# **ORIGINAL ARTICLE**



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# Skin barrier response to active chlorine hand disinfectant—An experimental study comparing skin barrier response to active chlorine hand disinfectant and alcohol-based hand rub on healthy skin and eczematous skin

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Abstract

Background: Alcohol-based hand rub (ABHR) is widely used for hand disinfection in the health care sector. ABHR is, however, known to cause discomfort when applied on damaged skin emphasizing the unmet need for alternative and better tolerated types of disinfectants. Active chlorine hand disinfectants (ACHDs) are potential new candidates; however, the effect on the skin barrier function compared to ABHR remains to be assessed.

Materials and methods: In Study A, the forearm skin of healthy adults was repeatedly exposed to ACHD and ABHR. Skin barrier function was assessed by measurement of transepidermal water loss, electrical conductance, pH, and erythema at baseline and at follow-up after 2 days, and subjective discomfort was likewise assessed. Study B was performed in the same way; however, in order to induce an experimental irritant contact dermatitis, sodium lauryl sulfate patch tests were applied to forearms before exposure to ACHD and ABHR.

Results: In both studies, the skin barrier function was unaffected after repetitive exposure to ACHD and ABHR, and with no significant differences between the products. Subjective discomfort was reported as sporadic or very mild in relation to both products.

Conclusion: Our results illustrate that use of ACHD does not affect the skin barrier function negatively, neither in intact skin nor in skin with experimentally induced contact dermatitis. Future studies should include real-life evaluation of skin barrier function and subjective discomfort following ACHD use in individuals with and without hand eczema.

#### KEYWORDS

active chlorine hand disinfectant, alcohol-based hand rub, hand eczema, skin barrier function, sodium lauryl sulfate, transepidermal water loss

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# 1 | INTRODUCTION

The 1-year prevalence of hand eczema (HE) in the general population is around 10% and even higher among health care workers (HCWs) with a 1-year prevalence of 21%.<sup>1,2</sup> In the health care sector, HE is most often induced by wet work,<sup>3</sup> currently defined as having wet hands for >2 h, hand washing >20 times, or wearing occlusive gloves for >2 h per working day.<sup>4</sup> Alcohol-based hand rub (ABHR) is another common exposure, which is recommended either in combination with hand washing, or in preference to hand washing, when the hands are not visibly dirty.<sup>5</sup> While frequent hand washings are known to cause impairment of skin barrier function leading to HE, due to the irritant effects of water and detergents.<sup>3,6,7</sup> ABHR has been assessed as harmless to the skin barrier function in numerous studies.<sup>6,8,9</sup> However, data are based on studies applying ABHR on dry skin, and results have recently been questioned in a study exploring the irritant effect of ABHR on wet skin indicating that the hydration of the skin may affect the damaging potential of ABHR.<sup>10</sup>

Further, when ABHR is applied on skin with eczematous lesions or otherwise damaged skin, the alcohol causes a sensation of burning and stinging.<sup>11,12</sup> This subjective discomfort, which is difficult to tolerate, is anticipated to influence the compliance with hand disinfection in a negative direction. As hand hygiene is one of the outmost important preventive measures to prevent transmission of microorganisms,<sup>13,14</sup> a lacking hand hygiene compliance among HCWs with HE will potentially make up a risk for hospital acquired infections, since more than 50% of all HE patients are colonized with pathogenic bacteria (i.e., *Staphylococcus aureus*).<sup>15–20</sup>

Facing these challenges from an aspect of nosocomial infections, there is an unmet need for a new disinfecting device that does not cause subjective discomfort to individuals with HE or otherwise impaired skin barrier function. An active chlorine hand disinfectant (ACHD) is a potential new candidate to meet the criteria for a new disinfection solution. The product is based on hypochlorous acid (HOCI), which is a part of the innate immune system in humans,<sup>21,22</sup> and acetic acid used for decades in medicine and in the product acting as a buffer in order to optimize the pH.<sup>23</sup> ACHD complies with European requirements regarding testing of hygienic hand rubs in in vivo studies. Both compounds in the product are known for their antimicrobial and anti-biofilm properties against pathogenic bacteria, including S. aureus.<sup>21,22,24–27</sup> and have been used in the treatment of wounds and eczema.<sup>23,28-30</sup> However, data on possible irritant effects of the product on the skin and whether it has any negative effects on the skin barrier are lacking.

The aim of the present study was to examine the skin barrier response to ACHD compared with ABHR on intact skin and on skin with experimentally induced irritant contact dermatitis in healthy individuals, respectively. Furthermore, subjective discomfort and clinical signs of irritation in relation to the application of ACHD and ABHR, respectively, were evaluated.

# 2 | METHODS AND MATERIALS

Two independent experimental studies were performed. Study A examined the skin barrier function after repeated exposure to ACHD and ABHR on healthy intact skin, while Study B assessed the skin barrier function after repeated exposure to ACHD and ABHR on experimentally induced irritant contact dermatitis.

#### 2.1 | Subjects

Healthy volunteers were included in Study A and Study B. Exclusion criteria were age <18 years, previous or current skin disease, pregnancy or lactating, and use of leave-on-products on volar forearms within 24 h before the study. The subjects were instructed to avoid application of water, detergents, moisturizers, or any other leave-on products on the volar forearms during the investigation.

#### 2.2 | Materials

The ACHD (SafeDes, SoftOx Solutions AS, Norway) contains 160 ppm ( $\pm$ 24 ppm) hypochlorous acid (HOCl) and 0.25% acetic acid (HOAc) and is approved according to EN 1500, EN 13727, and EN 13624. The ABHR used in this study was based on 85% ethanol, glycerol, and <5% isopropyl alcohol.

#### 2.3 | Procedure

# 2.3.1 | Study A

Study A was conducted from February to May 2020 at the Department of Dermatology, Bispebjerg and Frederiksberg Hospital, Copenhagen. For an overview of the study procedure, see Figure 1. On day 1, three test areas of  $5 \times 5$  cm were marked on skin of the volar forearms: area "ACHD" for ACHD, area "ABHR" for ABHR, and area "C" as a control. The three test areas on the forearms were randomized. After skin barrier assessments at day 1, ACHD and ABHR were repeatedly applied on area ACHD and ABHR, respectively, with a soaked cotton-pad for 30 s and afterwards air-dried. The applications were performed 20 times with a 10-min interval on day <u>1</u> and repeated on day <u>2</u>, giving a total of 40 applications <u>on</u> each area. Skin barrier assessments were performed again on day 3 (Figure 1).

A pilot study for the application procedure was performed prior to the study in order to achieve the most optimal setting.

#### 2.3.2 | Study B

The study was conducted from June to September 2020 at the Department of Dermatology, Bispebjerg and Frederiksberg





TEWL, transepidermal water loss; ACHD, active chlorine hand disinfectant; ABHR, alcohol-based hand rubs Subjective discomfort was rated by the participants after each application of ACHD and ABHR, respectively. Clinical evaluation of the ACHD and ABHR area was performed at day 1, day 2 and day 3.



#### FIGURE 2 Overview of study procedure in Study B

TEWL, transepidermal water loss; SLS, sodium lauryl sulphate; ACHD, active chlorine hand disinfectant; ABHR, alcohol-based hand rubs Subjective discomfort was rated by the participants after each application of ACHD and ABHR, respectively. Clinical evaluation of the ACHD, ABHR and control patch area was performed at day 1, day 2 and day 3.

Hospital, Copenhagen. An overview of the study procedure is given in Figure 2. On day 0, four test areas of  $5 \times 5$  cm were marked on the skin of the volar forearms: area "ACHD" for ACHD, area "ABHR" for ABHR, area "CP" for control patch, and area "C" as a control. The four test areas on the forearms were randomized. Irritant contact dermatitis was induced on area ACHD, area ABHR and area CP by applying sodium lauryl sulfate (SLS) patches, and area C was left untouched. As recommended in guidelines,<sup>31</sup> each of the three patch tests were prepared by applying 60  $\mu$ l of the SLS solution on a filter paper disc, placed on a 12 mm Finn Chamber, and immediately placed on areas ACHD, ABHR, and CP, respectively. The participants were instructed to remove the patches after 24 h. All participants received a text message as a reminder to remove the patches. The skin barrier assessments on day 1 were performed 1 h after removal of the patches. ACHD and ABHR were repeatedly applied on area ACHD and area ABHR, respectively, as in accordance with Study A. Skin barrier assessments were performed again on day 3 (Figure 2).

A pilot study for the application of the patch tests and the application procedure was performed prior to the study in order to achieve the most optimal setting for the study.

#### 2.3.3 Skin barrier assessments

The marked skin areas were measured by transepidermal water loss (TEWL), electrical conductance, pH, and colormeasurements<sup>32--36</sup> using DermaLab Combo (Cortex Technology, Hadsund, Denmark)<sup>37</sup> in accordance with guidelines.<sup>38--41</sup> TEWL was assessed after 20 min of acclimatization. The same room was used for skin barrier assessments on all participants in both Study A and Study B, and data on the room temperature and humidity were collected prior to the TEWL measurements. Windows and doors were closed during the measurements to prevent influence from draught or wind. The measurements were performed at approximately the same time of the day for each individual participant to minimize possible circadian rhythm effects. Three consecutive measurements were performed on the respective areas as recommended in the guidelines.<sup>40</sup> Although the temperature and humidity changed during the study due to seasonal changes, the participants served as their own controls and the participation in each study lasted up to only 4 days.

TEWL represents the passive diffusion of condensed water through the outermost skin layer, stratum corneum, while the water content in stratum corneum is represented by the electrical conductance (i.e.

**TABLE 1** Study A: Comparison of skin barrier function at baseline and day 3 on the three different application areas: ACHD (area ACHD), alcohol-based hand rub (ABHR) (area ACHD), and control (area C), respectively

		Day 1	Day 3	p-Value	p-Value <sup>*</sup>
TEWL (g/m <sup>2</sup> /h)	ACHD	4.04 (2.81-4.87)	3.97 (2.62–4.87)	0.60	0.14
	ABHR	3.97 (3.39-5.18)	4.15 (3.34–5.05)	0.91	
	Control	4.32 (3.23-5.16)	4.19 (3.52–5.37)	0.70	
Electrical conductance (mSv)	ACHD	64.50 (58.50-72.00)	63.50 (55.00-73.50)	0.33	0.67
	ABHR	61.50 (58.25-65.50)	69.00 (61.75-75.00)	0.01	
	Control	56.50 (48.25-63.00)	64.50 (55.25-68.00)	0.01	
pH	ACHD	6.07 (5.79-6.29)	5.48 (5.23-5.72)	<0.01	0.15
	ABHR	6.05 (5.77-6.29)	5.52 (5.38–5.70)	<0.01	
	Control	6.05 (5.75-6.18)	5.50 (5.36-5.67)	<0.01	
Erythema	ACHD	8.35 (7.90-9.90)	8.70 (7.43-10.03)	0.63	0.66
	ABHR	8.45 (7.65-9.78)	8.65 (7.13-9.38)	0.32	
	Control	8.35 (7.23-9.88)	8.90 (7.23-10.58)	0.08	

Note: Comparison of skin barrier function at baseline and <u>at day</u> 3 at the three different application sites assessed by TEWL, electrical conductance, pH, and erythema. Median values with 25 and 75 percentile are shown. Wilcoxon signed rank test was used to evaluate differences between the paired data. *p*-Values shown in bold are statistically significant.

Abbreviations: ABHR, alcohol-based hand rubs; ACHD, active chlorine hand disinfectant; TEWL, transepidermal water loss.

\*p-Value for ACHD skin barrier assessment on day 3 compared to corresponding control values on day 3.

hydration). A disrupted skin barrier seen in, for example, dermatitis is characterized by elevated TEWL values and reduced electrical conductance values,<sup>42</sup> although the electrical conductance may also be increased in case of more severe damage of the barrier. On healthy skin, pH ranges between approximately 5 and  $6.5^{34}$  while elevated values have been reported in patients with dermatitis.<sup>43</sup> With respect to skin color, erythema reflects a dilatation of the capillaries in the dermis indicating inflammation.<sup>39</sup>

# 2.3.4 | Subjective discomfort and clinical score

The participants were asked to rate discomfort (burning, itchy sensation) on a visual analogue scale (VAS) from 0 to 10 (10 being the most severe discomfort) after application of ACHD and ABHR, respectively.

For examination of a clinical skin reaction, the visual scale proposed by Frosch and Kligman was used to score erythema (0–4 points), scaling (0–3 points) and fissuring (0–3 points) with a maximum possible score of 10 points indicating severe erythema, scaling and fissuring.<sup>44</sup> The assessments were performed by the same investigator.

# 2.4 | Statistics

Standard descriptive statistics were used to characterize the study population. The Wilcoxon signed rank test was used to compare continuous paired data (TEWL, electrical conductance, pH, and erythema). Regarding the sample size, approximately 20 healthy volunteers were considered sufficient in this study.<sup>6</sup> Two-sided *p*-values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS Statistics 25.0.

# 2.4.1 | Ethical considerations

Study A and Study B were approved by the local Ethics Committee (project number H-19080907) and The Danish Data Protection Agency (project number P-2020-132). Written informed consent was obtained from each participant.

# 3 | RESULTS

# 3.1 Study A

In Study A, evaluating the skin barrier response after exposure to ACHD and ABHR on healthy intact skin, a total of 20 volunteers (13 females, 7 males) were included. All participants completed all three visits. The median age was 26 (range 18–64) years. Results of TEWL, electrical conductance, pH, and erythema measurements at day 1 and day 3 are given in Table 1. No significant differences were found for any of the three application sites (Table 1) between day 1 and 3 with respect to TEWL. Between day 1 and 3, the electrical conductance increased significantly at ABHR and control area, respectively, while no difference was found for ACHD. The pH values increased significantly from day 1 to 3<u>at</u> all three areas. Erythema was unchanged <u>at</u> the three areas from day 1 to 3.

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Day 0 Day 1 **Before SLS** After removal of patches **SLS** patches Day 3 p-Value p-Value\* TEWL (g/m<sup>2</sup>/h) ACHD 3.6 (2.7-5.7) 16.5 (12.2-19.8) 18.3 (12.7-22.0) 0.412 0.473 ABHR 3.1 (2.7-6.8) 15.2 (12.9-20.1) 16.2 (10.0-20.9) 0.972 Control patch 3.3 (2.7-6.9) 16.9 (12.5-20.9) 17.1 (11.0-23.0) 0.892 Control 3.4 (2.9-5.7) 3.8 (3.0-5.0) 3.4 (2.6-5.0) 0.986 ACHD 128 (99-161) Electrical conductance (mSv) 111 (83-157) 94 (74-152) 0.198 0.651 ABHR 105 (90-132) 102 (89-134) 164 (124-211) 0.021 107 (88-124) Control patch 115 (74-130) 134 (98-182) 0.071 Control 100 (89-138) 125 (91-145) 112 (96-152) 0.289 0.709 pН ACHD 5.3 (5.1-5.7) 5.0 (4.8-5.4) 5.3 (5.0-5.4) 0.020 ABHR 5.5 (5.2-5.6) 5.1 (4.8-5.3) 5.4 (5.1-5.5) 0.010 Control patch 5.4 (5.0-5.8) 5.0 (4.8-5.4) 5.3 (5.1-5.4) 0.031 5.2 (5.0-5.5) Control 5.4(5.1-5.7)5.2 (4.8-5.4) 0.059 Erythema ACHD 8.7 (8.0-11.0) 9.7 (8.6-12.1) 11.3 (9.4-12.6) 0.139 0.754 ABHR 8.9 (7.5-10.9) 10.8 (8.9-12.7) 10.7 (9.2-13.0) 0.071 Control patch 8.8 (7.8-11.1) 10.4 (8.6-13.9) 11.0 (8.7-13.5) 0.332 Control 9.3 (7.3-11.8) 8.9 (7.1-11.3) 9.3 (7.6-11.1) 0.970

**TABLE 2** Study B: Comparison of skin barrier function at day 1 and day 3 on the four different areas: Active chlorine hand disinfectant (ACHD) (area ACHD), alcohol-based hand rub (ABHR) (area ABHR), control patch (area CP), and control (area C), respectively

*Note*: Comparison of skin barrier function <u>at day 1 and at</u> day 3 at the four different sites assessed by TEWL, electrical conductance, pH, and erythema. Median values with 25 <u>and 75 percentiles</u> are shown. Wilcoxon signed rank test was used to evaluate differences between the paired data. *p*-Values shown in bold are statistically significant.

Abbreviations: ABHR, alcohol-based hand rubs; ACHD, active chlorine hand disinfectant; TEWL, transepidermal water loss.

\*p-Value for skin barrier assessment on day 1 compared to day 3.

\*\*p-Value for ACHD skin barrier assessment on day 3 compared to corresponding control patch values on day 3.

No significant differences were found for any of the skin barrier measurements when comparing ACHD area and the control area on day 3 (Table 1).

In Study A, two participants reported VAS scores for burning/itching of 1 and 2 points, respectively, after application of ABHR. No subjective discomfort was reported <u>for</u> the ACHD area. One participant developed mild redness on the site of ABHR corresponding to a Frosch Kligmann score of 1, that lasted for less than 30 min. No erythema, scaling or fissuring were found <u>at</u> the ACHD area.

#### 3.2 Study B

Study B evaluated the skin barrier response to ACHD and ABHR on SLS-induced irritant contact dermatitis. A total of 21 healthy volunteers (13 females, 8 males) were included and completed all four visits. The median age was 26 (range 18–65) years.

The skin barrier response from day 0 to 3 assessed by TEWL, electrical conductance, pH, and erythema is given in Table 2. No significant differences in TEWL were found for any of the four areas from day 1 to 3 (Table 2). No significant difference was found in electrical conductance between day 1 and 3 <u>at</u> the ACHD area, while a significant increase was observed <u>at</u> the area of ABHR from day 1 to 3 (Table 2). On day 3, electrical conductance at the ABHR area was higher than the ACHD area (p = 0.006), while no difference was observed when comparing ACHD area with the control patch area (Table 2).

The pH values significantly increased on day 3 as compared to day 1 on the ACHD area, ABHR area, and control patch area, respectively. No significant change in erythema was observed for any of the four areas (Table 2).

Details on subjective discomfort and clinical score for skin reactions are given in Tables 3 and 4, respectively. Four participants reported subjective discomfort due to ACHD on day 1 and three participants reported subjective discomfort on day 2. Of these, only one person reported discomfort on both days, giving a total of six participants reporting subjective discomfort due to ACHD in Study B. With regards to ABHR, five participants reported discomfort on day 1 and three reported discomfort on day 2. Of these, one participant reported discomfort on both days, giving a total of seven participants reporting subjective discomfort due to ABHR. Finally, a total of four participants reported subjective discomfort <u>to</u> both ACHD and ABHR during the investigation.

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	Subjective discomfort Yes (% of total)	p-Value <sup>*</sup>	Mean VAS score in participants reporting discomfort	Mean VAS score in total (n = 21)	p-Value**
ACHD	6 (28.6)	0.120	1.8	0.3	0.582
ABHR	7 (33.3)		2.0	0.4	
Control patch	0 (0)		0	0	

**TABLE 3**Study B: Subjective discomfort and mean visual analogue scale (VAS) scores reported by participants after application of activechlorine hand disinfectant (ACHD) and alcohol-based hand rub (ABHR)

Abbreviations: ABHR, alcohol-based hand rub; ACHD, active chlorine hand disinfectant.

\*p-Value for subjective discomfort to ACHD compared to ABHR. Fisher's exact test was used.

\*\*p-Value for mean VAS score for ACHD compared to ABHR. Wilcoxon signed rank test was used.

**TABLE 4**Study B: Mean values for skin reactions evaluated by theFrosch Kligman score

	Frosch Klign (0–10) Mear	nan score N	
	Day 1	Day 3	p-Value
ACHD	1.6	1.2	0.107
ABHR	1.5	1.4	0.580
Control patch	1.6	1.2	0.105

*Note*: The score was assessed before application on day 1 and hereafter again on day 3. The maximum Frosch Kligman score is 10. Wilcoxon signed rank test was used to evaluate differences between the paired data. Abbreviations: ACHD, active chlorine hand disinfectant; ABHR, alcoholbased hand rub.

# 4 DISCUSSION

This is the first study to evaluate the skin barrier response to ACHD in healthy skin and SLS-induced contact dermatitis, compared with the traditional ABHR. Our results confirm that the skin barrier function is unaffected by short-term applications of ACHD compared with ABHR assessed by non-invasive skin barrier measurements. Subjective discomfort was reported as very mild and only sporadically in relation to ACHD and ABHR, and clinical signs of skin reaction on the area of ACHD and ABHR were almost non-existing.

Our results show that the intact skin barrier function is not impaired by ACHD, and that ACHD does not lead to further impairment of an already disrupted skin barrier, since TEWL values were unaffected after repeated exposure to ACHD in Study A as well as in Study B. The increase in TEWL after SLS exposure and occlusion by patches is a wellknown occurrence, and since Agner et al. have shown that the TEWL values were stable between 1 and 3 h after removal of patches<sup>45</sup> the measurements in our study were performed 1 h after patch removal. The evaporimetry skin barrier measurement, TEWL, is validated and hence the best method for evaluation of skin barrier damage,<sup>32</sup> and the utility of the tool is confirmed by the continuous use of TEWL over decades as the primary outcome in several experimental studies evaluating the skin barrier response to for example SLS, ABHR, detergents, and topical products.<sup>8,46</sup>

Numerous studies have shown that the skin barrier evaluated by TEWL after application of ABHR is unaffected as in accordance with our results.<sup>6,8,9</sup> However, Plum et al. reported an increase in TEWL when the ABHR was applied on hydrated skin, which may mimic the real-life situation in busy work-settings in the health care sector.<sup>10</sup> Although the prevalence of subjective discomfort to ABHR on the SLSinduced dermatitis area was low in our study, due to the fact that the experimentally induced impairment of the skin barrier in Study B was mild, we know from previous studies that ABHR causes discomfort in more than every fourth HCW with HE.<sup>2,11</sup> Furthermore, Stutz et al. reported that 79.2% of the nurses suspected ABHR to be damaging to the skin barrier, thus increasing the risk of reduced compliance in relation to proper hand hygiene.<sup>11</sup> These findings emphasize the need for an alternative to ABHR for both HCWs with HE and for HCWs with challenged skin due to the high exposure to wet work in the health care sector.<sup>3</sup>

Alternatives to ABHR have not vet been successfully made available in the health care sector. Breidablik et al. suggested ozonized water as an alternative solution for disinfection of hands; however, the effectiveness in contrast to ABHR has been questioned and the irritant properties have not yet been tested.<sup>47,48</sup> Further, Kim et al. recently published a study examining a disinfecting solution with low concentrations of fermented ethanol, caprylic acid and citric acid as an alternative to the ethanol-based disinfectant; however, the solution has a pH value between 2.3-2.5 indicating non-optimal properties for use on skin.<sup>49</sup> Finally, a herbal-based hand disinfectant PureHands (Himalaya Drugs Company, India) containing coriander, neem and lime, among others, is another alternative, though the effectiveness against different bacteria remains to be concluded and no studies are available regarding the effect on the skin barrier.<sup>50</sup> Apart from being subjectively tolerable and harmless to the skin barrier, the alternative disinfectants should naturally adhere to regulations with respect to effectiveness against microorganisms.

Electrical conductance reflects the water content in the stratum corneum, and the method is very sensitive to exogenous factors such as the temperature and humidity.<sup>33,38,51</sup> We found no significant differences in the hydration after consecutive applications of ACHD during both study procedures indicating an unaffected skin barrier. The higher hydration on the area of ABHR in Study A and Study B is most likely explained by the moisturizing effect of glycerol added to the

ABHR solution.<sup>52,53</sup> although an additional damage to the skin cannot be excluded. ABHR with glycerol was chosen in the present study design since glycerol is added as an ingredient in almost all ABHR products used in the Danish health care sector. Atrux-Tallau et al. showed that glycerol increased the hydration in SLS-induced contact dermatitis, while the TEWL values remained high indicating that the skin barrier function assessed by TEWL is not restored by glycerol.<sup>54</sup> Sugarman et al. found that a decreased skin hydration and increased TEWL correlated with the severity of clinical symptoms in 38 patients with atopic dermatitis.<sup>42</sup> While this inverse relationship between hydration and TEWL found by Sugarman et al. indicated a damaged skin barrier, we found unaffected TEWL values at all areas in both intact and damaged skin, and significantly increased hydration only at the area of ABHR in both intact and damaged skin. Taken together, these results confirm that the skin barrier is not affected negatively by ACHD with respect to the hydration assessed by the electrical conductance.

In Study A, the pH values decreased significantly on day 3 as compared to baseline at all three test areas. During the study period, contact with water, soaps or other leave-on products on the forearms was not allowed, and several days without showering may therefore result in increased sebum production and thus a more acidic milieu.<sup>55,56</sup> In Study B, the pH values increased significantly on day 3 at the ACHD, ABHR and control patch areas. This is in line with previous findings evaluating the skin pH after SLS-exposure.<sup>43,57</sup> The increase in pH is most likely explained by the decreased level of lipids (e.g., ceramides) found in damaged skin.<sup>56</sup> The pH on day 1 was assessed 1 h after patch removal, thus in the early stage of a skin barrier disruption, and although an increase could be expected already at day 1, this was first observed at the assessments performed at day 3. Similar findings were reported by Wilhelm et al. reporting a decrease in the pH value on the forearms of healthy individuals immediately after inducing a skin barrier disruption with tape-stripping, while the pH value showed to increase in the subsequent days.<sup>58</sup>

In the present study, six and seven participants reported mild discomfort after repetitive applications of ACHD and ABHR, respectively. Nevertheless, the VAS score for discomfort was quite low and the participants reported discomfort only in relation to some of the applications of ACHD and ABHR. The skin barrier damage induced by the 1% SLS corresponded to a mild degree of dermatitis with redness and mild scaling, and not comparable to, for example, chronic HE with deep fissures. Compared to previous results, the prevalence of ABHR-related subjective discomfort was low in our study,<sup>2,11</sup> and the present results may therefore not reflect the discomfort in HCWs with chronic fissured HE using ABHR.

Using the Frosch Kligman score, the severity of the clinical skin reaction located to the ACHD area was similar to that of the control patch area <u>at</u> day 1 and day 3, while the skin reaction was more severe <u>at</u> the ABHR area albeit improved. This may indicate an enhanced improvement <u>on</u> the area of ACHD compared to the ABHR area. Although no difference was found in the skin color measurements evaluating erythema, the clinical Frosch and Kligman score may have identified differences between the areas since it evaluates not only the redness but also the scaling.

#### 4.1 | Strengths and limitations

The repetitive application procedure closely mimicked the daily life of many HCWs, making our study design and results reliable. Emollients were not allowed in our Study but could otherwise influence the results. Most of the participants in our study were <30 years, and since skin barrier properties depend on age, our results are not necessarily representative of all age groups. Although it can be argued that the actual irritancy of ACHD and ABHR may have been weakened because the measurements were performed almost 24 h after the last application, we decided to measure TEWL and electrical conductance on day 3 as they would otherwise only reflect the immediate hyper-hydration caused by the disinfectant solutions instead of the long-term effect of the intervention.<sup>38</sup> The study was performed on intact and experimentally induced contact dermatitis, and further data on the irritant properties of ACHD in patients with HE may be necessary in order to evaluate the usefulness for HCWs with HE, particularly with respect to subjective discomfort. The contact dermatitis induced by 1% SLS corresponded to a milder degree of dermatitis without deeper fissures, and the subjective discomfort may therefore not represent the true degree of discomfort that would have been experienced by patients with chronic HE.

# 5 CONCLUSION

Overall, our results show that the skin barrier function in intact skin and experimentally induced contact dermatitis is unaffected by repetitive exposure to ACHD as compared to ABHR. Our findings indicate that ACHD may be used as an alternative to the traditional ABHR by individuals with intact as well as challenged skin. Future studies should evaluate the skin barrier response as well as subjective discomfort to disinfectants in patients with chronic HE.

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#### CONFLICT OF INTEREST

Glenn Gundersen is Medical Director at SoftOx Solutions AS and Magnus Mustafa Fazli is Scientific Director at SoftOx Solutions AS. All other authors declare no conflict of interest.

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