healthcare workers may have occupational hand dermatitis, e.g., those reporting a frequency of handwashing exceeding 35 times per shift.¹⁵ A review of patients presenting with contact dermatitis revealed that almost half (60 of 124) of those with occupational hand dermatitis were healthcare workers.¹⁶ Irritant contact dermatitis is found among healthcare workers almost three times as often as allergic contact dermatitis.¹⁷ This is partly explained by the use of products for hand hygiene that lower the skin hydration after repetitive use.

Alcohol-based hand gels are becoming more popular for the post-contamination treatment of hands. Although their antimicrobial efficacy has been shown to be significantly lower than liquid alcohol-based hand rubs,^{7,8} gels are acceptable to healthcare workers. Sterillium Gel is the first alcohol-based hand gel that has a similar antimicrobial efficacy to liquid alcohol-based hand rubs (EN 1500), and seems therefore particularly appropriate for hospital use.

We have shown that Sterillium Gel has no clinically relevant potential for dermal irritation and sensitization, as shown by repetitive occlusive patch test, in which the test sample was allowed to volatilize prior to application but then occluded in order to avoid any volatilization from the treated skin area. This design is not based on the actual clinical practice, but due to the occlusion, is more demanding.

Ethanol, the active ingredient in the gel, is known to be 'safe and effective' for topical use.¹⁸

Although a lot of scientific work has been published about skin care ingredients such as glycerol for the hydration¹⁹ or panthenol for better regeneration of the skin barrier,²⁰ it is necessary to confirm the effect of the combined ingredients in the finished product.²¹

Sterillium Gel was found significantly to increase the skin hydration. This is probably explained by the glycerol which is known to increase skin hydration.²² This finding is very important for healthcare workers. Washing hands with soap and water is known to reduce skin hydration^{16,23,24} as does washing hands with antiseptic soaps,^{23,25} unlike alcohol-based liquid hand rubs.¹² Only one other alcohol-based hand gel (Purell, Gojo Industries, Akron, USA) has been tested on the skin for the hydration effect, which was not increased significantly by repetitive use.²⁴ Subclinical irritation can not be excluded because the transepidermal water loss (TEWL) was not assessed in this study, but the gel is unlikely to have caused a significant increase, because similar liquid products do not.¹² A remarkable increase of the mean skin hydration was seen between untreated baseline values. During the two week application period the mean values of the control fields were more or less identical, suggesting consistency of the control. Seasonal variations may have occurred during the two weeks, and may explain the lower baseline value at the beginning. Mean baseline values at the beginning were identical, supporting the validity of the measurements.

The findings reported here have now been confirmed in a multi-centre study in which 96 healthcare workers from four countries used the gel for four weeks of their normal working practice and rated it equal to or better than comparators. This study also reported on the antimicrobial spectrum of the gel using standard tests against bacteria, fungi and viruses, all of which it passed.²⁶

Many attempts have been made to improve compliance with hand hygiene. Skin care is certainly an important factor, and the perception that a product is beneficial to the skin should favour its regular use by healthcare workers.

References

1. Anonymous. Draft guideline for hand hygiene in healthcare settings. *Fed Reg* 2001; **66**: 56680.
2. Boyce J, Larson E. Methods to improve hand hygiene in healthcare settings. 11th Annual Meeting; Society for Healthcare Epidemiology of America (SHEA); Toronto, USA 2001.
3. Rotter ML. Arguments for the alcoholic hand disinfection. *J Hosp Infect* 2001; **48**: S4–S8.
4. Rotter ML. Handwashing and hand disinfection. In: Mayhall CG, Ed. *Hospital Epidemiology and Infection control*. 2nd edn. Philadelphia: Lippincott Williams & Wilkins, 1999: 1339–1355.
5. Pittet D, Hugonnet S, Harbarth S et al. Impact of a hospital-wide programme to improve compliance with hand hygiene. *Lancet* 2000; **356**: 1307–1312.
6. Schmidts-Winkler I. *Hand Disinfection in the Health Care Setting*. Hamburg: MediVerlag, 1997.
7. Pietsch H. Hand antiseptics: rubs versus scrubs, alcoholic solutions versus alcoholic gels. *J Hosp Infect* 2001; **48**: S33–S36.
8. Kramer A, Rudolph P, Kampf G, Pittet D. Limited efficacy of alcohol-based hand gels. *Lancet* 2002; **359**: 1489–1490.
9. Kampf G, Rudolf M. Spectrum of antimicrobial activity of Sterillium Gel, a new ethanol-based hand-gel. 12th Annual Scientific Meeting; Society for Healthcare Epidemiology of America (SHEA); Salt Lake City, USA 2002.
10. Pittet D. Improving compliance with hand hygiene in hospitals. *Infect Control Hosp Epidemiol* 2000; **21**: 381–386.
11. Lübke J, Ruffieux C, van Melle G, Perrenoud D. Irritancy of the skin disinfectant n-propanol. *Contact Dermatitis* 2001; **45**: 226–231.
12. Kramer A, Bernig T, Kampf G. Clinical double-blind trial on the dermal tolerance and user acceptability of six alcohol-based hand disinfectants for hygienic hand disinfection. *J Hosp Infect* 2002; **51**: 114–120.
13. Pittet D. Improving adherence to hand hygiene practice: a multidisciplinary approach. *Emerg Infect Dis* 2001; **7**: 234–240.
14. Altman DG. *Practical Statistics for Medical Research*. 1st edn. London: Chapman & Hall, 1991.
15. Forrester BG, Roth VS. Hand dermatitis in intensive care units. *J Occup Environ Med* 1998; **40**: 881–885.
16. Wilkinson SM. Effects of infection control measures on skin of healthcare workers. *Commun Dis Public Health* 2000; **3**: 305–306.
17. Nettis E, Colanardi MC, Soccio AL, Ferrannini A, Tursi A. Occupational irritant and allergic contact dermatitis among health care workers. *Contact Dermatitis* 2002; **46**: 101–107.
18. Anonymous. Tentative final monograph for health care antiseptic products; proposed rule. *Fed Reg* 1994; **59**: 31401–31452.
19. Jungermann E, Sonntag NOV. *Glycerine—a Key Cosmetic ingredient*. New York: Marcel Decker Inc., 1991.
20. Raab W, Kindl U, Daniels R. *Pflegekosmetik. Ein Leitfadens*. 3rd edn. Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1999.
21. Kampf G, Bielfeldt S, Pfannenbecker U, Rudolf M. Dermal and mucosal tolerance of a new antiseptic liquid soap. *Occup Environ Dermatol* 2001; **49**: 198–201.
22. Schürer N. Kosmetische Maßnahmen bei trockener Haut. In: Schürer N, Ed. *Die trockene Haut*.

- Stuttgart: Wissenschaftliche Verlagsgesellschaft, 2000: 86–91.
23. Larson E. Hygiene of the skin: when is clean too clean? *Emerg. Infect Dis* 2001; **7**: 225–230.
 24. Boyce JM, Kelliher S, Vallande N. Skin irritation and dryness associated with two hand-hygiene regimens: soap-and-water handwashing versus hand antiseptics with an alcoholic hand gel. *Infect Control Hosp Epidemiol.* 2000; **21**: 442–448.
 25. Sauermann G, Proske O, Keyhani R, Leneveu M-C, Pietsch H, Rohde B. Hautverträglichkeit von Sterillium und Hibiscrub in einer klinischen Vergleichsstudie. *Hyg Med* 1995; **20**: 184–189.
 26. Kampf G, Rudolf M, Labadie J-C, Barrett SP. Spectrum of antimicrobial activity and user acceptability of the hand disinfectant agent Sterillium® Gel. *J Hosp Infect* 2002; **52**: 141–147.