REVIEW ARTICLE



Natural Oils for Skin-Barrier Repair: Ancient Compounds Now Backed by Modern Science

Alexandra R. Vaughn^{1,2} · Ashley K. Clark¹ · Raja K. Sivamani^{1,3} · Vivian Y. Shi⁴

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Abstract Natural plant oils are commonly used as topical therapy worldwide. They are usually easily accessible and are relatively inexpensive options for skin care. Many natural oils possess specific compounds with antimicrobial, antioxidant, anti-inflammatory, and anti-itch properties, making them attractive alternative and complementary treatments for xerotic and inflammatory dermatoses associated with skin-barrier disruption. Unique characteristics of various oils are important when considering their use for topical skin care. Differing ratios of essential fatty acids are major determinants of the barrier repair benefits of natural oils. Oils with a higher linoleic acid to oleic acid ratio have better barrier repair potential, whereas oils with higher amounts of irritating oleic acid may be detrimental to skinbarrier function. Various extraction methods for oils exist,

⊠ Vivian Y. Shi vshi@email.arizona.edu

- ¹ Department of Dermatology, University of California–Davis, Sacramento, CA, USA
- ² Drexel University College of Medicine, Philadelphia, PA, USA
- ³ Department of Biological Sciences, California State University, Sacramento, CA, USA
- ⁴ Department of Medicine, Dermatology Division, Arizona Cancer Center, University of Arizona, PO BOX 245024, 1515 N. Campbell Ave., Building #222, Levy Bldg., 1906E, Tucson, AZ 85724-5024, USA

including cold pressing to make unrefined oils, heat and chemical distillation to make essential oils, and the addition of various chemicals to simulate a specific scent to make fragranced oils. The method of oil processing and refinement is an important component of selecting oil for skin care, and cold pressing is the preferred method of oil extraction as the heat- and chemical-free process preserves beneficial lipids and limits irritating byproducts. This review summarizes evidence on utility of natural plantbased oils in dermatology, particularly in repairing the natural skin-barrier function, with the focus on natural oils, including *Olea europaea* (olive oil), *Helianthus annus* (sunflower seed oil), *Cocos nucifera* (coconut oil), *Simmondsia chinesis* (jojoba oil), *Avena sativa* (oat oil), and *Argania spinosa* (argan oil).

Key Points

Certain natural plant-based, cold-pressed oils possess antioxidant, antimicrobial, and skin barrier repair properties, making them promising moisturizers for inflammatory skin conditions associated with barrier disruption.

Plant-based oils can have significantly varied effects from one another when applied to the skin; thus, there is a need to better understand their unique characteristics and optimal extraction methods.

Plant-based oils that are higher in linoleic acid, such as sunflower seed oil, may provide beneficial effects to the skin barrier, as opposed to oils higher in oleic acid, such as olive oil, which may be detrimental to the skin barrier.

1 Introduction

1.1 Normal Skin Barrier

As the largest organ, skin functions to protect us from environmental injuries, prevent microbial invasion, regulate temperature, and maintain hydration. Skin's infrastructure provides the necessary components to form a protective barrier. The most superficial layer of the epidermis, stratum corneum (SC), normally retains enough water and acts as a hydro-lipid film to function as a first-line defense against the outside world [1]. Moisture homeostasis is essential to maintaining skin's protective function and flexibility. The precise organization of the SC relies on the intricate arrangement of corneocytes, natural moisturizing factors (NMF), and an adequate level and ratio of intercellular lipids, forming a 'brick-and-mortar'-like barrier [2]. Lipid precursors include phospholipids, cholesterol, and glucosylceramide. The primary lipids forming the SC matrix are approximately 20% free fatty acids (FFAs), 20% cholesterol (CHOL), and 60% ceramides (CERs). These lipids are interspersed in organized layers called the lamellar phase of the SC [3]. In addition, skin-barrier efficacy may be determined by variations in lateral lipid packing in the SC [4]. An in vivo study using Raman Microscopy demonstrated that maximum lateral packing (and greatest barrier function) of SC lipids occurs at 20-40% of the depth of the SC, or about 4-8 µm from the surface. On the other hand, the more superficial lipids and the deeper lipids appeared more disordered, which researchers hypothesized contributed to weakened skin-barrier function [5]. Linoleic acid (LA) is an essential fatty acid (EFA) and an important building block for the intercellular lipid complex. A deficiency of LA leads to altered barrier, and patients with atopic dermatitis (AD) have been shown to have decreased LA metabolites in their SC. Additionally, intracellular keratin proteins and surface filaggrin (FLG) proteins help to maintain hydration of the SC [6]. The concentration and proportions of lipids, including CHOL, FFAs, and CERs, are essential to forming an effective skin barrier that prevents transepidermal water loss (TEWL) [7, 8]. Several NMFs are present within the corneocytes, including lactic acid, amino acids, urea, glycosaminoglycans, and break-down products from FLG protein degradation; they function to maintain SC moisture, pH balance, and flexibility. When dry weather or SC dehydration causes the normal corneocytes' water content to drop, barrier repair enzymes are activated to degrade FLG proteins to be incorporated into the lipid envelope to replenish NMFs in rebuilding the skin barrier. FLG can also undergo processing in the upper SC to release free amino acids to be incorporated into the NMF to restore skin moisture [9].

1.2 Skin-Barrier Dysfunction

A defective skin barrier enables entry of irritants, allergens, and microbes that, together with an exaggerated immune response, result in skin inflammation (Fig. 1). AD is the prototypic inflammatory skin condition with a defective skin-barrier function, which is characterized by increased TEWL, decreased SC hydration, increased pH, and decreased sebum levels. Several other chronic inflammatory skin conditions associated with skin-barrier deficiencies include psoriasis, ichthyosis, asteatotic eczema, and contact dermatitis [10, 11]. Additionally, there is an age-related decline in skin-barrier function and resultant loss of water accumulation in the SC, ultimately leading to loss of hydration [2]. Chronologically aged skin has globally decreased levels of SC lipids, NMFs, and water content [12].

Both exogenous and endogenous irritants and allergens can cause and exacerbate skin-barrier dysfunction by damaging barrier-structural proteins, eliminating NMF, and altering important lipid-based structures [7]. Mounting an overly exaggerated immune response to environmental irritants, as well as genetic or acquired mutations in barrierrepairing genes can further disrupt barrier structure and function [13]. For instance, FLG gene mutation leads to FLG deficiency and impaired skin barrier, and is a strong risk for development of AD [14]. Similar pathogenic mechanisms occur in multiple inflammatory skin diseases, including both AD and psoriasis. Dysfunction of skinbarrier function is implicated as one component of psoriasis pathogenesis; however, interactions between immune cells and epidermal keratinocytes is more prominent in psoriasis than AD [15]. The majority of patients with AD do not have FLG mutations (FLG mutations are only reported in 25-50% of patients with AD), which underscores the importance of other genetics and environmental factors in the pathogenesis of AD [16]. Skin-barrier dysfunction also leads to an altered skin microbiome and allows pathological organisms to flourish and predominate, further promoting skin-barrier breakdown and inflammation [17]. A defective skin barrier is associated with increased SC pH, which also promotes barrier breakdown and inflammation [18]. Additionally, increased SC pH prevents proper function of barrier repairing enzymes, which require mildly acidic pH for optimal function [19]. Defective tight junction proteins beneath the SC may also contribute to the pathogenesis of AD. Deficiency in tight junction adhesive proteins called claudin-1 (CLDN1) jeopardizes skin-barrier integrity, leading to increased TEWL and heightened T helper 2 (T_h 2) polarity [20], all which have been implicated in eczematous dermatoses. Additionally, deficient delivery of long-chain CERs in sweat may also contribute to eczematous conditions [21].

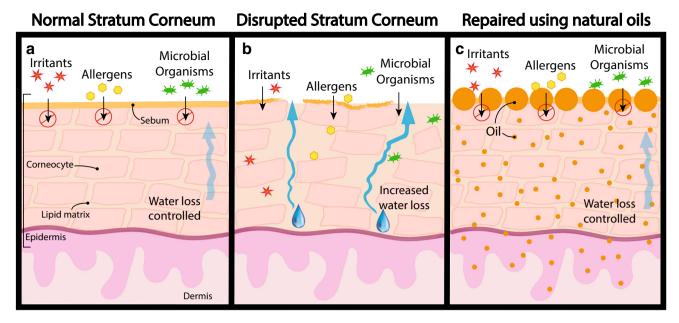


Fig. 1 Skin-barrier repair using natural oils. **a** Healthy skin barrier protects against moisture evaporation, irritants, allergens, and microbial invasion. The stratum corneum (SC) is an important part of the skin barrier and is composed of organized corneocytes, epidermal tight junctions, natural moisturizing factors, and intracellular lipids that are essential to maintaining moisture and optimal SC. **b** SC disruption is characterized by increased trans-epidermal water loss,

1.3 Skin-Barrier Repair

There is an unremitting search by both providers and patients for the 'ideal' moisturizer to repair the skin barrier. Patient preference often determines compliance and the effectiveness of a moisturizer [22]. Moisturizers repair the skin barrier through two major mechanisms: (i) providing hydration via hydrophilic constituents such as glycerol, and (ii) preventing TEWL via hydrophobic constituents such as petrolatum to occlude the skin. There is also evidence that hydrophobic constituents such as petrolatum may diffuse into the intercellular space in the SC to enhance the structural integrity of the barrier [23]. Other moisturizing ingredients in topical repair preparations include CERs, dimethicone, hyaluronic acid, Butyrospermum parkii (shea butter), and natural oils such as Simmondsia chinesis (jojoba oil) and Helianthus annus (sunflower oil). Together, the components of moisturizers work by increasing SC water content and enhancing corneocyte adhesion, keeping the SC smooth and flexible [8]. The SC acts as a permeability barrier by limiting entry of potential irritants from the outside world and by preventing the escape of water from the body. In turn, important components within the SC, including NMFs, keratin, and FLG, help to form, degrade, and regenerate the permeability barrier in order to maintain sufficient hydration for effective skin-barrier function. Oils and oil-based moisturizers improve SC

decreased SC hydration, and increased pH. A disrupted skin barrier is involved in the pathogenesis of various skin diseases including atopic dermatitis and contact dermatitis. **c** Natural oils may help repair the skin barrier by replenishing intracellular lipids, creating an occlusive seal, improving SC hydration, decreasing inflammation, and reducing microbes

hydration by occluding the skin, thereby limiting the escape of water so that more water is trapped within the SC [24]. van Logtestijn et al. suggest topical oil application not only improves hydration through occlusion, but also causes a depth-dependent increase in hydration throughout the entire SC, which is maximal at the middle top layer [25]. This coincides with findings by Choe et al., which demonstrated that lateral packing of lipids and intercellular lipid conformation are maximized at 20–40% of the SC depth, and correlates with highest skin-barrier function [5].

A pillar of treatment for inflammatory dermatoses involves restoring skin-barrier function in order to maintain moisture, which in turn prevents entry of irritants, allergens, and microbes, and controls pruritus. Over-the-counter emollients may contain allergenic and irritating chemicals, such as preservatives and fragrances, which both consumers and providers are unaware of due to the proprietary nature of the ingredients. On the other hand, prescription skin-barrier repair emollients tend to be expensive and therefore not easily accessible to many patients. As a result, patients and caregivers often seek alternative treatment options [10]. The use of natural, preservative-free alternatives is an attractive option for barrier repair. For thousands of years, cultures all over the world have used natural plant-based oils to maintain vitality and wellness in various ways, including skin health and beauty [26]. There is a large variety of natural oils with varying lipid compositions. Generally, natural oils are relatively inexpensive and widely available [27, 28]. However, despite their regular use by many in skin care, there is a paucity of studies examining their role in restoring skin-barrier function. Processing steps used to produce commercially available oils are important determinants of the skin benefits of oils, since certain processing methods can produce irritating byproducts that may further disrupt the skin barrier. In this review, we summarize current evidence on the utility of natural plant-based oils in dermatology, particularly in repairing the natural skin-barrier function, with the focus on widely used natural oils, including Olea europaea (olive oil; OO), H. annus (sunflower seed oil; SFO), Cocos nucifera (coconut oil; CO), S. chinesis (jojoba oil; JO), Avena sativa (oat oil) and Argania spinosa (argan oil; AO).

2 Natural Oil Lipid Composition

Oils are compounds that consist mainly of glycerides, formed from a condensation reaction between fatty acids and glycerol. As opposed to animal fats, with the exception of fish oils, most plant-derived oils are liquid at room temperature. Most plant-based oils are low in saturated fats and high in polyunsaturated and monounsaturated fats. One exception is coconut oil, which is a semi-solid at room temperature and contains a high amount of saturated fat [1].

There are dozens of different types of oils, each with unique characteristics. Plant-based oils consist of varying proportions of monounsaturated (MUFAs), polyunsaturated (PUFAs) fatty acids, and saturated fatty acids (SFAs). Additionally, different oils have distinct compositions of fatty acids of varying chain lengths and grades of saturation. Fatty acid chain lengths are denoted by the length of their carbon backbones. For example, a short-chain fatty acid has six or fewer carbons in its backbone (C6:0), medium-chain fatty acids have ≤ 12 carbons (C12:0), and long-chain fatty acids have 12-22 carbons. Different oils also contain varying levels of omega-3 and omega-6 PUFAs. A summary of various natural oils and their chemical compositions can be found in Table 1. Additional structural differences between oils include unique side chains and degree of saturation. Certain natural oils are unstable and can undergo degradation and oxidation, creating irritating chemicals, and can lead to spoilage or growth of microorganisms. Thus, the different characteristics of oils highlight the importance of thoughtful selection for skin moisturization.

3 Natural Oil Extraction and Refinement—A Process That Defines 'Virginity'

Natural oils are categorized based on how they are processed prior to becoming commercially available. Classifications include fixed oils and essential oils, and it is important to distinguish one from another since they are significantly different in terms of their chemistry, physical properties, and mechanisms of action. Fixed oils are not volatile at room temperature, while essential oils are composed of aromatic compounds that volatilize at room temperature. Fixed oils can be further characterized based on whether they are nonvirgin, virgin, or extra virgin. Extra virgin oils are entirely unrefined and produced through cold pressing. Virgin oils are also cold pressed, yet they are slightly more acidic than extra virgin oil. For example, OO acidity is determined by numerous factors such as the variety of the olives used (some olives are naturally more acidic) and duration of time the olives sit before they are used to produce olive oil [29]. Nevertheless, it has not been established whether the acidity level between extra virgin oils and virgin oils influences their utility for skin care. Nonvirgin oils are refined by applying heat and chemicals, which can compromise the fatty acids and the nutrients within the oil. Commercially available refined oils are often mixed with other oils of unknown quantities and purity to enhance their extraction, which can make their overall composition uncertain. The original constituents within natural oils can be removed or altered after refinement. Oil extraction methods are important to consider when selecting oils as moisturizers, since unrefined oils retain the most nutrients and unaltered fatty acids, and are likely less irritating to the skin.

3.1 Cold-Pressed Oils

Cold-pressed oils are produced by screw-pressing the entire kernel and seed from the plant at room temperature, without the addition of chemicals (Fig. 2). Cold-pressed oils may contain naturally occurring residues, such as wax, which can act as a hydrophobic component to occlude the SC, decrease TEWL, and promote barrier repair. For example, extra virgin olive oil (EVOO) is entirely *unrefined* and produced through cold pressing. EVOO contains the least amount of acid, approximately 1% or less, which is determined by the level of free acids in the oil, one of which is oleic acid [29]. Higher acidity correlates to higher free oleic acid content, which can be harmful to the skin barrier by disrupting SC pH (normally between 5 and 6) and altering barrier-forming enzymatic activities within the SC.

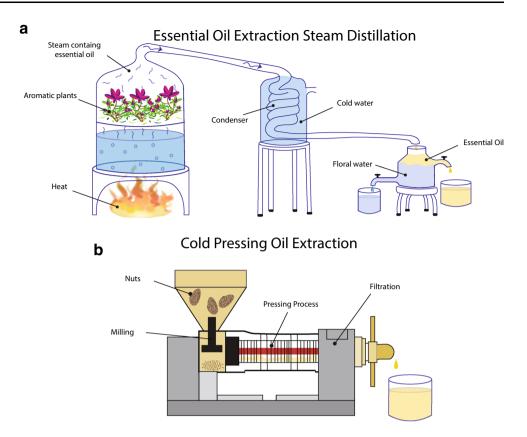
Table 1 Na	Natural oils, fatty acid composition, and evidence f	osition, and evidence for skin-barrier repair	ir			
Oil	Latin name	Origin	% Oleic acid composition	% Linoleic acid composition	% Other fatty acids	Evidence for skin-barrier repair
Almond	Oleum amygdalae	Mediterranean region of the Middle East	64–82	8–28	80	
Apricot kernel	Prunus armeniaca, Armeniaca vulgaris	Armenia, Persia, South Africa	62–76	19–33	4-7.5	
Argan	Argania spinosa	Morocco	43-49	29–36	4-15	AO improved skin elasticity in forearms of 60 postmenopausal women who were also consuming either OO or AO. No control group [83] AO significantly reduced sebum production in 20 volunteers with oily skin [84]
A vocado Castor	Persea americana Ricinus communis	Mexico South Asia	72.8	8.6	10–19	,
Coconut	Cocos nucifera	Multiple	5-10	1–2.5	85-90	CO contains monolaurin, which has been shown to be antimicrobial [45] Virgin CO significantly reduced SCORAD index
						and TEWL in 117 children with AD after 8 weeks compared with group receiving mineral oil [48] CO just as effective as mineral oil in improving skin hydration and increasing skin lipids in 34 adults with xerosis. There was no significant change in TEWL or SC pH [34]
						After 4 weeks of treatment with either CO or OO, only 5% of subjects receiving CO remained positive for <i>Staphylococcus aureus</i> (77% positive at baseline), while 50% of those receiving OO remained positive (5% positive at baseline) [34]
Grape seed [34]	Vitis vinifera	Mediterranean, central Europe, Morocco, Portugal, and Iran	12–22	65–85	2–10	Compared with 14 other natural oils, GSO contained the highest percentage of LA and provided significant protection against sodium lauryl sulfate-induced irritant contact dermatitis [5]
Hempseed	Cannabis sativa	Multiple	9.85	51.96	40	
Jojoba	Simmondsia chinensis	USA, Mexico	11.2	S	~ 85	JO is actually a wax with unique fatty alcohol esters that make it especially resistant to degradation [85] Due to its high wax composition (50% wax), JO is reported to be the closest match to natural human sebum (26% wax) [54] JO may be equal to almond oil and mineral oil in its occlusive abilities, but petrolatum may be superior in its occlusive and penetrative abilities [55, 56]
KuiKui Nut	Aleurites moluccans	Hawaii	17–34	27–52	1.5-34	

Table 1 continued	ntinued					
Oil	Latin name	Origin	% Oleic acid composition	% Linoleic acid composition	% Other fatty acids	Evidence for skin-barrier repair
Mustard seed	Brassica nigra or Brassica hirta	India, Bangladesh, Pakistan	12	15	73	MO significantly delayed skin-barrier repair compared with SFO, soybean oil, and OO [24] MO increases blood vessel permeability and triggers acute inflammation within the skin [1]
Oat [62]	Avena sativa	Worldwide	28.4-40.3	36.6–45.8	~ 23	Oat oil has anti-inflammatory and anti-itch properties, possibly due to phytochemicals called avenanthramides [75, 76] Oat oil may upregulate ceramide synthesis by acting on PPARs [77]
						In a study using an emollient containing A. sativa, there was significant improvement in SCORAD in 108 children with AD after 3 months (no control group) [78]
						Oat-oil-based lotion significantly improved dryness, scaling, roughness, and itch in 29 subjects with dry skin after 2 weeks (no control group) [79]
						Oat-oil-based lotion was as effective as ceramide- based cream at improving TEWL and moisturization in 35 subjects with dry skin (no control group) [79]
Olive	Olea europaea	Spain	55.28	17.84	~ 24	After 4 weeks of treatment with either OO or SFO, the OO significantly increased TEWL, decreased SC thickness, and induced mild erythema [79]
						Neonates randomized to receive either Bepanthen [®] (water-in-oil emollient), an OO cream (30% OO/ 70% lanolin), or no emollient for 4 weeks. OO cream more effective than Bepanthen [®] at preventing dermatitis at Weeks 2, 3, and 4 [42]
Palm kernel	Elaeis guineensis	Africa, Brazil	36.6	9.1	\sim 54	Palm oil has high LA content and also demonstrative protective effects against sodium lauryl sulfate- induced irritant contact dermatitis [85]
Safflower oil [85]	Carthamus tinctorius	Asia and Africa	13–20	2–9	78	SAF use in massage of neonates caused significant rise in triglycerides and LA levels [50]
Shea butter [51]	Butyrospermum parkii	Netherlands	46.4	6.6	45-47	

Table 1 continued	tinued					
Oil	Latin name	Origin	% Oleic acid composition	% Linoleic acid composition	% Other fatty acids	Evidence for skin-barrier repair
Sunflower [38]	Helianthus annus	Southwestern US and Northern Mexico	24.3	61.5	Ś	 LA is the predominate fatty acid in SFO [38] SFO significantly increased skin hydration by 12–18% after 4 weeks of treatment in 19 adults with and without AD [43] SOD may reduce inflammation by acting on PPAR- α [66] 2% SOD cream is as effective as topical steroid in improving SCORAD and subjective quality of life in children with AD [68] Use of 2% SOD cream provides steroid-sparing effects in 86 children with AD [68] In a mouse study, SFO was not as effective as Aquaphor[®] at reducing TEWL, but was significantly more effective than MO, OO, and soybean oil [1] After 10 days of SFO treatment in preterm infants, TEWL significantly increased and skin hydration decreased [69]
						atter 4 weeks in neonates compared with no on treatment [70]
-						

AD atopic dermatitis, AO argan oil, CO coconut oil, GSO grape seed oil, JO jojoba oil, LA linoleic acid, MO mustard oil, OO olive oil, PPAR-α peroxisome proliferator-activated receptor-alpha, SAF safflower oil, SC stratum corneum, SCORAD SCORing Atopic Dermatitis, SFO sunflower oil, SOD sunflower oil distillate, TEWL trans-epidermal water loss

Fig. 2 Oil extraction methods. **a** Steam distillation is one method used to produce essential oils. Through the use of heat, volatile compounds are removed and steam is produced containing the oil, which is then condensed and produced as essential oil. Chemicals may be added to aid production of essential oils in a process called chemical extraction. b Cold pressing is the method used to produce unrefined, natural or 'virgin' oils. The entire seed or kernel is slowly pressed under high pressure without adding heat or chemicals, producing entirely unrefined oil that retains its waxy residues and beneficial fatty acids



3.2 Essential Oils

Essential oils are produced by adding heat, and represent the volatile fraction of oils within the plant (Fig. 2) [30]. Unlike fixed oils that are composed of fatty acids and glycerides, essential oils are composed of more volatile compounds such as terpenes and terpenoids.

3.3 Fragranced Oils

Fragranced oils are synthetic fragrance compounds that have been added to a fixed oil to give it a scent. Fragranced oils are made by adding a combination of a number of scent-based ingredients in order to impart a scent to the fixed oil. Much like how fragrances may be irritating in emollients and moisturizers, fragrances that have been added to oils may be irritating as well.

4 Natural Oils for Skin-Barrier Repair

Natural plant oils are used commonly as topical skin care therapy worldwide, as they are relatively inexpensive and readily available options [31]. Some oils possess specific compounds with antimicrobial and antioxidant properties. Coconut oil contains an antimicrobial compound called monolaurin, and *Vitis vinifera* (grape seed oil, GSO) contains potent antioxidants called procyanidin B1, B2, and C1. Monolaurin, or lauric acid, is believed to exert antimicrobial activity by disrupting membranes of microbial organisms [32, 33]. Proanthocyanidins are a class of polyphenols found in many different plants, and are believed to possess not only potent antioxidant power, but anticarcinogenic and antibacterial also properties [33, 34, 35]. Unique ratios of different EFAs are major determinants of a natural oil's barrier repair benefit. For instance, oils with a higher LA to oleic acid (OA) ratio are better at skin-barrier repair, whereas oils with higher levels of irritating OA may be detrimental to skin-barrier function [36]. The LA content is an integral component in the structural maintenance of the lamellar phase SC lipid matrix [1], and plays a direct role in improving skin-barrier permeability in clinical and in vitro studies [36, 37]. Conversely, OA appears to disrupt lamellar lipid arrangement and increase skin permeability [38, 39]. Although no standard value of an LA to OA ratio has been set as a boundary between positive and negative barrier actions, some commonly used oils have either a predominant LA or OA content. For instance, LA content in GSO and SFO can reach over 60% of the fatty acid profile, while the OA content of OO and AO reaches over 60% and these oils have a much smaller proportion of LA. Another consideration regarding natural oils is their ability to penetrate the SC. For instance, as characterized by Choe et al., lateral packing of SC lipids is variable depending on the depth level of the SC, which may affect the ability of oils to penetrate [5].

4.1 Olive Oil

OO originates from the fruit of O. europaea trees that are indigenous to the Mediterranean basin. It has been used for skin care for centuries across the world, including ancient Egypt and Greece, and has recently gain popularity in Europe, Latin America, and Asia [40-42]. A study in the UK estimated that 52% of newborn nursery units recommend OO for newborn skin care [28]. There is an appreciable amount of evidence examining the effects of topical OO on skin-barrier biophysical properties. A study by Danby et al. compared the effect of OO and SFO (not specified as virgin by the authors) on barrier function in two cohorts of adults with and without a history of AD [43]. Cohort 1, consisting of six adults with a history of AD, applied OO to one forearm twice daily for 5 weeks while the other forearm acted as the control. In cohort 1, the TEWL was 2.3 times higher on the OO-treated forearms than the controls (p < 0.001), and the OO-treated forearms had SCs that were approximately 23% thinner than the control forearms. Cohort 2 consisted of six adults with a history of AD and six adults without any history of skin disease, and applied OO to one arm and SFO to the other arm twice daily for 4 weeks. In cohort 2, OO sites had caused mild skin erythema and a significant increase in TEWL (9.89 g/m²/h higher than SF, p = 0.01) compared with the SFO-treated skin in patients with and without AD. In contrast, SFO significantly increased skin hydration by 12-18% and did not induce erythema. There was no change in TEWL or SC thickness in SFO-treated skin compared with baseline. These findings are consistent with mouse studies, which have also shown that OO impairs skin-barrier function [1].

The skin barrier does not become fully functional until a few weeks after birth, therefore skin care of premature neonates is essential to aid their immature skin barrier. However, guidelines for appropriate skin care of immature neonates are not clearly defined. An Austrian group compared the efficacy between a commonly used water-based lanolin cream (Bepanthen[®]) and an oil-based lanolin cream by randomizing neonates into three group to receive either Bepanthen[®] (proprietary water-based cream containing lanolin, petrolatum, and dexpanthenol), an OO cream (30% OO/70% lanolin), or no emollient [42]. Infants from the two treatment groups had Bepanthen[®] or OO cream applied to their entire body within 24 h of birth and then twice daily for 4 weeks. Skin dryness and irritation were assessed with a 4-point scale. At 4 weeks, the Bepanthen[®] group and OO cream group both had significantly lower degrees of peeling and scaling dermatitis compared with the group receiving no emollient (p < 0.001). In fact, the OO cream was more effective than the Bepanthen[®] cream in preventing dermatitis at weeks 2, 3, and 4. The authors concluded OO might be beneficial for the skin of premature infants. However, these results could be confounded by the effect of the lanolin cream rather than the OO, since the OO cream was comprised of 70% lanolin. Additionally, other ingredients in the proprietary Bepanthen[®] cream and OO cream could have affected these findings.

Although some evidence is conflicting, overall current evidence concludes that topical OO, superimposed on other environmental factors, could impair skin-barrier function and worsen symptoms of AD. In currently published studies, authors did not specify how the OO was processed or whether it was virgin, extra virgin, or non-virgin. Therefore, it is unclear what other chemicals were contained in the OOs that have been studied.

4.2 Coconut Oil

CO originates from the C. nucifera tree from the Indian-Indonesian region. It has gained popularity across the world for cooking and skin care. CO has antimicrobial activity and skin-barrier repairing properties in various skin conditions including xerosis, AD, and acne [44]. It contains monolaurin, a monoglyceride formed from lauric acid, a short-chain fatty acid with antibacterial activity against Propionibacterium acnes, Staphylococcus aureus (SA), and S. epidermidis [45]. Monolaurin has robust antibacterial and antiviral activity and activity against yeast biofilms in cell studies [46, 47]. In a double-blinded, randomized controlled trial by Evangelista et al., 117 children with moderate to severe AD were given either virgin CO or mineral oil to apply over their entire body twice daily [48]. Both the mineral oil and CO groups had reduction in SCORAD (SCORing Atopic Dermatitis) index (68.23 versus 38.13%, respectively) at 8 weeks compared with baseline, but the reduction in the CO group was significantly higher than the mineral oil group at all time points (p < 0.001). Likewise, both groups had decreases in TEWL (70.07% in the CO group and 35.36% in the mineral oil group), but the CO group had significantly lower TEWL throughout the study (p < 0.001). The reduction in TEWL by the oils is likely due to their ability to occlude the skin and prevent water escaping from the SC. Capacitance measurements were used to evaluate emollient effects of the moisturizers, resulting in an increasing trend in both groups and only a statistically significant (p = 0.0309) difference after 8 weeks, with the CO group (mean increase to 42.3 from 32.0) having higher capacitance than the mineral oil group (mean increase to 37.49 from 31.31). In a similar study on 34 women aged 17-65

years old with mild to moderate xerosis, Agero and Verallo-Rowell found that extra virgin CO and mineral oil (twice weekly application for 2 weeks) similarly improved hydration and increased skin surface lipids, without significantly altering TEWL and pH [49]. Based on this study, CO is just as effective a moisturizer as mineral oil and can be a safe, antimicrobial alternative in patients with AD and xerosis.

In a separate double-blind controlled trial, Verallo-Rowell et al. compared the moisturizing and antibacterial properties of virgin CO with virgin OO in adult patients with AD [34]. Subjects in each group were assessed for SA culture before and after use. Only 5% of subjects receiving CO remained positive for SA, while 50% in the OO group remained positive. Both oils significantly decreased the objective-SCORAD severity index (O-SSI) after 4 weeks, but the decrease in the CO group was greater. However, this study had skewed preliminary data, with over 75% of subjects randomized to CO testing positive for SA at baseline and thus suboptimal study design limits the interpretation of the final results.

Nangia et al. studied the skin-barrier function after twice daily application of CO (not specified by researchers as virgin) for 7 days in combination with massage in very low birth weight neonates. Compared with the neonates who received no oil massage, those in the CO group had a significant decrease (14.06% decrease versus 7.99% decrease in the control group) in TEWL (p < 0.01) at 72 h [50]. A separate study of neonates in India by Solanki et al. randomized neonates to receive topical safflower oil (SAF) or CO four times per day for 5 days or no oil [51]. The authors took a unique analytic approach by measuring serum triglycerides (TGs) and fatty acid profiles after oil massage. Interestingly, blood TGs were significantly elevated in all groups at Day 5 (oil and no oil), but the quantum increase (proportionate change from baseline calculated as proportionate change = post-oil/pre-oil) was significantly higher in the oil groups compared with control (p < 0.05). The increase in blood TGs in the no-oil group may be due to dietary factors such as expanding diet as the infant grows or as part of the normal developmental process. The SAF group had a significant increase in blood linoleic acid, while the CO group had a significant rise in blood saturated fats. These findings reflect the importance of careful selections of oils for neonatal massage, since they demonstrate that oils may be absorbed percutaneously and that the specific type of oil can alter the neonate's blood lipids [51].

4.3 Safflower Seed Oil

SAF comes from the seeds of the *Carthamus tinctorius* plant, and is used commonly as a cooking oil, to produce

margarine, and in cosmetics. SAF is colorless, flavorless, and rich in linoleic acid (approximately 78% LA) [52]. As previously described in the study by Solanki et al., neonates who received massages four times daily for 5 days with SAF had a statistically significant rise in blood triglycerides and blood levels of LA and arachidonic acid (AA) [51]. The notion that topical application of oils can penetrate through the skin to affect blood lipid levels is an important consideration when using oils for neonatal massage. The high LA content in SAF supports the idea that its use on the skin would be beneficial to the skin barrier, however clinical studies using SAF are currently lacking.

4.4 Jojoba Oil

JO, also known as jojoba liquid wax, is extracted from the seeds of the S. chinesis plant. It is traditionally used by Mexicans and Native Americans for hair care and eczema, among other skin care purposes [53]. JO is actually classified as a wax with unique fatty alcohol esters, making it especially resistant to degradation, and it also possesses a high oxidative stability [54]. Unlike any other plant-based oil, JO comprises up to 50% wax esters, making it a close match to natural human sebum, which is reported to consist of approximately 26% wax esters [55, 56]. These unique properties may make JO a good repair option for skin conditions with defective and altered sebaceous barriers, such as AD, psoriasis, seborrheic dermatitis, and rosacea [57]. Reports have demonstrated that JO can improve acne [58], psoriasis [59], and wounds [60].

Stamates et al. assessed skin hydration status in nine adults and seven infants with normal skin after treatment with petrolatum, paraffin (mineral oil), JO, and AO [24]. The researchers used Raman microspectroscopy, which measures SC swelling and penetration of the topical agent into the SC [24]. The degree of SC swelling was used to determine the occlusive properties of the oils. Water and lipid concentrations were measured with Raman microspectroscopy and an algorithm was used to calculate SC penetration of the oils based on those measurements. Measurements were taken before, and 30 and 90 min after nine healthy adult volunteers applied the oils to designated areas on their forearms. There was no significant different in skin penetration or SC swelling (10-20%) between the three oils, but petrolatum showed significantly higher SC swelling (40-60%) and therefore the greatest occlusive ability. JO, almond oil and mineral oil appear to be comparable in their occlusive abilities, but petrolatum appears to have superior occlusive and penetration ability based on the Raman measurements.

4.5 Mustard Oil

Mustard oil (MO) is extracted from Brassica nigra and B. hurta seeds and is used widely in cooking and skin moisturization in South Asia due to its affordability. In 2016, the FDA prohibited cold-pressed MO from being imported into the US due to its high content of erucic acid, which can cause cardiac toxicities when ingested by animals [61]. As discussed previously in a study by Darmstedt et al., MO significantly delayed skin-barrier repair in neonates when compared with SFO, soybean oil, and OO [1]. Additionally, MO is known to increase blood vessel permeability and trigger acute inflammation within the skin [62]. In a separate study in Bangladesh, over 400 families were surveyed to determine the prevalence of oil massage of newborns and which oils are most commonly used [63]. According to the results, 88% of study participants used MO on a regular basis. Due to its immense everyday use in many countries, further evaluations are needed to evaluate the safety and efficacy of MO.

4.6 Sunflower Oil

SFO is derived from the seeds of H. annus plants in Southwest United States and Northern Mexico, and is traditionally used in cooking. SFO is a popular treatment choice for AD and neonatal skin care. Studies have examined the effect of SFO on the biophysical properties of the SC. As mentioned previously in Sect. 4.1, in the study by Danby et al., SFO had more desirable effects on the skin barrier compared with OO [43]. LA is the predominate fatty acid in SFO and skin-barrier lipids, and can improve skin-barrier function by activating peroxisome proliferator-activated receptor-alpha (PPAR- α), which regulates keratinocyte proliferation and accelerates skinbarrier repair, as demonstrated by in vitro studies and animal models [64, 65]. LA agonism at PPAR- α receptors stimulates differentiation of keratinocytes, enhances skinbarrier function, and improves skin lipid metabolism. Sunflower oil distillate (SOD) produced through distillation of SFO is becoming increasingly incorporated into skincare products due to its ability to reduce inflammation and activate PPAR- α in vitro [66]. De Belilovsky et al. compared a cream containing 2% SOD versus topical steroid (hydrocortisone butyro-propionate 1 mg/g) in 40 children with AD. After 3 weeks of twice-daily applications, both groups had significant improvement in SCORAD grading of their AD and subjective quality of life scores with no difference between the groups [67]. Furthermore, in a separate study by Msika et al., 86 children with AD were randomized to receive either a topical steroid (0.05%) desonide) or 2% SOD cream. Application of the topical steroid plus the SOD cream every other day was just as effective as twice daily application of topical steroid at improving lichenification, excoriation, and quality of life, thereby demonstrating an encouraging steroid-sparing result [68]. This study further adds to the theory that linoleic acid may be an important essential fatty acid for restoration of skin-barrier function.

In a mouse study by Darmstadt et al., the epidermal skin barrier was assessed after applying MO, SFO, OO, soybean oil, and Aquaphor[®] (a petrolatum-based emollient) [1]. Whether the vegetable oils were virgin versus nonvirgin was not specified. Aquaphor[®] led to the greatest significant reduction in TEWL after 5 h, followed closely by SFO. On the other hand, MO significantly increased TEWL and olive oil did as well to a lesser extent. Kanti et al. studied the effects of SFO oil on skin-barrier properties of preterm infants [69]. After 10 days of SFO application, TEWL significantly increased while skin hydration decreased until the SFO was stopped. However, conflicting data exists on the beneficial effects of SFO on skin-barrier function, and Kanti et al. postulates that contrasting results have come from adult or in vitro studies or did not use appropriately objective measures. For instance, in a study comparing SFO, OO, and no oil in neonatal skin care, both oil groups had significantly improved skin hydration compared with the no-oil group after 4 weeks; however, the no-oil group had significant improvement in lamellar structure compared with the other groups [70]. It is possible that the use of oils in preterm infants needs to be carefully utilized as they may retard the normal maturation of preterm neonatal skin.

4.7 Oat Oil

Oat oil comes from A. sativa and has been used for various eczematous skin conditions [71, 72]. Oat oil is rich in polyunsaturated fatty acids, composed of up to 36-46% LA and 28-40% OA. The high LA component is postulated to contribute most to the skin-barrier function [73, 74]. Many over-the-counter oatmeal colloidal emollients claim to soothe and protect irritated or eczematous skin. Oats may reduce irritation in various xerotic dermatoses through its anti-inflammatory and anti-itch properties, likely mediated by phytochemicals called avenanthramides [75, 76]. Avenanthramides have been shown to inhibit activation of NF-kB, an important regulator of pro-inflammatory proteins, and may also reduce inflammation when applied to the skin by inhibiting cytokines [75]. In vitro keratinocyte studies have shown that oat oil can upregulate the expression of CER-processing genes and increase CER levels by 70%, through activation of PPARs [77].

In a 3-month open-label study, an emollient containing *A. sativa* was assessed in 108 children with moderate AD aged between 6 months and 6 years old. Compared with

baseline, there was a statistically significant improvement $(48.6 \pm 73.6\%, p < 0.001)$ in SCORAD index and 100% tolerance by all subjects after 3 months [78]. However, results cannot be solely attributed to the oat oil, since the emollient contained various other ingredients including evening primrose oil, glycerin, and mineral oil. In another study by Southall et al., which also did not include a control group, 29 subjects (of unspecified ages) with severe xerosis and itch applied an oat-oil-based lotion to their lower legs twice daily. After 2 weeks, there was significant improvement in clinical evaluation of dryness, scaling, and roughness (p < 0.05), improvement in itch (p < 0.05), and decreased TEWL after 7 and 14 days of use [79]. A separate 5-week study compared an oat-oil-based lotion with a CER-based cream in 35 subjects with moderate dry skin. The oat-based moisturizer was as effective as the ceramidebased cream in improving TEWL and moisturization [79]. It is important to note that data from these studies is supplied by the manufacturer and additional published data such as percent change in endpoint parameters is unavailable. Additionally, the vehicles for the oat-based and ceramide-based moisturizers were not the same, so it is difficult to distinguish which specific ingredients led to the results. Oat oil has also been reported in several cases to be a contact allergen, inducing both immediate and delayed hypersensitivity reactions when used in personal care products [80].

4.8 Argan Oil

AO comes from the *A. spinosa* plant originating in Morocco, and is touted as the beauty secret of Moroccan women for centuries. AO is traditionally used in cooking and in skin and hair care products. It is most commonly used to enhance hair luster, reduce dry skin, and to cure brittle fingernails [81]. Edible AO is obtained from cold-pressed roasted argan kernels, while non-roasted argan kernels are used for beauty argan oil [82]. Recently, AO has become a popular ingredient in skin serums and topical products, with claims of antioxidant power, wrinkle-reducing abilities, and even claims to reduce sebum production.

In a study by Boucetta et al. to assess the effect of AO on skin elasticity, 60 postmenopausal women were randomized to consume either 25 mL/day of AO or 25 mL/day of OO for 2 months, and all 60 participants also applied ten drops of AO to their volar forearms once per day [83]. Skin elasticity was measured using Cutometer and Reviscometer. The women who consumed AO had a significant increase in skin elasticity (p < 0.001), while those who consumed OO had no significant change in skin elasticity. Topical application of AO led to a statistically significant increase in gross elasticity, net elasticity, and biological elasticity (p < 0.001) at 2 months compared with baseline. However, it is important to note there was no control group.

AO has been used as acne treatment in Moroccan folk medicine. To test this, Dobrev evaluated the ability of a skin cream containing argan oil to reduce sebum production in 20 adult volunteers with oily skin. After applying the AO formulation to their faces twice daily for 4 weeks, the subjects had a 33% reduction in physician's visual assessment of the severity of oily skin (p < 0.001). Additionally, forehead and cheeks had a 20% reduction in sebum production (p < 0.001) and the percentage area covered by sebum decreased significantly by 42% (p < 0.001) [84].

4.9 Grape Seed Oil and Palm Kernel Oil

GSO is derived from Vitis vinifera plants in the Mediterranean, central Europe, Morocco, Portugal, and Iran, and is commonly used in cooking, as a moisturizer in cosmetics, and as a carrier oil in aromatherapy massage. Schliemann-Willers et al. compared 14 different natural oils in the prevention of irritant contact dermatitis (ICD) in 20 healthy adult volunteers, and found that oils with a higher ratio of LA compared with OA had the most protective effects [85]. In this study, GSO and palm kernel oils (PKO), which contained the highest percentage of LA, provided a significant protective effect against sodium lauryl sulfate (SLS)-induced ICD. The authors hypothesized that a high OA to LA ratio increases TEWL and disrupts SC lipid organization [85]. These results are consistent with the study by Danby et al. that demonstrated SFO, which contains higher LA, had more beneficial effects on the skin than OO, which is higher in OA content [43].

5 Conclusion

Natural oils are commonly used in skin care both alone and in combination with other ingredients to help hydrate and soothe the skin. Natural ingredients, including oils and other botanicals, are considered by health-savvy consumers to be readily available, affordable, safe, gentle, and aesthetically attractive [31]. However, unique characteristic differences exist between oils that have been demonstrated in clinical studies with their application to the skin. On that note, companies claim benefits of oil-containing products without robust clinical data, and studies are small in subject number and some have suboptimal study design and randomization. In addition, many studies did not specify the virginity or refinement status of the oils used. Natural oils, such as SFO, that contain high percentages of EFAs, such as LA, have been shown in both humans and animals to

provide beneficial effects to the skin barrier [43]. On the other hand, oils with higher OA content, such as OO, can be irritating and detrimental to the integrity of the skin barrier when used as a moisturizer. The method of oil processing and refinement is an important component of selecting oil for skin care. Cold pressing is the preferred method of extraction, as it uses no heat or chemicals, thereby preserving beneficial lipids and limiting irritating byproducts. Several studies have examined the role of natural oils in neonatal skin care regimens, to help protect and improve the integrity of the immature skin barrier, with promising results. Carefully selected natural, cold-pressed oils could be used in addition to, or in place of, other conventional moisturizers to provide SC hydration and improve skin-barrier function. On average, studies used small doses of oils (2-4 mL per application) massaged onto designated areas of skin, or whole body application such as in neonatal skin care, two to four times daily [45, 48, 77, 82]. While topical application of cold-pressed oils appear to be safe, adverse effects may include burning, erythema, or an allergic reaction. Plant oils have been reported to induce allergic contact dermatitis in some individuals, with essential oils having a greater incidence than cold-pressed fixed oils [86]. There have also been reports of skin cancer associated with exposure to mineral oil [87], although associations between natural plant oils and skin cancers have not been reported. Overall, natural oils have also been shown to possess anti-inflammatory and anti-itch properties (oat oil) [75], as well as antimicrobial properties (CO) [45]. The ideal natural oil emollient should have the following properties: anti-inflammatory, anti-microbial, barrier repairing, low potential for irritation or allergy, and should be readily available and economical.

6 Future Directions

The use of natural oils in skin care dates back centuries, and there continues to be growing interest devoted to identifying and developing botanical-based ingredients for skin health products. Whether compositions with high LA versus OA truly translates into better barrier repair requires further investigation. There are currently no standardized dosing recommendations on various natural oils, but this is an area that deserve future investigation. More research is needed to shed light on how these natural oils can be safely incorporated into emollients or used in combination to treat various skin diseases. The stark variation in the characteristics and effects of natural oils on the skin emphasizes the need for more evidence to educate healthcare professionals on how plant-based natural oil-containing products may be used in skin care.

Compliance with ethical standards

Conflict of interest ARV, AKC, RKS and VYS report no relevant conflicts of interest.

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