

ORIGINAL RESEARCH

The Comparative Effects of Various Moisturizers on Epidermal Barrier Function Recovery After Bathing in Atopic Dermatitis

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ABSTRACT

Background/Aims: An important pillar of AD management involves moisturizer application following bathing to restore epidermal barrier function (EBF). In this study, we aim to bring additional evidence to the “soak-and-smear” regimen, comparing EBF recovery by various moisturizers following bathing in AD and healthy subjects.

Methods: Volar forearms of 10 AD patients and 10 healthy controls were immersed in water for 10 minutes to simulate bathing. Immediately after bathing, ceramide-containing emollient (CER), a humectant (10% glycerin, GLY), an occlusant (white petrolatum, PETR), and aloe vera 5% extract (ALOE) were applied to separate test sites on the forearm. One test site did not receive any moisturizer and served as control. EBF parameters (hydration, TEWL, and pH) were recorded at baseline, and 15, 30, and 60-minutes post-bathing.

Results: AD and controls shared similar trends. ALOE had the most significant pH decrease while GLY had the highest pH increase. Hydration significantly increased in all moisturizers compared to control. GLY led to the highest increase, peaking at 15-minutes for both AD and healthy subjects. AD subjects had higher hydration following CER than healthy subjects throughout the entire study. All four moisturizers increased TEWL compared to control, though PETR had the lowest initial TEWL increase.

Conclusion: All moisturizers had an immediate effect on improving SC hydration. Their initial effects on TEWL increase recovers toward control levels by 60-minutes. Future studies are needed to examine the effect of repeated moisturizer post-bathing over longer study periods.

INTRODUCTION

Atopic dermatitis (AD) is a remitting-relapsing inflammatory skin condition characterized by xerosis, itching, and eczematous lesions. Patients have defective epidermal barrier function (EBF) associated with decreased ceramide levels and stratum corneum (SC) hydration, and increased transepidermal water loss (TEWL) and pH.¹ Management recommendations emphasize the “soak and smear” technique, by applying moisturizers immediately after bathing.² Few studies have reported the quantitative effect of moisturizers on EBF following bathing, and even less have compared the various ingredients. The goal of this study is to compare EBF recovery among various moisturizers after bathing in AD and healthy subjects. The moisturizers tested encompass a wide spectrum of barrier-repairing properties and include a ceramide-containing emollient (CER), humectant (10% glycerin, GLY), occlusive (white petrolatum, PETR), and aloe vera 5% extract (ALOE).

METHODS

The study was approved by the institutional review board at the University of California, Davis (IRB# 523979) and registered on clinicaltrials.gov (NCT02594969). Following informed consent, ten patients with AD (mean age 26.3 years, range 12-45 years; 5 mild, 3 moderate, 2 severe) and ten healthy volunteers (mean age 28.5 years, range 22-34 years) participated in this study.

CER (Valeant Pharmaceuticals, USA) and PETR (Covidien, USA) were purchased commercially. GLY 10% solution was prepared in phosphate-buffered saline. For ALOE extraction, 2.5g of fresh aloe vera leaf was added to 50mL sterile water, heated at 80°C while stirred for 30-minutes, cooled to

room temperature, then centrifuged at 2000rpm for 10 minutes followed by serial filtering.

Testing was conducted on volar forearms. None of the subjects bathed or applied topical moisturizers or medications for 12-hours prior to the study session. Test arms were immersed in room temperature non-ionized water for 10-minutes, followed by dab-drying with towels. EBF including hydration (MoistureMeter SC, Delfin Technologies, Inc., USA), TEWL (Tewameter, Courage and Khazaka, Germany) and pH (Dry Skin pH Meter, Hanna Instruments, USA) were measured immediately post-immersion. Within 3-minutes post-bath, 0.2ml of each of the four moisturizers were applied to separate 1-inch² spots on the forearm, and gently massaged until no residual product was visible. The control spot did not receive any moisturizer. EBF were measured again at 15, 30 and 60-minutes post-bathing. Participants were asked to report skin discomfort, including itching, burning or pain at any time during the study.

RESULTS

Outcome measures are presented in Table 1. EBF status changes were compared to post-bath values. Time course changes in EBF are presented in Figure 1. AD and healthy subjects had very similar trends. None of the participants reported discomfort. No increased erythema or signs of irritation were observed in any of the participants.

Table 1. Outcome Measures. Percent differences in epidermal barrier function (EBF) (pH, hydration, and TEWL) compared to control (no moisturizer).

AD	pH			HYDRATION			TEWL		
	15MIN	30MIN	60MIN	15MIN	30MIN	60MIN	15MIN	30MIN	60MIN
CER	97.5%	100.5%	102.4%	442.9%*	394.4%*	413.2%*	493.5%	219.9%*	240.7%
GLY	106.1%	107.1%*	103.6%	828.3%*	722.9%*	684.3%*	379.4%*	179.0%*	218.5%*
PETR	96.3%	99.0%	97.5%	173.4%	315.7%*	382.8%*	181.7%	207.5%*	182.4%*
ALOE	88.2%*	94.1%*	92.3%*	328.2%*	256.9%*	269.7%*	246.2%*	202.0%*	184.8%*

HEALTHY	pH			HYDRATION			TEWL		
	15MIN	30MIN	60MIN	15MIN	30MIN	60MIN	15MIN	30MIN	60MIN
CER	99.2%	100.3%	98.1%	334.7%*	282.7%*	296.7%*	573.7%*	242.9%*	164.8%
GLY	110.4%*	108.3%*	100.7%*	815.2%*	695.1%*	639.4%*	455.0%*	206.1%*	171.3%
PETR	102.2%	99.1%	97.0%	96.8%	217.7%*	343.4%*	242.3%*	209.9%*	220.0%*
ALOE	91.2%	94.1%	91.1%	471.5%*	303.0%*	268.7%*	291.5%*	221.9%*	285.8%*

EBF values were measured three-times to calculate average values. Hydration and TEWL were normalized to post-bath values. Statistical analysis was performed using two-tailed-paired T-test. Results were compared to post-bath values. Differences in EBF were considered statistically significant when p-values were ≤ 0.05 . * = $p < 0.05$.

AD, atopic dermatitis; TEWL, transepidermal water loss; CER, ceramide-containing emollient cream; GLY, 10% glycerin; PETR, white petrolatum; ALOE, 5% aloe vera extract.

ALOE is associated with the most significant decrease in absolute pH values throughout all time points in all subjects, nadir at 15-minutes (88.2% in AD, 91.2% in healthy). In contrast, GLY is associated with highest pH increase, values peaking at 15-minutes (106.1% in AD, 110.4% in healthy). There was no statistical difference in mean pH between CER and PETR compared to control in both AD and healthy subjects at all time points measured.

All four moisturizers increased hydration compared to control. GLY led to the highest increase, peaking at 15-minutes for both AD (828.3%) and healthy (815.2%) subjects. PETR led to initial hydration decrease with nadir at 15-minutes, followed by rapid

recovery by 60-minutes. AD subjects had higher hydration following CER (442.9% \rightarrow 394.4% \rightarrow 413.2%) than healthy subjects (334.7% \rightarrow 282.7% \rightarrow 296.7%) throughout the entire study.

To our surprise, all four moisturizers increased TEWL compared to control throughout the entire study period. CER is associated with the highest initial TEWL among all moisturizers, peaking at 15-minutes (493.5% in AD, 573.7% in healthy), followed by rapid decrease by 60-minutes (240.7% in AD, 164.8% in healthy). PETR is associated with the lowest initial TEWL among all moisturizers at 15-minutes (246.2% in AD, 242.3% in healthy), followed by steady maintenance throughout the study.

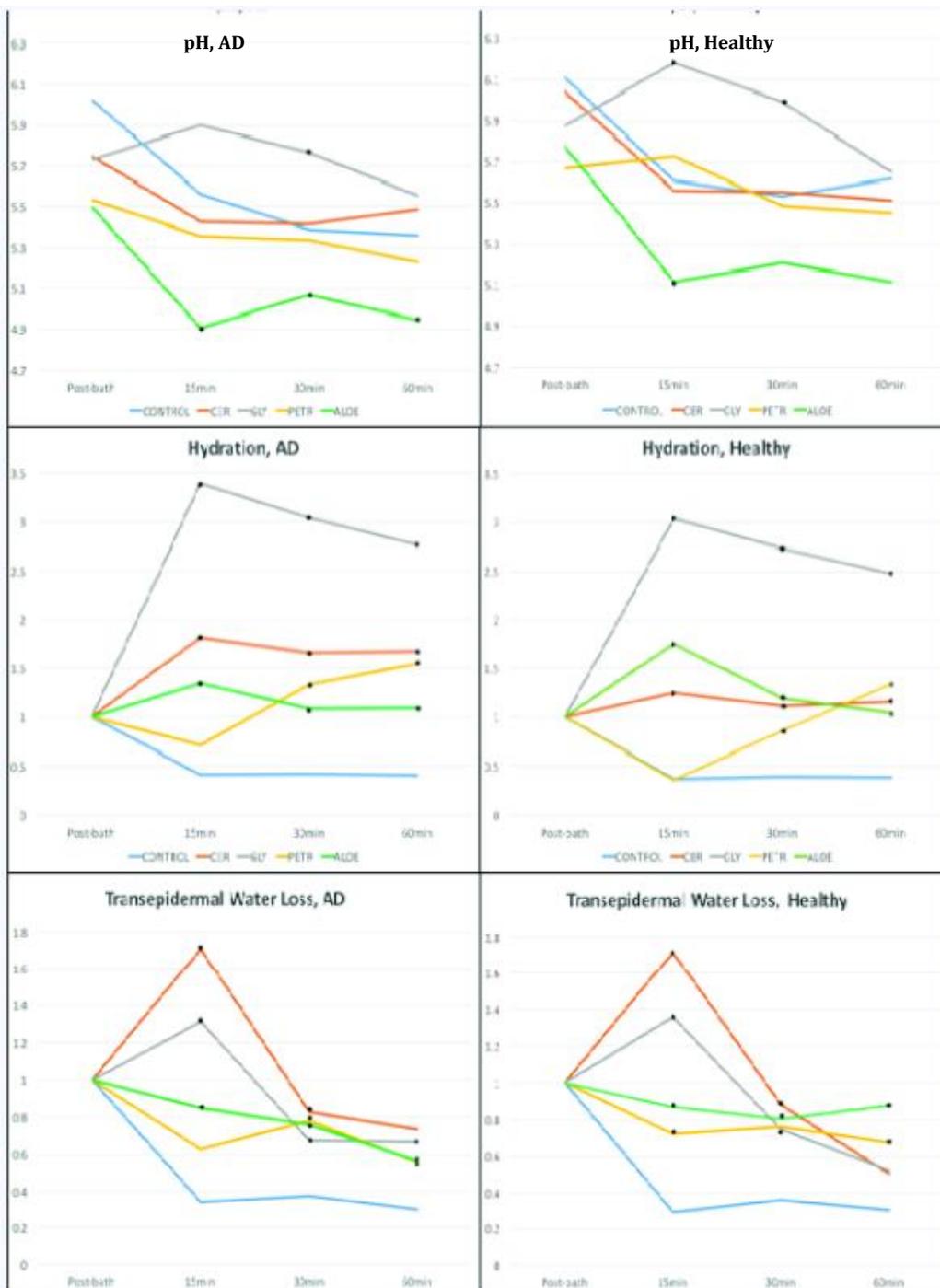


Figure 1. Changes in epidermal barrier function (EBF) due to various moisturizers post-bathing. Hydration and TEWL values are normalized to baseline reading. Percent post-bath of pH hydration, and TEWL vs. time are graphed for AD and healthy participants. All 3 parameters were measured 3 times to obtain an average value with standard deviation. pH values for 3 healthy subjects were not obtained due to equipment malfunction.

DISCUSSION/CONCLUSIONS

This study aimed to bring additional evidence to the “soak-and-smear” regimen by examining the effect of various types of moisturizers on EBF recovery post-bathing. We have previously demonstrated that bathing temporarily introduces moisture to the skin with a peak in hydration status immediately post-bathing in AD and healthy subjects [3]. In the current study, ALOE is best at lowering SC pH. GLY is best at introducing SC hydration. CER led to the most rapid TEWL increase. PETR is superior at limiting TEWL at the initial phase. Overall, moisturizers had an immediate effect on SC hydration status, whereas their effect on TEWL is delayed, but slowly recovers toward control levels by 60-minutes.

Our study duration was limited by practical considerations of subject patience with participants sitting in the room during the entire study period. We did not follow the EBF measurements beyond 60-minutes post-bathing, which may explain that despite trending towards baseline, TEWL status after moisturizer application was higher than control. The initial TEWL increase within the first 60-minutes may be due to increased local water concentration after bathing and hydrating effects of the moisturizers. Future studies are needed to examine the effect of repeated moisturizer use throughout the day following bathing or with repeated daily bathing, as recommended in real life practice.

Conflict of Interest Disclosures: Dr. Shi has equity in DermVeda and is a paid advisor for Melno Therapeutics and the National Eczema Association, as well as a paid preceptor for Novartis. Dr. Sivamani is a scientific advisor for DermVeda. The remainder of the authors have no relevant conflicts of interest.

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