

Effect of emollients on skin barrier function in patients with atopic dermatitis: a systematic review and meta-analysis

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Abstract

Introduction: Atopic dermatitis (AD) primarily arises from skin barrier dysfunction. Emollients serve as a primary management modality for AD patients. They can enhance skin barrier function through multiple mechanisms. However, previous research has not established definitive conclusions about their effectiveness or ideal usage duration. This study systematically analyzes emollients' actual barrier-repairing effects by synthesizing current evidence.

Methods: We screened 14 relevant studies from four databases: PubMed, Embase, Web of Science, and Cochrane Library. Ten of these human randomized controlled trials were included in the meta-analysis, which mainly examined the effects of emollients on transepidermal water loss (TEWL), skin hydration (capacitance value), and skin acidity (pH). We further compared the effects of different application times on TEWL in subgroups. Data were analyzed using Review Manager 5.4, and the results are expressed as effect estimates with 95% confidence intervals (CIs).

Results: The TEWL values of AD patients using emollients were significantly lower than those of the control group, with statistical significance at 2 weeks and 4 weeks of continuous use. Skin capacitance values were significantly higher in the emollient group than in the control group, and there was no significant difference in skin pH between the two groups of patients.

Conclusions: The combined data suggest that emollients can reduce TEWL values and improve skin hydration in patients with AD, with statistically significant effects observed after 2 weeks and 4 weeks of continuous use. However, the improvement of skin pH by emollients has not been confirmed, and the efficacy of use for ≥ 6 weeks remains inconclusive due to limited evidence. More research is needed to explore this in the future.

Keywords: moisturizer, transepidermal water loss, skin hydration, skin surface pH

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Introduction

Atopic dermatitis (AD) is a prevalent chronic inflammatory skin disease, showing a rising global incidence. Epidemiologic studies indicate that AD prevalence in developed countries reaches up to 15% to 30% (1). Although AD predominantly affects infants and young children, chronic cases often involve recurrent flare-ups lacking remission periods, with eczematous lesions frequently persisting into adulthood (2, 3). AD pathogenesis arises from the interplay of genetic predisposition, immune dysregulation, skin barrier dysfunction, and environmental triggers. Collectively, these mechanisms drive the chronic inflammation and recurrent exacerbations central to AD pathophysiology (4). Current AD management prioritizes skin barrier restoration, pruritus control, and inflammation mitigation (5, 6). Restoring skin barrier function is a cornerstone of AD management because it is essential for maintaining cutaneous homeostasis, minimizing transepidermal water loss (TEWL), and defending against exogenous irritants and allergens (7). AD is marked by a compromised skin barrier, which is demonstrated by increased TEWL, lower hydration levels in the stratum corneum, and an altered lipid composition (8, 9). It is important to note that in patients with AD the synthesis of intercellular lipids, especially ceramides, cholesterol, and free fatty acids (FFAs), occurs in lower amounts and presents irregular molar ratios (10). In healthy skin, these lipids assemble into multilayered membrane structures at an equimolar ratio (1:1:1), constituting the "mortar" in the "brick-and-mortar" model, which

ensures epidermal barrier integrity and optimal hydration (11). Topical formulations containing ceramide-, cholesterol-, and FFA-mimetic lipids aim to correct these deficiencies, thereby restoring barrier function and mitigating AD flare severity (12). Emollients are foundational therapies in AD management, exerting clinically significant, multifunctional effects on skin barrier restoration (13). Emollients address the characteristic lipid deficiencies in AD skin—such as reduced or imbalanced ceramides, fatty acids, and cholesterol—by replenishing these components, thereby repairing stratum corneum integrity, improving water retention, and reducing TEWL. For instance, Kawana et al. (14) demonstrated that emollients containing ceramides structurally and functionally emulate natural ceramides, occupying intercellular spaces within the stratum corneum to restore barrier compactness. A meta-analysis revealed that the introduction of emollients at an early stage notably decreases the occurrence of AD in infants (15). However, there is no clear evidence-grade research to support the use of emollients as primary care for patients with AD over 2 years old. Recent improvements in non-invasive methods allow for accurate evaluation of skin barrier function, mainly by measuring stratum corneum moisture levels and TEWL (16). A key pathophysiological feature of AD is elevated skin surface pH (rising from the healthy range of 4.1–5.8 to 7.0–8.0), which disrupts barrier function and enzymatic activity. Consequently, emollient formulation pH has emerged as a critical therapeutic consideration. Emollients formulated with pH-adjusted compositions (4.0–5.5), acidic components, and physiological lipid ratios may

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synergistically enhance barrier repair; however, optimizing sustained buffering systems and personalized pH-adaptive regimens requires further investigation (17). Considerable heterogeneity persists across current evidence regarding emollient efficacy in restoring skin barrier function among patients with AD. Variability in emollient types, compositions, and formulations likely contributes to inconsistent clinical efficacy, and the optimal duration of emollient use for skin barrier repair in mild-to-moderate AD remains undefined. Differences in methodology—such as study design, sample size, measures of outcomes, and length of follow-up—add to the complexity of interpreting the results. A comprehensive review and meta-analysis of the current evidence has thus become imperative to integrate the effects of emollients on skin barrier impairment related to AD. This process has established evidence-based clinical recommendations while having guided the development of tailored emollient strategies that have demonstrated enhanced skin barrier recovery and have contributed to improved long-term patient outcomes.

Methods

This study was pre-registered in the PROSPERO database (CRD42024575950) and prepared following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (18).

Search strategy

To conduct a thorough systematic search of the literature, both controlled vocabulary and free text terms, along with the Boolean operators “AND” and “OR,” were utilized. The following text words were searched for, appearing in all fields of the article: (“Emollient” OR “Emollients” OR “Moisturizer” OR “moistener”) AND (“atopic dermatitis” OR “Dermatitis, Atopic” OR “Atopic Dermatitis”). Four databases—PubMed, Embase, Web of Science, and Cochrane Library—were searched without time limit. The search methods are described in full in Table S1. Only English randomized controlled trials (RCTs) were selected for this article.

Eligibility criteria

A study was deemed eligible if it satisfied all the following criteria for inclusion: 1) it was a full-length article published in a peer-reviewed journal, 2) the research involved patients diagnosed with mild to moderate AD aged 2 years or older, 3) it assessed factors linked to skin barrier function, including TEWL along with other endpoint indicators, 4) the product investigated had to comprise emollient components, and 5) it presented relevant qualitative or quantitative data concerning skin barrier function both prior to and following treatment.

Conversely, a study was excluded if it fulfilled one or more of the criteria for exclusion: 1) it was published in a non-peer-reviewed outlet (such as a website or non-peer-reviewed journal), 2) it appeared solely in abstract form, 3) the research involved animal models or cell lines, 4) it utilized other topical treatments alongside emollients as part of the therapeutic approach, 5) it was categorized as a secondary study (including narrative reviews, systematic reviews, meta-analyses, conference notes, etc.), 6) it focused on diseases not associated with AD, 7) it was identified as a duplicate publication, or 8) study participants were younger than 2 years of age.

Study selection

Two reviewers, Q. Y. and W. Z., evaluated the titles and abstracts independently. When the studies potentially met the inclusion criteria, full texts were imported into Endnote (version 21, Clarivate Analytics, Philadelphia, PA, USA). Subsequently, Q. Y. and W. Z. independently examined these full texts and assessed them based on the previously mentioned criteria to determine final eligibility.

Data extraction

The following data were extracted: authors' names and year of publication, study population (age, sex, and country), diagnostic criteria for AD, products and sites tested, number and form of people in each group (intervention or control), duration of the study in days, and transcription of the main endpoints, measuring instruments, and the presence or absence of adverse events into a table. Data that were captured included baseline and endpoint measurements (means) along with their variability measured by standard deviation (*SD*), or standard error of the mean (*SEM*), which were obtained using the GetData Graph Digitizer (version 2.26, GetData Graph Digitizer, Moscow, Russia) (19) because most publications present the results in an image. These values were transcribed into an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA) capturing the following outcomes: TEWL, skin capacitance values, and skin surface pH. Values were obtained at various duration points because certain chosen studies conducted endpoint measurements at multiple crucial intervals throughout the study period. Throughout the process of gathering data, we sought the input of fellow researchers to address and find solutions to any problems that emerged.

Quality assessment

The quality of the methodology in the studies was evaluated using the risk of bias (RoB) system from the Cochrane Collaboration (20), which encompasses seven elements: generation of random sequences, concealment of allocation, blinding of both subjects and personnel, blinding in outcome assessment, handling of incomplete outcome data, selective reporting, and additional biases. According to the standards set forth in the Cochrane Handbook, there are three assessment options: green indicates a low risk of bias, yellow represents an unclear risk of bias, and red signifies a high risk of bias (20).

Statistical analysis

Studies that were RCTs were categorized based on the similarities of outcomes associated with skin barrier function. A meta-analysis was conducted separately for each category utilizing Review Manager 5.4 (Nordic Cochrane Centre, Copenhagen, Denmark) (21). For the statistical evaluations, a random effects model was employed to compute both the mean and the *SD* for continuous variables. The mean was established by calculating the difference between the endpoint value and the baseline value. In cases in which the RCTs provided *SD*s for both the baseline and endpoint in both the intervention and control groups, the *SD* of the change in relation to the baseline was derived using the following formula:

$$SD_{change} = \sqrt{SD_{change}^2 + SD_{final}^2 - (2 \times Corr \times SD_{baseline} \times SD_{final})}$$

Evaluation of heterogeneity

The heterogeneity statistics were calculated for each graph's legend using a forest plot. The I^2 index reflects the level of variation in effect sizes attributed to heterogeneity instead of sampling error within the overall variability among the studies. For instance, a 0% I^2 value signifies that the entire variation in effect sizes identified is caused by sampling error, whereas a 100% I^2 indicates that all observed variations are due to true effect variability. Typically, I^2 values are classified as low (0%–25%), moderate (25%–50%), high (50%–75%), and very high (75%–100%) heterogeneity (24, 25).

Results

Identification of studies

The literature search revealed a total of 1,546 records, as illustrated in Figure 1. Among these, 230 were identified by PubMed, 382 by Embase, 644 by Cochrane Library, and 290 by Web of Science. A total of 258 duplicates were removed from the 1,546 records, leaving 1,288 records for title and abstract screening. After

screening titles and abstracts, 1,109 items unrelated to the topic—comprising reviews, systematic evaluations, meta-analyses, conference proceedings, and non-human studies—were eliminated. Consequently, 179 records remained that were deemed potentially relevant, and their full texts were reviewed for eligibility. Ultimately, 165 articles were excluded based on the criteria detailed in Figure 1, leading to the inclusion of 14 full-text publications from the initial 179.

Risk of bias within studies

The risk of bias assessment across the 14 included studies is summarized in Figure 2a (percentage across all studies) and Figure 2b (judgment for each individual study). Random sequence generation: seven studies (50%) were judged as low risk and seven (50%) as unclear risk. Allocation concealment: seven studies (50%) were judged as low risk and seven (50%) as unclear risk. Blinding of participants and personnel: three studies (21%) were judged as low risk and 11 (79%) as unclear risk. Blinding of outcome assessment: 13 studies (93%) were judged as low risk and one study (7%) as unclear risk. Incomplete outcome data: all 14 studies (100%)

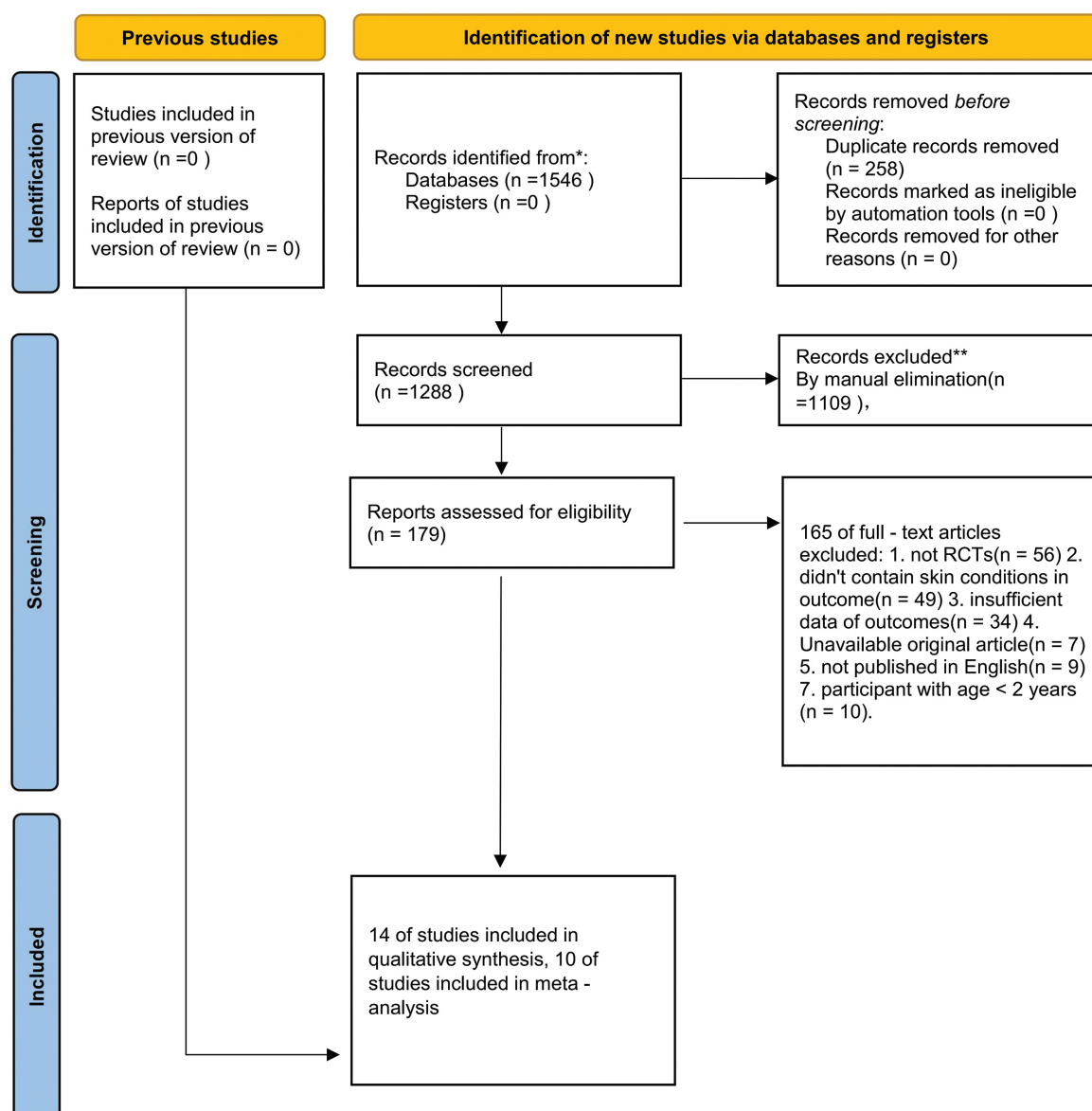


Figure 1 | Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram for systematic reviews that included searches of databases and registers only.

were judged as low risk. Selective reporting: all 14 studies (100%) were judged as low risk. Other bias: all 14 studies (100%) were judged as unclear risk. No study was judged as high risk of bias in any domain.

Research features

Table 1 summarizes the main characteristics of the 14 clinical studies. Eight of these studies included AD patients with Hani-



Figure 2 | a) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all studies. Domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), other bias. Classification: low risk of bias, unclear risk of bias, high risk of bias. b) Risk of bias summary: review authors' judgements about each risk of bias domain for each study. + = low risk of bias, ? = unclear risk of bias, - = high risk of bias.

fin and Rajka's diagnostic criteria, and Angelova-Fischer et al. (26) and Andrew et al. (27) included volunteers with UK working party diagnostic criteria. The studies were conducted in various countries, including Sweden, the United States, the UK, Germany, and South Korea. Three studies tested products containing urea ingredients (28–30); Kircik et al. (31) and Danby et al. (32) tested hydrogel or lotion emollients, respectively; and six studies tested specific emollients such as Cetaphil® Restoraderm® Body Moisturizer (CRM), emollients containing *Lactobacillus sakei* proBio 65, KAM-3008 cream, and so on. The frequency of emollient use by the experimental group was twice a day in all 14 studies, and the dosage could not be derived from precise data due to geographic, environmental, and personal factors. The duration of the test ranged from 1 to 8 weeks, and most of the studies performed measurements on forearm skin. The study by Danby et al. (32) conducted two sets of clinical trials providing values of skin barrier measurements in patients with AD applying diprobase cream or diprobase gel, and this was considered two different sets of data extracted from the study. The experiments by Danby et al. (30) tested three emollients (glycerin cream, paraffin cream, and urea glycerin cream) and were considered three different sets of data. Most of the experiments ranged in duration from 4 to 8 weeks, and TEWL values were extracted for subgroup analyses at different key time points.

Transepidermal water loss

Figure 3a shows a forest plot of the meta-analysis of TEWL values for the nine studies. For this outcome, the use of emollients resulted in a statistically significant reduction in TEWL with low heterogeneity ($I^2 = 18\%$, $Z = 3.39$, $p = 0.0007$, standardized mean difference [SMD] = -0.27 , 95% CI = -0.43 , -0.12).

Figure 3b shows a forest plot of skin TEWL values after different time cycles of emollient use in nine studies. Three of these provided data on TEWL values after 1 week of emollient use ($Z = 0.48$, $p = 0.63$), with moderate heterogeneity ($I^2 = 37\%$, SMD = 0.08 , 95% CI = -0.24 , 0.40). Three studies provided data on TEWL values after 2 weeks of emollient use ($Z = 2.89$, $p = 0.004$), with moderate heterogeneity ($I^2 = 55\%$, SMD = -0.52 , 95% CI = -0.88 , -0.17). Nine studies provided data on TEWL values after 4 weeks of emollient use ($Z = 2.92$, $p = 0.004$), with low heterogeneity ($I^2 = 22\%$, SMD = -0.25 , 95% CI = -0.42 , -0.08). Two studies provided data on TEWL values for ≥ 6 weeks of use ($Z = 1.71$, $p = 0.09$), with low heterogeneity ($I^2 = 0\%$, SMD = -0.32 , 95% CI = -0.69 , 0.05).

Skin hydration

In five studies assessing skin capacitance values between treatment and control groups, the use of emollients significantly improved skin capacitance results as shown in Figure 4a (SMD = 0.55 , 95% CI = 0.2 , 0.89 , $Z = 3.11$, $p = 0.002$), with moderate heterogeneity ($I^2 = 61\%$). After performing a sensitivity analysis (as shown in Fig. 4b) and removing one comparison arm (diprobase gel formulation) from the study by Danby et al. (32), the results showed lower heterogeneity ($I^2 = 12\%$), with a statistically significant effect remaining (SMD = 0.43 , 95% CI = 0.20 , 0.67 , $Z = 3.61$, $p = 0.0003$).

Skin surface pH

In studies assessing skin pH (shown in Fig. 5), no significant differences were found in skin surface pH between the treatment and control groups ($Z = 0.27$, $p = 0.79$), with moderate heterogeneity ($I^2 = 52\%$, SMD = -0.04 , 95% CI = -0.34 , 0.26). No significant differences were observed after sensitivity analyses, which may be due to differences in measurement equipment and the relatively low variability of skin pH, which is more difficult to measure accurately.

Discussion

Transepidermal water loss

The meta-analysis of TEWL values included nine studies using different types of emollients, and the results showed that emollients significantly reduced TEWL values in AD patients (SMD = -0.27 , 95% CI = -0.43 , -0.12), which indicates favorable recovery of skin physiological function. Subgroup analyses were performed based on the duration of emollient use: pooled data from three studies showed no statistically significant difference and a small total effect size after 1 week of emollient use; three studies provided TEWL values after 2 weeks of emollient use, with statistically significant results (SMD = -0.52 , 95% CI = -0.88 , -0.17); and nine studies provided data on TEWL values after 4 weeks of emollient use, with statistically significant differences (SMD = -0.25 , 95% CI = -0.42 , -0.08). Two studies provided data on TEWL values for ≥ 6 weeks of use (SMD = -0.32 , 95% CI = -0.69 , 0.05), but, due to the small number of studies, the results may be false positive.

It can be inferred that continuous use of emollients for 2 to 4 weeks in patients with mild-to-moderate AD significantly reduces TEWL values, whereas studies with ≥ 6 weeks of use did not show statistical significance, likely due to insufficient sample sizes and the limited number of studies. TEWL is the gold-standard objective measure for assessing skin barrier integrity (33), quantifying the stratum corneum's capacity to retain water. Barrier dysfunction disrupts the lipid bilayer's continuity (e.g., ceramides and cholesterol), thereby elevating TEWL. In patients with AD, TEWL values may exceed $20 \text{ g/m}^2/\text{h}$ (34), correlating directly with reduced natural moisturizing factor (NMF) levels caused by filaggrin (FLG) mutations (35). TEWL values are elevated in patients with AD compared to healthy individuals. The deficiency of FLG-derived amino acid metabolites, which maintain stratum corneum hydration and enhance barrier integrity by reducing intercellular gaps, renders elevated TEWL a biomarker for early-stage AD. However, TEWL measurements are influenced by ambient temperature, humidity, instrumentation (e.g., discrepancies of up to 15% between closed-chamber probes such as the VapoMeter and open-chamber devices such as the SkinTes), and physiological variability. A meta-analysis by Akdeniz et al. (36) identified substantial heterogeneity in TEWL reference values for healthy adults (e.g., $12\text{--}18 \text{ g/m}^2/\text{h}$ on the forehead) and highlighted the need for standardized measurement protocols.

Nevertheless, the limited number of studies necessitates further research incorporating time-dependent analyses as a primary focus. The molecular mechanism underlying the efficacy of prolonged emollient use likely involves two sequential phases: 1)

emollient-supplemented ceramides must first penetrate the stratum corneum and reorganize residual natural lipids into a lamellar structure (approximately 7–14 days), and 2) subsequent activation of the peroxisome proliferator-activated receptor (PPAR) signaling pathway upregulates lipid-synthesizing gene expression (21–28 days post-application), culminating in sustained barrier function improvement (37). Second, prolonged emollient use in AD patients exerts delayed immunomodulatory effects because the Th2-dominant immune response characteristic of AD forms a vicious cycle with barrier dysfunction. Barrier restoration by emollients mitigates pathogen-associated molecular pattern (PAMP) penetration, thereby suppressing alarmins such as thymic stromal lymphopoietin (TSLP) (38). This process involves phenotypic modulation of Langerhans cells, which suppress T-cell activation through time-dependent cumulative mechanisms. In conclusion, although prolonged emollient use (> 2 weeks) significantly reduces TEWL in

AD patients, heterogeneity in emollient formulations, dosage regimens, and the absence of RCTs evaluating > 6-week applications underscore the necessity for standardized clinical trials to establish stepwise efficacy thresholds for optimizing emollient therapy in AD.

Skin hydration

In the evaluation of skin capacitance values, the pooled results showed a statistically significant improvement in the emollient group compared with the control group (SMD = 0.55, 95% CI = 0.2, 0.89, $p = 0.002$), with moderate heterogeneity. After sensitivity analysis excluding the Diprobase gel arm from Danby et al. (32), heterogeneity decreased to a low level ($I^2 = 12\%$), and the effect remained statistically significant (SMD = 0.43, 95% CI = 0.20, 0.67, $p = 0.0003$). Skin capacitance is a secondary metric for evaluating skin barrier integrity, widely utilized to assess hydration status.

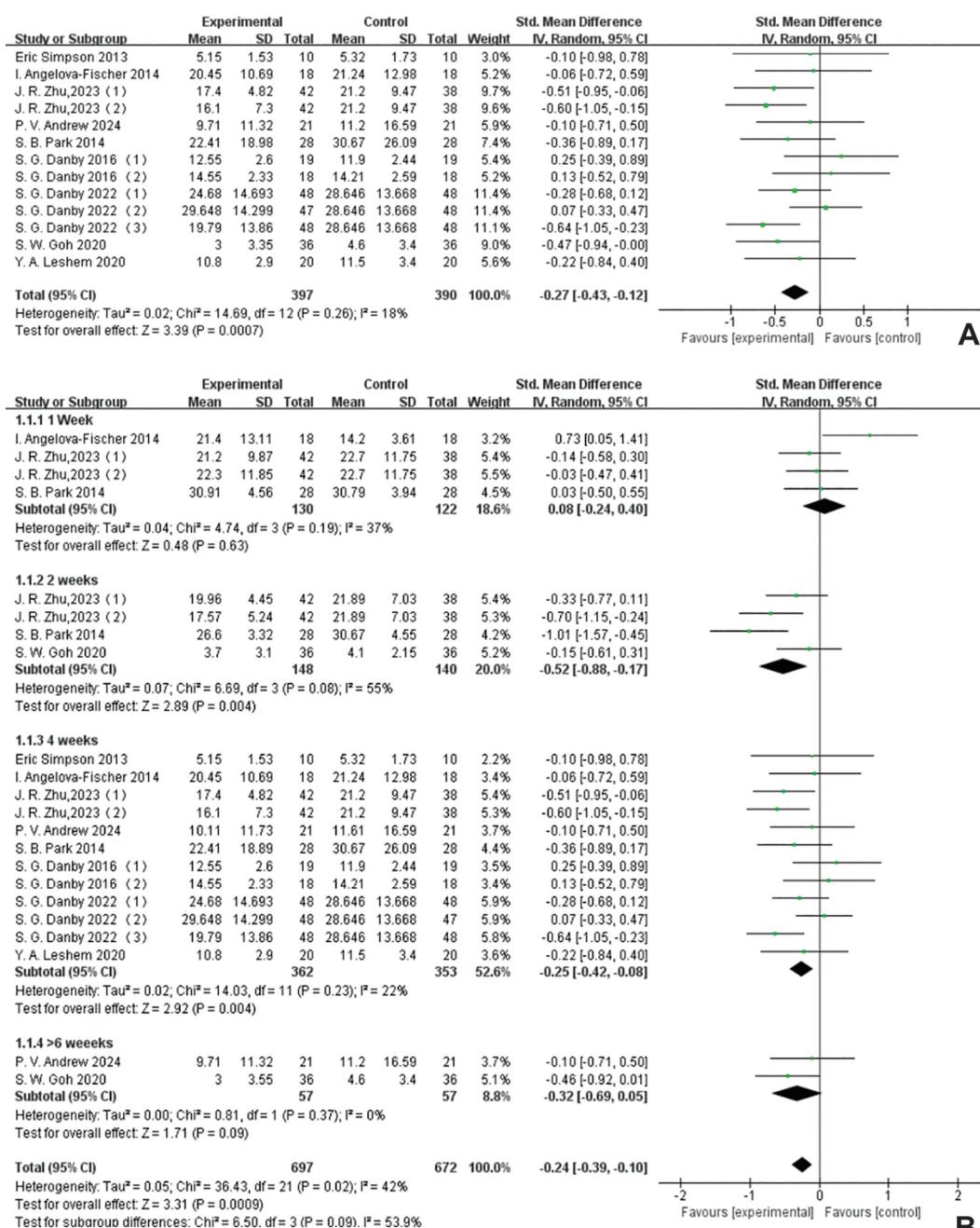


Figure 3 | a) Forest plot of meta-analysis for TEWL values in the studies. Comparison: emollient intervention vs. control group, outcome: TEWL change from baseline, effect model: random effects model. b) Forest plot of subgroup analysis for TEWL values by different intervention durations. Subgroups: 1 week, 2 weeks, 4 weeks, ≥ 6 weeks of emollient use; comparison: emollient intervention vs. control group; effect model: random effects model. SMD = standardized mean difference. TEWL = transepidermal water loss, CI = confidence interval.

Measurements rely on the skin’s electrical properties, particularly variations in dielectric constant and conductive pathway density. Elevated moisture levels correlate with increased dielectric constants and conductive pathway density, thereby reducing impedance (39). Park et al. (40) demonstrated that emollients containing lactobacilli extend capacitance value improvements by modulating the microbiome-immune axis.

Second, exogenous factors—including surfactants, detergents, hard water, *Staphylococcus aureus* colonization, and concurrent moisturizer use—may confound capacitance measurements. The CM825 Corneometer (CK Electronic, Cologne, Germany) was employed in most studies, with moisturizers applied twice daily. However, heterogeneous application sites, lack of standardized cleansing protocols, and short study durations across geographically diverse cohorts introduced variability. Uncontrolled environmental exposures during these studies likely acted as confounding variables, compromising the validity of emollient efficacy conclusions in this meta-analysis. In addition, differences in emollient composition affect efficacy. Andrew et al. (27) demonstrated that formulations containing ceramides and lactates simultaneously elevated capacitance values and reduced skin pH, whereas occlusive agents alone (e.g., petroleum jelly) provided only transient TEWL improvement. This divergence suggests that capacitance changes reflect not only hydration but also dynamic lipid metabolic activity and structural protein regulation. Transient capacitance elevations correlate with short-term hydration, whereas complete barrier restoration necessitates multifaceted interventions.

Skin surface pH

The meta-analysis revealed no significant differences in skin surface pH between treatment and control groups, potentially attributable to variability in the pH of products tested across studies and formulation complexity. Furthermore, pH may lack the sensitivity required to detect subtle physiological changes under these experimental conditions. Although emollients are first-line therapies for enhancing barrier function in AD patients, their impact on skin surface pH remains debated. This meta-analysis found no significant alteration in skin pH following emollient use, yet barrier function improved, suggesting that pH-independent molecular mechanisms underlie their efficacy.

Healthy skin surface pH is optimally maintained within a weakly acidic range (4.0–5.5), a microenvironment essential for barrier homeostasis. An acidic microenvironment enhances stratum corneum integrity by activating β -glucocerebrosidase and acidic sphingomyelinase, enzymes that facilitate ceramide synthesis and lipid matrix organization (41, 42). In patients with AD, lesion site pH frequently exceeds 6.0, activating serine proteases (e.g., kallikrein 5/7), disrupting the stratified organization of stratum corneum lipids, and triggering Th2-dominant inflammation (43). Notably, some emollients—even without significantly lowering pH—directly restore the lipid barrier through replenishment of physiological lipids (e.g., ceramides, cholesterol, and free fatty acids) (37). Lóden et al. (28) demonstrated that emollients containing urea, although they do not significantly modulate pH,

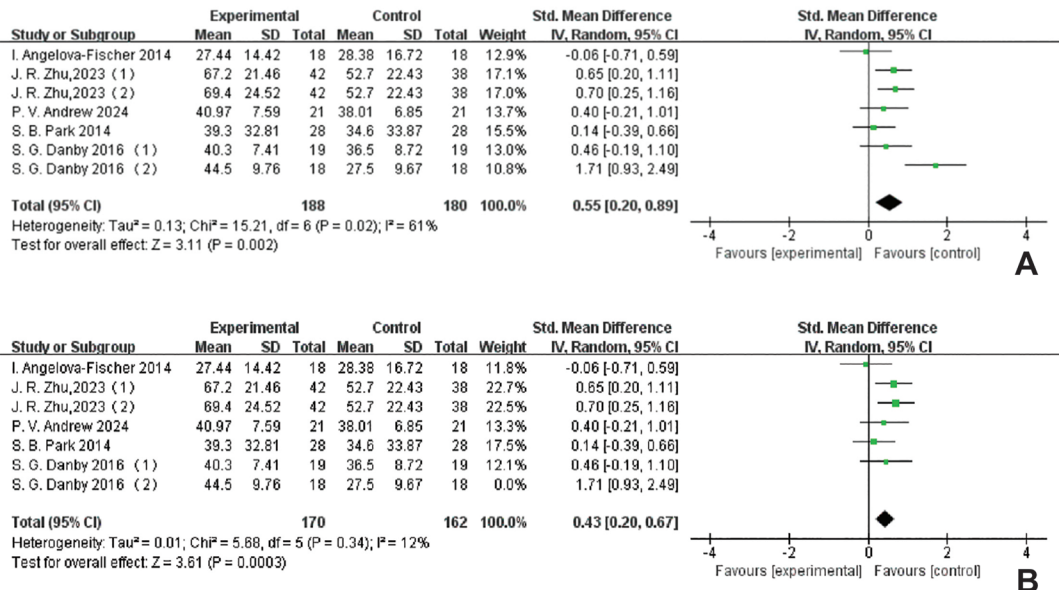


Figure 4 | a) Forest plot of meta-analysis for skin capacitance values in the studies. Comparison: emollient intervention vs. control group, outcome: skin hydration (capacitance) change from baseline, effect model: random effects model. b) Forest plot of sensitivity analysis for skin capacitance values after excluding the study by Danby et al. (32). Comparison: emollient intervention vs. control group, outcome: skin hydration (capacitance) change from baseline, effect model: random effects model.

TEWL = transepidermal water loss, SMD = standardized mean difference, CI = confidence interval.

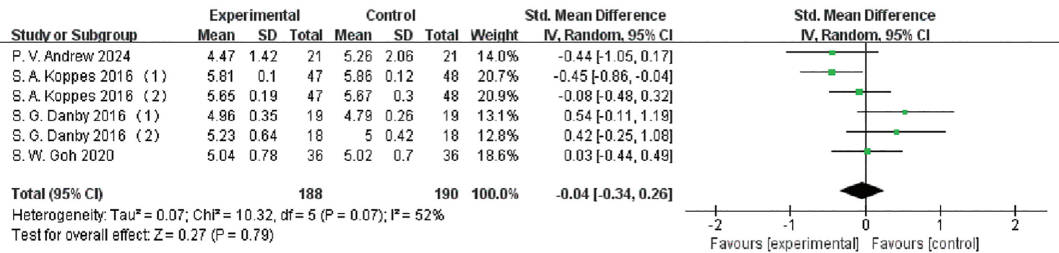


Figure 5 | Forest plot of meta-analysis for skin surface pH values in the studies. Comparison: emollient intervention vs. control group, outcome: skin surface pH change from baseline, effect model: random effects model.

SMD = standardized mean difference, CI = confidence interval.

markedly reduced irritant sensitivity in AD patients via enhanced hydration and reduced TEWL. This implies that emollients circumvent pH-dependent repair mechanisms through lipid restoration and anti-inflammatory activity.

Acidic emollients, however, may restore barrier integrity and lipid synthesis by reestablishing the skin's physiological acidic milieu, inhibiting serine proteases (e.g., kallikrein 5), attenuating desquamation, and modulating lipid-processing enzymes (e.g., acidic sphingomyelinas and β -glucocerebrosidase) (44). Emerging evidence underscores that emollient pH critically influences barrier restoration and lipid formation in AD patients. Neutral-pH emollients (e.g., petroleum jelly or mineral oil) primarily exert occlusive effects rather than actively modulating the skin's microenvironment. Although these formulations transiently mitigate transepidermal water loss, their long-term efficacy is constrained by failure to address pH-dependent enzymatic dysregulation. Andrew et al. (27) reported that acidic emollients containing zinc lactobionate upregulated antimicrobial peptide expression (e.g., human β -defensin-2) via acidic microenvironment restoration, a benefit absent in pH-neutral counterparts. In summary, pH is a single facet of emollient mechanisms, with effects extending beyond pH modulation. Future studies must elucidate the long-term impact of pH-tailored emollients on microbiome-immune crosstalk.

Among the 14 studies analyzed (26–32, 40, 45, 56–60), three incorporated urea (28–30), one tested a formulation containing niacinamide (45), and one utilized an emollient buffered with zinc lactobionate (27). The remaining studies either did not disclose formulation details or employed multi-component formulations. Emollients exert their therapeutic effects via multiple mechanisms: lipid replenishment, reducing transepidermal water loss, enhancing keratinocyte differentiation, modulating skin pH and microbiota, and exhibiting anti-inflammatory and antioxidant properties (46, 47). Common formulations include ceramides, glycerol, and urea, which restore the stratum corneum's "brick wall" structure by replenishing epidermal lipid reservoirs, thereby mitigating transepidermal water loss (48). A meta-analysis demonstrated that emollients containing ceramides significantly reduced TEWL and glucocorticoid dependence in eczema patients (49). N-palmitoyl serine (PS), a ceramide precursor, modulates ceramide synthesis during interleukin (IL)-4-mediated inflammation via CB1 receptor activation. PS treatment attenuates IL-4-induced inflammatory signaling and restores lipid metabolic balance in the stratum corneum (50). Other ingredients (e.g., glycerol or petroleum jelly) enhance epidermal hydration and barrier integrity (51). Niacinamide and vitamin C exhibit bioactive properties, stimulating keratinocyte proliferation and differentiation to accelerate barrier restoration (52). One study demonstrated that eicosapentaenoic acid in jojoba oil elevated prostaglandin E₂ (PGE₂) and tumor necrosis factor- α (TNF- α) levels, whereas components such as glycerol and urea attenuated the production of these inflammatory mediators (53). However, none of the studies empirically evaluated these molecular markers, highlighting the need for future research integrating molecular mechanistic insights with clinical datasets to advance targeted emollient therapies.

Constraints and suggestions for future work

Several limitations must be acknowledged regarding the modestly positive outcomes. First, the primary limitation stems from the limited number of clinical trials (10 studies) in the meta-analysis, coupled with small sample sizes (under 100 participants per study); consequently, these findings should be interpreted as preliminary in nature. This is because subgroup analyses and funnel plot asymmetry lack sufficient statistical power to reliably distinguish chance from true differences or detect potential reporting bias when fewer than 10 studies are included (54). Second, the use of GetData Graph Digitizer for data extraction could introduce limitations on the statistical power and accuracy of the analysis. Heterogeneity in emollient formulations across studies may confound the observed positive outcomes because the therapeutic effects could be partially attributable to variability in formulation vehicles. Quality assessment of the studies revealed that the RoB in most trials was predominantly unclear, leading to an overall reduction in methodological rigor. Furthermore, potential conflicts of interest stemming from commercial funding in certain studies further undermine the reliability of the findings. Such biases may arise from factors including reliance on subjective dermatologic assessments, selective outcome reporting, or biased presentation of results in commercially supported trials (55). The majority of clinical studies adopted a split-body design, leading to limited inclusion of RCTs. This contributed to a restricted evidence base and reduced sample sizes, with the smallest groups comprising only 15 participants ($n = 15$ per group). Second, confounding effects from participants' dietary habits and lifestyle factors could not be fully controlled, potentially influencing outcome validity. Furthermore, the heterogeneity of emollient formulations—each with distinct compositions and multifactorial mechanisms of action—was not comprehensively addressed in this analysis. No significant adverse events were reported in most studies, indicating that emollient use is likely well tolerated.

Conclusions

Thus, although emollients significantly improved certain indices of skin barrier function in patients with AD (TEWL and skin capacitance), no statistically significant improvement was detected in skin surface pH. Nevertheless, to the best of our knowledge, this study provides the first systematic investigation of topical emollients as a daily intervention for restoring skin barrier function in AD. Our findings suggest that emollients reduce TEWL in mild-to-moderate AD when used for 2 to 4 weeks; however, the lack of statistical significance for prolonged use (≥ 6 weeks) may reflect the limited number of available studies. This highlights the need for future trials to define stepwise efficacy expectations based on duration and formulation. Anticipating growing interest in skin barrier restoration, future RCTs should prioritize defining optimal emollient duration of use and identifying active ingredients to develop targeted therapeutic strategies. Such advancements may ultimately translate into safer, more effective emollient formulations capable of addressing the impaired skin barrier in AD.

Table 1 | Full details of all studies in the systematic review.

Author, year; location	Study population			Intervention	Control	Test product, pH	Test evaluation time	Test area	Outcome	
	Sample size, sex (M:F)	Age, years	Diagnostic criteria						Instrument	Indicators
Lodén et al. (1999) (28); Sweden	n = 15 (4:11)	32–46	Hanifin and Rajka	Test product	No treatment	5% urea in oil-in- water emulsion; pH 5.0	10, 20 days	Forearm	EP1 Evaporimeter (ServoMed, Stockholm, Sweden); CM-820 Corneometer (CK Electronic, Cologne, Germany)	TEWL, patch test reactions, stratum corneum hydration (AU)
Kircik et al. (2012) (31); USA	n = 20 (9:11)	12–65	Hanifin and Rajka	Test product	Eucerin lotion	Hydrogel vehicle and Eucerin lotion; NR	Baseline, 14 days	Upper and lower extremities	Tewameter® 300 (Courage + Khazaka Electronic, Cologne, Germany); Corneometer® 825 (CK Electronic, Cologne, Germany)	TEWL, stratum corneum hydration (AU), dry skin clinical scores
Simpson et al. (2013) (56); USA	n = 20 (4:16)	18–65	NR	Test product	No treatment	Cetaphil® Restoraderm® Body Moisturizer (CRM), pH 5.5	Baseline, 27 days	Right or left lower leg	CM825 Corneometer (CK Electronic, Cologne, Germany)	TEWL, stratum corneum hydration (AU), dry skin clinical scores
Angelova-Fischer et al. (2014) (26); Germany	n = 20 (4:16)	12–65	UK Working Party	1st week apply arm AC; 2nd week apply arm AC+AL	1st week apply arm AC; 2nd week apply arm HC+AL	AC: <i>Glycyrrhiza</i> <i>inflata</i> root extract etc.; HC: 1% hydrocortisone; AL: licochalcone A etc.; pH NR	Baseline, 7, 28 days	Forearms	CL400 Skin Colorimeter (Courage + Khazaka Electronic, Cologne, Germany); TM300 Tewameter (Courage + Khazaka Electronic, Cologne, Germany); CM825 Corneometer (CK Electronic, Cologne, Germany)	SCORAD, itch severity assessment; TEWL; skin hydration; lesional skin <i>Staphylococcus aureus</i> colonization
Park et al. (2014) (40); South Korea	n = 30 (20:10)	3–37	Hanifin and Rajka	Test product	General emollient	Emollient containing <i>Lactobacillus</i> <i>sakei</i> proBio 65 and general emollient; pH NR	Baseline, 7, 14, 28 days	Forearms, arms	TM210 Tewameter (Courage + Khazaka Electronic, Cologne, Germany); CM825 Corneometer (CK Electronic, Cologne, Germany)	Investigator's global assessment; TEWL; Skin Capacitance; Visual Analog Scale for Pruritus
Bomstein et al. (2015) (57); Israel	n = 20 (5:15)	19–67	Hanifin and Rajka	Test product	No treatment	KAM-3008 cream; pH NR	7, 14, 21 days	One side of body	Evaporimeter (Cortex Technology, Hadsund, Denmark); CM825 Corneometer (CK Electronic, Cologne, Germany)	SCORAD scale, TEWL, skin hydration
Danby et al. (2016) (32); UK	n = 37 (28:9)	29–37	Self-reported history of AD	Test product	No treatment	Diprobase® cream, pH 4.92; Doublebase™ gel, pH 7.13	28 days	Forearm	AF200 AquaFlux condensing chamber probe (Biox Systems Ltd., London, UK); MX18 Mexameter (CK Electronic, Cologne, Germany); PH905 Skin Surface pH Meter (Courage + Khazaka Electronic, Cologne, Germany); CM825 Corneometer (CK Electronic, Cologne, Germany)	TEWL, stratum corneum integrity and hydration, pH, and skin redness

Table 1 | Continued.

Author, year; location	Study population			Intervention	Control	Test product, pH	Test evaluation time	Test area	Outcome	
	Sample size, sex (M:F)	Age, years	Diagnostic criteria						Instrument	Indicators
Koppes et al. (2016) (58); Netherlands	n = 95 (35:60)	21–51	Hanifin and Rajka	Cer-Mg cream or HC	Cer-Mg + EM	HC; EM; Cer-Mg; pH NR	0, 21, 42 days	One side of body	Tewameter 300 (Courage + Khazaka Electronic, Cologne, Germany); SC Compact Moisture Meter (Courage + Khazaka Electronic, Cologne, Germany); skin pH meter (Courage + Khazaka Electronic, Cologne, Germany); erythema meter (Courage + Khazaka Electronic, Cologne, Germany)	SCORAD, TEWL, skin surface pH and erythema
Nasrollahi et al. (2018) (29); Iran	n = 20 (8:12)	2–45	NR	Test product	Water-in-oil (w/o) emulsion containing Eucerin with 5% urea	Emulsion-free with 1.5% LA; Eucerin with 5% urea; pH NR	0, 14, 21 days	One side of body	MPA 580 Cutometer® (Courage + Khazaka Electronic, Cologne, Germany); DUB Skin Scanner (Taberna Pro Medicum, Lübeck, Germany)	SCORAD, subcutaneous hydration, pH, sebum, temperature and ultrasound characterization of skin
Goh et al. (2020) (59); Malaysia	n = 36 (6:30)	12–65	Hanifin and Rajka	Test product	Standard commercial moisturizer	pH-modified moisturizer; standard commercial moisturizer; pH 7.32–7.58	0, 14, 42 days	Forearms, abdomen, shins	Hanna Instruments HI99181 (Hanna Instruments, Woonsocket, RI, USA); TM300 Tewameter (Courage + Khazaka Electronic, Cologne, Germany)	pH, TEWL, SCORAD
Leshem et al. (2020) (60); USA	n = 22 (10:10)	17–67	Hanifin and Rajka	Test product	No treatment	Cetaphil cream; Aveeno eczema therapy moisturizing cream; CeraVe moisturizing cream; Vaseline 100% pure petroleum jelly; pH NR	0, 28 days	Forearm	CM 820 Corneometer (CK Electronic, Cologne, Germany)	TEWL, capacitance, pH, and TEWL after tape stripping
Danby et al. (2022) (30); UK	n = 49 (20:29)	19–81	NR	Test product	No treatment	Urea-glycerin cream, glycerin cream, simple paraffinic cream without moisturizer; pH NR	0, 14, 28 days	Forearm	Colourimeter (Courage + Khazaka Electronic, Cologne, Germany); CM825 Corneometer (CK Electronic, Cologne, Germany); AF200 AquaFlux condensing chamber probe (Biox Systems Ltd., London, UK)	Sodium lauryl sulfate challenge, TEWL, hydration and natural moisturizing factor levels

Table 1 | Continued.

Author, year; location	Study population			Intervention	Control	Test product, pH	Test evaluation time	Test area	Outcome	
	Sample size, sex (M:F)	Age, years	Diagnostic criteria						Instrument	Indicators
Zhu et al. (2023) (45); China	n = 122	12–65	Hanfin and Rajka	Group T1 used an emollient containing niacinamide; group T2 used emollient after applying a cleansing gel containing niacinamide	Moisturizer no. 1	Moisturizer no. 1; emollients containing niacinamide; cleansing gel with niacinamide; pH NR	0, 7, 14, 28 days	Face	Corneometer CM825 (CK Electronic, Cologne, Germany)	SCORAD and PP-NRS, POEM and DLQI, TEWL and stratum corneum water content
Andrew et al. (2024) (27); UK	n = 21 (9:14)	19–81	UK Working Party	Test product	Carrier cream	Test cream (LCP) consisting of emollient base with zinc lactobionate buffer system, glycerin, and physiological lipids (ceramides, free fatty acids, and cholesterol) at pH 4.0; vehicle consisted of same base emollient, adjusted to pH 7.0	0, 28, 56 days	Entire palmar surface of forearm	CM825 Corneometer (CK Electronic, Cologne, Germany); AF200 AquaFlux condensate chamber probe (Biox Systems Ltd, London, UK); 905 Skin- pH-Meter (Courage + Khazaka Electronic, Cologne, Germany)	TEWL, skin hydration, skin sensitivity to sodium dodecyl sulfate and pancreatic rennet-like protease activity

AC = a formulation of *Glycyrrhiza inflata* root extract, etc., AD = atopic dermatitis, AL = an emollient containing licochalcone A, etc., AU = water content of the stratum corneum, Cer-Mg = ceramides and magnesium, DLQI = Dermatology Life Quality Index, EM = emollients, F = female, HC = hydrocortisone, LA = linoleic acid, LCP = test cream, M = male, NR = not reported, POEM = Patient-Oriented Eczema Measure, PP-NRS = Peak Pruritus Numerical Rating Scale, SCORAD = SCORing Atopic Dermatitis, TEWL = transepidermal water loss, UK = United Kingdom, USA = United States of America.

References

- Wollenberg A, Christen-Zäch S, Taieb A, Paul C, Thyssen JP, de Bruin-Weller M, et al. ETFAD/EADV eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol*. 2020;34:2717–44.
- Saeki H, Ohya Y, Furuta J, Arakawa H, Ichijima S, Katsunuma T, et al. English version of clinical practice guidelines for the management of atopic dermatitis 2021. *J Dermatol*. 2022;49:e315–75.
- Mortz CG, Andersen KE, Dellgren C, Barington T, Bindslev-Jensen C. Atopic dermatitis from adolescence to adulthood in the TOACS cohort: prevalence, persistence and comorbidities. *Allergy*. 2015;70:836–45.
- Lu Z, Xiao S, Chen W, Zhu R, Yang H, Steinhoff M, et al. IL-20 promotes cutaneous inflammation and peripheral itch sensation in atopic dermatitis. *FASEB J*. 2022;36:e22334.
- Roesner LM, Heratizadeh A. Barrier defect in atopic dermatitis—possibilities and limits of basic skin therapy. *Allergol Sel*. 2021;5:287–92.
- van den Bogaard EH, Elias PM, Goleva E, Berdyshev E, Smits JPH, Danby SG, et al. Targeting skin barrier function in atopic dermatitis. *J Allergy Clin Immunol Pract*. 2023;11:1335–46.
- Zhu TH, Zhu TR, Tran KA, Sivamani RK, Shi VY. Epithelial barrier dysfunctions in atopic dermatitis: a skin–gut–lung model linking microbiome alteration and immune dysregulation. *Br J Dermatol*. 2018;179:570–81.
- Fölster-Holst R, Reimer R, Neumann C, Proksch E, Rodríguez E, Weidinger S, et al. Comparison of epidermal barrier integrity in adults with classic atopic dermatitis, atopic prurigo and non-atopic prurigo nodularis. *Biology*. 2021;10:1008.
- Tokudome Y. Influence of oral administration of lactic acid bacteria metabolites on skin barrier function and water content in a murine model of atopic dermatitis. *Nutrients*. 2018;10:1858.
- Berdyshev E, Goleva E, Bronova I, Dyjack N, Rios C, Jung J, et al. Lipid abnormalities in atopic skin are driven by type 2 cytokines. *JCI Insight*. 2018;3:e98006.
- Yang G, Seok JK, Kang HC, Cho YY, Lee HS, Lee JY. Skin barrier abnormalities and immune dysfunction in atopic dermatitis. *Int J Mol Sci*. 2020;21:2867.
- Janssens M, van Smeden J, Gooris GS, Bras W, Portale G, Caspers PJ, et al. Increase in short-chain ceramides correlates with an altered lipid organization and decreased barrier function in atopic eczema patients. *J Lipid Res*. 2012;53:2755–66.
- Alvarenga JM, Bieber T, Torres T. Emerging biologic therapies for the treatment of atopic dermatitis. *Drugs*. 2024;84:1379–94.
- Kawana M, Miyamoto M, Ohno Y, Kihara A. Comparative profiling and comprehensive quantification of stratum corneum ceramides in humans and mice by LC/MS/MS. *J Lipid Res*. 2020;61:884–95.
- Kelleher MM, Cro S, Cornelius V, Lodrup Carlsen KC, Skjerven HO, Rehbinder EM, et al. Skin care interventions in infants for preventing eczema and food allergy. *Cochrane Database Syst Rev*. 2021;2:CD013534.
- Mori T, Ishida K, Mukumoto S, Yamada Y, Imokawa G, Kabashima K, et al. Comparison of skin barrier function and sensory nerve electric current perception threshold between IgE-high extrinsic and IgE-normal intrinsic types of atopic dermatitis. *Br J Dermatol*. 2010;162:83–90.
- Proksch E. pH in nature, humans and skin. *J Dermatol*. 2018;45:1044–52.
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8:336–41.
- Digitizer GG. GetData-Graph-Digitizer 2.26 [accessed 2024 Dec 19]. Available from: <http://Getdata-Graph-Digitizer.Com/>.
- Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
- The Nordic Cochrane Centre. Review Manager (Revman). Version 5.4. Copenhagen, Denmark: The Nordic Cochrane Centre; 2020 [accessed 2024 Dec 19]. Available from: <https://Training.Cochrane.Org/Onlinelearning/Core-Software-Cochrane-Reviews/Revman>.
- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane handbook for systematic reviews of interventions. Version 6.3. Cochrane; 2022 [cited 2022 February]. www.Training.Cochrane.Org/Handbook. Available from: <https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current>.
- Ursoniu S, Sahebkar A, Serban MC, Banach M. Lipid profile and glucose changes after supplementation with astaxanthin: a systematic review and meta-analysis of randomized controlled trials. *Arch Med Sci*. 2015;11:253–66.
- Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–60.
- Borenstein M, Hedges L, Higgins J, Rothstein H. Identifying and quantifying heterogeneity. In: *Introduction to meta-analysis*. Chichester, UK: John Wiley & Sons; 2021. p. 99–117.
- Angelova-Fischer I, Neufang G, Jung K, Fischer TW, Zillikens D. A randomized, investigator-blinded efficacy assessment study of stand-alone emollient use in mild to moderately severe atopic dermatitis flares. *J Eur Acad Dermatol Venereol*. 2014;28:9–15.
- Andrew PV, Pinnock A, Poyner A, Brown K, Chittock J, Kay LJ, et al. Maintenance of an acidic skin surface with a novel zinc lactobionate emollient preparation improves skin barrier function in patients with atopic dermatitis. *Dermatol Ther*. 2024;14:391–408.
- Lodén M, Andersson AC, Lindberg M. Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (Cano-derm®). *Br J Dermatol*. 1999;140:264–7.
- Nasrollahi SA, Ayatollahi A, Yazdanparast T, Samadi A, Hosseini H, Shamsipour M, et al. Comparison of linoleic acid-containing water-in-oil emulsion with urea-containing water-in-oil emulsion in the treatment of atopic dermatitis: a randomized clinical trial. *Clin Cosmet Investig Dermatol*. 2018;11:21–8.
- Danby SG, Andrew PV, Taylor RN, Kay LJ, Chittock J, Pinnock A, et al. Different types of emollient cream exhibit diverse physiological effects on the skin barrier in adults with atopic dermatitis. *Clin Exp Dermatol*. 2022;47:1154–64.
- Kircik LH. Transepidermal water loss (TEWL) and corneometry with hydrogel vehicle in the treatment of atopic dermatitis: a randomized, investigator-blind pilot study. *J Drugs Dermatol*. 2012;11:210–4.
- Danby SG, Chalmers J, Brown K, Williams HC, Cork MJ. A functional mechanistic study of the effect of emollients on the structure and function of the skin barrier. *Br J Dermatol*. 2016;175:1011–9.
- Alexander H, Brown S, Danby S, Flohr C. Research techniques made simple: transepidermal water loss measurement as a research tool. *J Invest Dermatol*. 2018;138:2295–300.e1.
- Simonsen L, Fullerton A. Development of an in vitro skin permeation model simulating atopic dermatitis skin for the evaluation of dermatological products. *Skin Pharmacol Physiol*. 2007;20:230–6.
- Cole C, Krobath K, Schurch NJ, Sandilands A, Sherstnev A, O'Regan GM, et al. Filaggrin-stratified transcriptomic analysis of pediatric skin identifies mechanistic pathways in patients with atopic dermatitis. *J Allergy Clin Immunol*. 2014;134:82–91.
- Akdeniz M, Gabriel S, Lichterfeld-Kottner A, Blume-Peytavi U, Kottner J. Transepidermal water loss in healthy adults: a systematic review and meta-analysis update. *Br J Dermatol*. 2018;179:1049–55.
- Fujii M. The pathogenic and therapeutic implications of ceramide abnormalities in atopic dermatitis. *Cells*. 2021;10:2386.
- Brunner PM, Guttman-Yassky E, Leung DYM. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *J Allergy Clin Immunol*. 2017;139:S65–76.
- Gidado IM, Qassem M, Triantis IF, Kyriacou PA. Review of advances in the measurement of skin hydration based on sensing of optical and electrical tissue properties. *Sensors*. 2022;22:7151.
- Park SB, Im M, Lee Y, Lee JH, Lim J, Park YH, et al. Effect of emollients containing vegetable-derived lactobacillus in the treatment of atopic dermatitis symptoms: split-body clinical trial. *Ann Dermatol*. 2014;26:150–5.
- Illic D, Bollinger JM, Gelb MH, Mauro TM. SPLA2 and the epidermal barrier. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2014;1841:416–21.
- Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. *Acta Derm Venereol*. 2013;93:261–7.
- Lee HJ, Lee SH. Epidermal permeability barrier defects and barrier repair therapy in atopic dermatitis. *Allergy Asthma Immunol Res*. 2014;6:276–87.
- Baker P, Huang C, Radi R, Moll SB, Jules E, Arbiser JL. Skin barrier function: the interplay of physical, chemical, and immunologic properties. *Cells*. 2023;12:2745.
- Zhu JR, Wang J, Wang SS. A single-center, randomized, controlled study on the efficacy of niacinamide-containing body emollients combined with cleansing gel in the treatment of mild atopic dermatitis. *Skin Res Technol*. 2023;29:e13475.
- Kang SY, Um JY, Chung BY, Lee SY, Park JS, Kim JC, et al. Moisturizer in patients with inflammatory skin diseases. *Medicina*. 2022;58:888.
- Lei D, Ye L, Wen S, Zhang J, Zhang L, Man MQ. Preventive and therapeutic benefits of natural ingredients in photo-induced epidermal dysfunction. *Skin Pharmacol Physiol*. 2024;37:1–18.
- Palonciová M, Vávrová K, Sovová Ž, DeVane R, Otyepka M, Berka K. Structural changes in ceramide bilayers rationalize increased permeation through stratum corneum models with shorter acyl tails. *J Phys Chem B*. 2015;119:9811–9.
- van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. *Cochrane Database Syst Rev*. 2017;2:CD012119.
- Shin KO, Kim S, Park BD, Uchida Y, Park K. N-palmitoyl serinol stimulates ceramide production through a CB1-dependent mechanism in in vitro model of skin inflammation. *Int J Mol Sci*. 2021;22:8302.
- Yang B, Lv C, Ye L, Wang Z, Kim Y, Luo W, et al. Stratum corneum hydration inversely correlates with certain serum cytokine levels in the elderly, possibly contributing to inflammaging. *Immun Ageing*. 2023;20:7.
- Barnes TM, Mijaljica D, Townley JP, Spada F, Harrison IP. Vehicles for drug delivery and cosmetic moisturizers: review and comparison. *Pharmaceutics*. 2021;13:2012.

53. Wang X, Lai Q, Zheng B, Ye L, Wen S, Yan Y, et al. Prevalence and severity of dermatological condition-associated skin pain in the Chinese. *J Pain Res.* 2020; 13:1201–7.
54. Song F, Gilbody S. Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1998;316:471.
55. Yaphe J, Edman R, Knishkowsky B, Herman J. The association between funding by commercial interests and study outcome in randomized controlled drug trials. *Fam Pract.* 2001;18:565–8.
56. Simpson E, Böhlring A, Bielfeldt S, Bosc C, Kerrouche N. Improvement of skin barrier function in atopic dermatitis patients with a new moisturizer containing a ceramide precursor. *J Dermatolog Treat.* 2013;24:122–5.
57. Bomstein Y, Rozenblat S. Treatment of atopic dermatitis with KAM-3008, a barrier-based, non-steroidal topical cream. *J Dermatolog Treat.* 2015;26:426–30.
58. Koppes SA, Charles F, Lammers L, Frings-Dresen M, Kezic S, Rustemeyer T. Efficacy of a cream containing ceramides and magnesium in the treatment of mild to moderate atopic dermatitis: a randomized, double-blind, emollient- and hydrocortisone-controlled trial. *Acta Derm Venereol.* 2016;96:948–53.
59. Goh SW, Jamil A, Safian N, Md Nor N, Muhammad N, Saharudin NL. A randomized half-body, double blind, controlled trial on the effects of a pH-modified moisturizer vs. standard moisturizer in mild to moderate atopic dermatitis. *An Bras Dermatol.* 2020;95:320–5.
60. Leshem YA, Wong A, McClanahan D, Simpson EL. The effects of common over-the-counter moisturizers on skin barrier function: a randomized, observer-blind, within-patient, controlled study. *Dermatitis.* 2020;31:309–15.