Effect of Olive and Sunflower Seed Oil on the Adult Skin Barrier: Implications for Neonatal Skin Care

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Abstract: Natural oils are advocated and used throughout the world as part of neonatal skin care, but there is an absence of evidence to support this practice. The goal of the current study was to ascertain the effect of olive oil and sunflower seed oil on the biophysical properties of the skin. Nineteen adult volunteers with and without a history of atopic dermatitis were recruited into two randomized forearm-controlled mechanistic studies. The first cohort applied six drops of olive oil to one forearm twice daily for 5 weeks. The second cohort applied six drops of olive oil to one forearm and six drops of sunflower seed oil to the other twice daily for 4 weeks. The effect of the treatments was evaluated by determining stratum corneum integrity and cohesion, intercorneocyte cohesion, moisturization, skin-surface pH, and erythema. Topical application of olive oil for 4 weeks caused a significant reduction in stratum corneum integrity and induced mild erythema in volunteers with and without a history of atopic dermatitis. Sunflower seed oil preserved stratum corneum integrity, did not cause erythema, and improved hydration in the same volunteers. In contrast to sunflower seed oil, topical treatment with olive oil significantly damages the skin barrier, and therefore has the potential to promote the development of, and exacerbate existing, atopic dermatitis. The use of olive oil for the treatment of dry skin and infant massage should therefore be discouraged. These findings challenge the unfounded belief that all natural oils are beneficial for the skin and highlight the need for further research.

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Various types of oils are used as part of neonatal skin care regimens around the globe (1–6). Oils are advocated therapeutically as part of baby massage (2), recommended for the prevention and treatment of dry skin (7,8), and used in the treatment of cradle cap (9). Oils have been used as part of massage therapy for generations (1–4). Although it is thought that the tactile stimulation of babies is beneficial (1,10), benefits related to application of the oil per se have also been recorded (2,11). Certain natural oils soften the skin and provide moisturization (8), possess antimicrobial activity (12–14), display anti-inflammatory properties (15,16), and reduce skin irritation (17). Randomized controlled trials of the clinical effect of topically applied sunflower seed oil (SSO) and almond oil have reported significant benefits, such as fewer nosocomial infections and quicker recovery of dermatologic conditions (11–13,18). These benefits can be linked, at least in part, to improved skin barrier function (18,19). Only a single study, conducted in mice, has evaluated the effect of a variety of natural oils on the biophysical properties of the skin barrier in vivo (19). SSO was found to promote skin barrier repair, but olive oil, mustard seed oil, and soybean oil significantly inhibited its repair (19). Furthermore, mustard seed oil was found to disrupt the ultrastructural properties of the epidermis and cause cutaneous inflammation and is a known trigger of contact dermatitis (CD; 19,20). A defect of the skin barrier is the primary event in the development of atopic dermatitis (AD; 21), a chronic condition that affects up to 30% of children (22). Negative environmental factors play a prominent role in determining the skin barrier defect (21). The potentially negative effects of some natural oils on the skin barrier therefore present the risk of greater susceptibility to AD and compound the difficulties that 76% of patients experience in managing the condition (23). Given that the majority of cases of AD arise during the first year of life (24), while the skin barrier is undergoing a period of “optimization” before reaching adult status (25,26), the risk to neonatal skin is greatest.

In the United Kingdom, a recent survey of oil use found that 52% of maternity and neonatal units recommend the use of oil for infant skin care (5). Olive oil was most frequently recommended (82%), followed by SSO (21%). Further qualitative work found that midwives and health visitors regularly recommend the use of natural oil for babies' dry skin (7). Their belief in the safety of natural oils and the desire to offer a cheap solution to the problem of dry skin influences their preference. Despite the absence of robust evidence, health professionals believe that oils do “more good than harm” and, because they are a “traditional” product, have not considered the need to base their advice on empirical evidence. The aim of this study was to ascertain the safety and effect of commonly used natural oils on the biophysical properties of the skin in humans. As a precaution, based on the damaging effects of olive oil applied to the skin of mice (19), this initial mechanistic study was performed in adults with and without a history of AD. Volunteers with a history of AD, having the propensity for a defective skin barrier, are likely to be most susceptible to the effects of topically applied oils.

MATERIALS AND METHODS

Subjects

Two cohorts of volunteers (aged ≥ 18 years) were recruited. Volunteers who were pregnant, breastfeeding, or using prescription immunomodulatory medication in the last 6 months were excluded. Volunteers refrained from using topical products on the treatment sites for at least 7 days before and during participation. Informed consent was obtained from each participant. The National Health Services Trent Multi Centre Research Ethics Committee approved this mechanistic study (reference 04/MREC/70).

Cohort 1 consisted of seven volunteers (five female and two male, mean age 46 ± 5.7 years) with a self-reported previous history of AD (no symptoms for 6 months).

Cohort 2 consisted of 12 volunteers (mean age 34 ± 4.0 years), 6 (4 female and 2 male, mean age 37 ± 6.7 years) with no history of skin disease and 6 (5 female and 1 male, mean age 32 ± 5.4 years) with a self-reported previous history of AD (no symptoms for 6 months).

Treatment

A randomized observer-blind forearm-controlled design was employed. Treatments were applied to the volar side of the forearm, 3 cm below the elbow flexure and 3 cm above the wrist. Participants, after a demonstration, applied the oils at home to replicate normal skin massage.

The cohort 1 treatment regimen consisted of six drops (~31 µL/drop) of olive oil to the designated forearm twice daily for 5 weeks. The opposite forearm acted as an untreated control.

The cohort 2 treatment regimen consisted of six drops olive oil to one forearm and six drops of SSO to the other twice daily for 4 weeks.
RESULTS

Effect of Olive Oil on the Skin Barrier

Seven volunteers applied six drops of olive oil (−0.189 g/100 cm² area of skin) to the skin of one forearm twice daily for 5 weeks (0.131 ± 0.0161 g/cm² total over 69 applications). The frequency of application is in line with the traditional practice of performing infant massage one to four times per day for the first several months of their lives (1,2). To minimize the burden on volunteers, the duration of the treatment regimen was kept to 5 weeks, in line with published trials and previous studies on emollients (28,31). The amount applied was determined empirically as the quantity needed to cover the skin without excess runoff. This is less than normally applied during neonatal massage (5–20 mL per massage) according to the published literature (2,11). For comparison, 0.571 g/100 cm² was applied in one randomized controlled trial of topical oils (13). The biophysical properties of the skin were assessed at the end of treatment (Figs. 1 and 2). TEWL measurement is a validated method of determining skin (permeability) barrier function (28). There was no significant difference in TEWL between the treated and untreated sites, suggesting that the treatment did not have a lasting effect on skin barrier function. To assess the underlying condition of the skin barrier, tape stripping was performed in conjunction with TEWL measurements to experimentally damage the SC (validated previously; 28). The resulting rate at which TEWL increases with each successive tape strip depends on the structural integrity and thickness of the SC, subject to the effect of any applied treatments. As can be seen in Fig. 1A, TEWL increased at a significantly greater rate on the site treated with olive oil than on the untreated site. In every case, TEWL reached 90 g/m² per hour on the treated site first. On average, TEWL, after 25 tape strips, was 2.3 (0.31 SEM, n = 7) times higher on the treated site than on the untreated control (p < 0.001). This finding suggests that the skin barrier is structurally weakened (more permeable) or thinner after olive oil application. The fact that this defect is apparent only after experimentally induced damage fits well with the proposed existence of a “skin barrier reserve” (21).

On both sites there was a general decrease in the amount of protein (related to the number of corneocytes) that each tape strip removed with increasing depth, indicating a progressive increase in intercorneocyte cohesion consistent with the process of desquamation (Fig. 1B). Intercorneocyte cohesion can be affected by changes in hydration level and

### TABLE 1. Specifications of Natural Oils Used in This Study

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Carbon number</th>
<th>Olive oil</th>
<th>Sunflower seed oil</th>
<th>Content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmitic acid</td>
<td>C16:0</td>
<td>10.5</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Oleic acid</td>
<td>C18:1</td>
<td>76.3</td>
<td>27.3</td>
<td></td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>C18:2</td>
<td>4.6</td>
<td>60.9</td>
<td></td>
</tr>
<tr>
<td>Linolenic acid</td>
<td>C18:3</td>
<td>0.7</td>
<td>0.1</td>
<td></td>
</tr>
</tbody>
</table>

Volunteers were asked to leave the skin uncovered for at least 30 minutes after each application. Olive oil (Sigma, Gillingham, UK) and SSO (William Hodge­son & Co., Congleton, UK) were allocated in opaque dropper bottles. The choice of supplier was based on the provision of a detailed certificate of composition (Table 1).

### Biophysical Measurements

Measurements were performed in a room maintained at 21 ± 2°C and 38% to 50% relative humidity (27). Volunteers, assessed separately, were asked to sit in a resting position with their forearms exposed for 30 minutes before measurements to acclimatize the test areas. The last application of oils was made 12 to 24 hours before the final session to avoid interference of residues with the measurements.

Skin-surface pH, stratum corneum (SC) hydration, and erythema were measured using skin pH meter (PH905), corneometer (CM825), and mexameter (MX 18), respectively (CK Electronic GmbH, Cologne, Germany). All measurements were based on the average of nine readings. Transepidermal water loss (TEWL) was measured using an AquaFlux AF200 (Biox Systems Ltd., London, UK). Tape stripping was performed in conjunction with TEWL as previously described (28). The amount of protein that each disc removed was immediately determined using infrared densitometry (SquameScan 850A; CuDerm, Dallas, TX, USA) as previously reported (29). Total SC thickness (H) was estimated from the relationship between the cumulative amount of protein removed and TEWL based on Fick's first law using a previously published nonlinear model (29,30).

### Statistical Analysis

Results were analyzed using Graphpad Prism v5.0c (Graphpad Software Inc., La Jolla, CA, USA). The Student t test and analysis of variance were used to evaluate statistical significance, and p < 0.05 was considered significant. Results were shown as means ± standard errors of the mean.
Figure 1. The effect of olive oil on stratum corneum (SC) integrity. Seven volunteers applied olive oil twice daily to one forearm for 5 weeks. The opposite forearm was left untreated as a control. (A) Transepidermal water loss (TEWL) measured in conjunction with tape stripping. (A) Repeated-measures two-way analysis of variance reported a statistically significant effect of tape stripping, the treatment, and the interaction between the two. Asterisks indicate the results of a Bonferroni Posttest (**p < 0.001). (B) Average amount of protein removed by every five discs used to strip the skin. There was a significant difference between the treatments after 25 and 30 tape strips (Bonferroni Posttest, *p < 0.05).

Figure 2. The effect of topical olive oil on stratum corneum (SC) thickness. Total SC thickness calculated based on Fick's first law from the relationship between transepidermal water loss and the thickness of the SC removed by tape stripping. *p < 0.05, determined using a paired t test.

Effect of SSO Compared with Olive Oil on the Skin Barrier

Twelve volunteers, six with a history of AD and six with no history of skin disease, applied six drops of olive oil (0.193 g/100 cm$^2$) to one forearm and six drops of SSO (0.183 g/100 cm$^2$) to the other twice daily for 4 weeks (0.106 ± 0.0100 g/cm$^2$ of olive oil and 0.101 ± 0.0085 g/cm$^2$ of SSO total over 55 applications). The treatment was shortened from 5 to 4 weeks to ascertain whether olive oil exerted the same effects after a shorter duration. The biophysical properties of the skin were assessed before and after treatment (Fig. 3).

Like with the first cohort, treatment with olive oil significantly decreased SC integrity in volunteers with a history of AD (Fig. 3A). A similar reduction was observed in healthy volunteers, although the effect was restricted to deeper SC layers. After 20 tape strips, TEWL was 9.89 g/m$^2$/hour higher after treatment with olive oil on average for all volunteers (p = 0.01). The fact that treatment with olive oil also led to a greater decrease in skin barrier function (significantly greater basal TEWL by 2.5 g/m$^2$/hour, p = 0.04) in volunteers with a history of AD than in volunteers with no history of skin disease suggests that the greater cohesion of granular keratinocytes, which may be brought about by topical products. After (16–24 hours) the last application of oil, there was no significant difference in the amount of protein that the first 20 discs removed from each site, indicating that the oil did not affect the cohesiveness of the SC. The difference in the rate at which TEWL increased during tape stripping is therefore not a result of differences in the amount of SC removed, but after 25 tape strips there was a significant difference in the amount of protein removed, indicating greater cohesion at the site treated with olive oil. This coincides with the point at which the SC is completely removed in some volunteers (30) and, given the greater cohesion of granular keratinocytes, suggests that the SC has been completely removed sooner. In agreement with this, there was a significant difference in the thickness of the SC (Fig. 2). On average, the SC was ~23% thinner on the site treated with olive oil than the control.
with healthy skin suggests that they are more susceptible to its negative effects.

In contrast, treatment with SSO had no significant effect on skin barrier function or SC integrity in either group of volunteers (Fig. 3B). Baseline TEWL was on average 0.787 g/m²/hour higher after treatment with SSO for all volunteers. After 20 tape strips, TEWL was 0.38 g/m²/hour lower on average after treatment. As discussed earlier, greater increases in TEWL during tape stripping may indicate thinner SC. In agreement with this, SC thickness was 0.988 ± 0.6418 µm less after treatment with olive oil but was unchanged after treatment with SSO (data not shown). The effect of the treatments was similar in each cohort.

A greater rate of desquamation could explain the effect of olive oil on SC thickness. A number of factors, including SC pH, regulate desquamation (21). To determine whether altered SC pH plays a role in SC thinning in response to topically applied olive oil, skin surface pH was measured before and after treatment (Table 2). Skin surface pH was affected only in volunteers with no history of skin disease treated with SSO. In this case, pH was high, although it remained within the normal range for healthy skin.

Because topical oils are used to moisturize the skin, SC hydration was assessed before and after treatment (32). SC hydration was slightly higher 16 to 24 hours after the topical application of olive oil and SSO, although it was significantly higher only after SSO treatment (Table 2). The greatest improvement was observed in the group with a history of AD (18% ± 7.1% greater).

To assess the potential irritancy of the oils, skin redness was also measured (33). Skin redness was greater than baseline measurements on the sites treated with olive oil but not SSO, independent of skin type, suggesting that olive oil induced cutaneous irritation and inflammation or acted as a modest vasodilator (Table 2).

**DISCUSSION**

Olive oil applied twice daily for 4 weeks (less than a tablespoonful) caused a significant reduction in SC integrity and thickness, failed to impart a significant effect on SC hydration, and induced mild erythema in volunteers with and without a history of AD. The study population was predominantly female in both cohorts, so the observed effect could be sex associated, with a greater or lesser effect in males, and therefore requires further investigation. The properties of the test sites are similar between males and females, and there are currently no reports of a sex effect with respect to the use of topical oils (34). The observed negative effects of olive oil are not common to all natural oils. SSO, when used in the same way, preserved SC integrity, did not cause erythema, and improved skin hydration by 12% to 18% in the same volunteers when assessed the day after the last application of oil. For reference, neonatal skin is 40% dryer than adult skin when assessed using the same method (35). This finding is in stark contrast to current practice, wherein olive oil is more frequently recommended (5). The contrasting effects of olive oil and SSO on the skin is unsurprising given their different composition of phytochemicals. In agreement with the findings presented here, topically applied olive oil has previously been shown to inhibit skin barrier repair of experimentally damaged skin in mice, whereas SSO promoted repair (19).
It has been suggested that the ratio of oleic acid (OA) to linoleic acid (LA) in natural oils determines their effects on the skin (19, 36). When a panel of 14 natural oils were compared for their ability to prevent experimentally induced irritant contact dermatitis in humans, positive effects (based on clinical scoring of irritation, TEWL, and chromometry) were associated with low OA and high LA content (36). Olive oil contains 55% to 83% OA, which at 5% significantly increases TEWL when applied to the skin (37). A significant increase in baseline TEWL was observed after olive oil application in volunteers with a history of AD in this study. Also significant is the lasting effect of olive oil on SC integrity, similar to the effect of topical products containing harsh surfactants and potent topical corticosteroids (28, 38).

OA is a well-documented skin penetration enhancer (39). It enhances penetration by decreasing the conformational order of SC lipids and by inducing lipid phase separation (39, 40). Although LA is also a reported penetration enhancer (39), the topical application of OA increases TEWL to a greater extent (41).

In addition to direct effects on lipid structure, OA was shown to suppress skin barrier homeostasis through its action on the NMDA cell-surface receptor expressed by epidermal keratinocytes (42). Consistent with the effects of OA, the poorer integrity and thickness of the skin after treatment with olive oil support a mechanism whereby it disrupts the lipid structure of the SC (43) and inhibits homeostasis (21). Mild erythema was also observed at the sites treated using olive oil in this study. OA has also been shown to induce cutaneous irritation, including modulation of cytokine production and infiltration of inflammatory cells (33, 44). Moreover, reports of CD after exposure to olive oil have prompted recommendations to avoid its use (45).

In contrast to OA, LA, the predominate fatty acid in SSO, has been shown to exert positive effects on the skin barrier (19). This is attributed to its potent activation of peroxisome proliferator-activated receptor-alpha (PPAR-α) compared with mild activation by OA (46). PPAR-α, a nuclear receptor expressed by keratinocytes, is involved in regulating keratinocyte proliferation, inflammation, and skin barrier homeostasis in response to a range of lipid metabolites. In rats and mice, PPAR-α activators accelerate skin barrier development and repair (46). A number of clinical studies have recently reported the beneficial effects of LA for the treatment of AD (47, 48). SSO extracts have been shown to improve skin condition, reduce the severity of AD, hydrate the skin, and be steroid-sparing (18, 47). When applied to the skin of
healthy volunteers for 48 hours under occlusion, SSO was found to reduce basal TEWL and blood flow, although the difference was not significant (17). The data presented here demonstrate that topically applied SSO preserves the integrity of intact skin in volunteers with and without a history of AD and moisturizes.

The greatest distinction between the effects of SSO and olive oil on the skin barrier was observed in volunteers with a history of AD. These volunteers are predisposed to a defective skin barrier (21), characterized by an abnormal lipid profile, with fewer omega-6 unsaturated fatty acids (e.g., LA) and more monounsaturated fatty acids (e.g., OA; 49). This shift is associated with poorer skin barrier function and greater severity of disease (50). Topical application of an excess of OA in olive oil may therefore exacerbate this defect. The skin of neonates has features similar to those of AD (21,25) and is therefore likely to be more susceptible to the negative effects of topical oils. In neonates and patients with AD, it is also important to consider the potential allergenicity of protein residues found in natural oils when assessing their safety (51).

The starkly contrasting effects of the oils tested here emphasizes the need for evidence to enable health care professionals to make informed choices on products used for skin care. SSO, of the composition tested, does not damage the skin barrier and moisturizes in adults. The implication is that SSO will have similar effects when applied to infant skin, but documented differences in the lipid composition of the infant barrier raise uncertainty, so further testing is required. In vitro research suggests that the benefits could be greater to the developing skin barrier than the intact adult barrier (46). Moreover, the adoption of topical therapy with SSO in preterm infants in Bangladesh significantly reduced mortality associated with enhanced skin barrier function (18). The notable problem is identifying oil varieties with a defined composition: a challenge faced when sourcing the oils tested, does not damage the skin barrier and moisturizes.

Topical olive oil could therefore, in combination with other environmental factors, exacerbate or promote the development of AD and CD (45). Given that infant skin is more susceptible to challenge than adult skin, it is reasonable to predict that the effect of olive oil would also be deleterious in infants, if not more so. It remains to be determined whether SSO is harmful to the infant skin barrier. To this end, the results of this report highlight the need to heed evidence over tradition. Further research in adults, and now infants, is required to assess the benefit and merits of natural oils for healthy and eczematous skin. Should their be a case for the continued use of natural oils, it is necessary to ensure that only oils with a positive effect are applied to the skin, particularly of infants, for whom the practice of massage is increasing in popularity (2).

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