

1 Review Article

2 **Application of seed oils and its bioactive compounds in sunscreen formulations**

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1 **Abstract**

2 The photoprotective skincare products are in high demand to meet the consumer market with
3 concern on skin health. Seed oils are commonly used as ingredients in many cosmetic
4 products due to their natural antioxidants and now being increasingly recognised for their
5 effects on skin health and photoprotection. This article briefly reviews the application of seed
6 oils in sunscreen development focusing on the antioxidants that contribute to photoprotection,
7 thus preventing UV-induced erythema and photoaging. The addition of seed oils that contain
8 specific natural bioactive compounds were discussed in the review. Besides that, seed oils
9 acting in molecular pathways that benefit in photoprotection were also summarized. Seed oils
10 (pomegranate seed oil, castor oil, cocoa butter, jojoba oil, rosehip oil, grapeseed oil, kenaf
11 seed oil and pumpkin seed oil) utilization have high potential to act as natural UV filters and
12 at the same time help in skin repairing. The seed oils contributed beneficial properties to the
13 sunscreen formulation by their synergistic effect with antioxidants, antiaging properties, anti-
14 inflammatory effect, and potential hormetic effect. The finding of specific bioactive
15 compound from seed oils provide better understanding on the contribution of seed oils in
16 sunscreen formulation.

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21 **Keywords:** Seed oil, photoprotection, antiaging, antioxidants, anti-inflammation

1 **1. Introduction**

2 Aging is a gradual and continuous degradation of the structural integrity and physiological
3 functions in human body. The process of skin aging has been divided into two categories,
4 which are intrinsic and extrinsic aging (Thring et al., 2009). Intrinsic skin aging is resulted
5 from the changing of skin elasticity from time to time. On the other hand, extrinsic skin aging
6 is more likely to be triggered by UV exposure, which is known as photoaging that accounts
7 for about 80 % of skin aging (Kwon et al., 2019). UV radiation consists of UV-A, -B, and -C
8 that differ in their wavelength, posing degree of side effects on skin. UVA and UVB radiation
9 elevate the alteration of skin connective tissue via the formation of reactive oxygen species
10 (ROS), lipid peroxides, and degradation of cell contents and enzymes. While UVC with the
11 longest wavelength is absorbed by the ozone layer and will not reach the earth. The UV-
12 induced free radicals promote harmful effect on human skin that trigger the process of aging
13 by activating DNA damage and formation of inflammatory cytokines to damage the
14 extracellular matrix (ECM) (Kwon et al., 2019). Besides that, UV radiation also promotes
15 collagen and elastin degradation while inhibits their formation, leading to the formation of
16 wrinkles (Leccia et al., 2019). This leads to the loss of skin elasticity.

17 Photoprotective products protect the skin by preventing and minimizing the damaging effects
18 of UV radiation. Sunscreen is an important part of a complete UV protection strategy.
19 According to the recommendation of the Skin Cancer Foundation, regular daily use of
20 sunscreen before going outdoor is crucial to decrease the risk of skin cancers. Sunscreen is
21 categorised into physical and chemical sunscreen. Physical sunscreen consists of mineral
22 titanium dioxide and/or zinc oxide. The physical sunscreen blocks and scatters the UV
23 radiation before they penetrate the skin. While for chemical sunscreen, it contains chemical
24 UV filters like avobenzone and octocrylene to absorb UV radiation before they damage the
25 skin. However, all active ingredients in sunscreen are chemically derived.

1 Nowadays, the use of natural ingredients in sunscreen formulation has gained significant
2 attention as they are supplied with antioxidants with beneficial properties (Radice et al.,
3 2016). Seed oils contain phytochemicals were proven in reducing the amount of synthetic
4 chemicals (Lacatusu et al., 2014; Chu et al., 2019) and play crucial roles in antiaging and skin
5 repair pathways (Kwon et al., 2019). The utilization of seed oil in sunscreen formulation is
6 important to fulfil consumers' needs to maintain healthy youth while providing adequate
7 protection against harmful UV radiation. This review focuses on the provision of sunscreen
8 fortified with seed oils and their role in photoprotection and skin health contribution. The
9 present review highlighted potential seed oils in sunscreen development with specific natural
10 bioactive compounds benefit in photoprotection, anti-inflammation and anti-photoaging.

11 **2. Potential seed oils in sunscreen development**

12 Vegetable oils have played important roles in the composition of cosmetics, act as emollients
13 and vehicles to carry other active substances (Yara-Varon et al., 2017). Seed oil is a vegetable
14 oil extracted from the seed by pressing and/or solvent extraction. Cosmetic formulations with
15 seed oils are designed to protect the skin against exogenous or endogenous damages. The
16 incorporation of seed oils in cosmetic products is crucial to provide moisturizing effect by
17 forming a skin barrier to prevent water loss (Sarkar et al., 2017). Also, seed oils showed
18 antiaging effects by supplying bioactive compounds that nourish the skin (Lin et al., 2017).
19 There are some skincare and personal care products with seed oils added, including skincare
20 lotions and creams, bath products, facial makeup, personal cleanliness, sunscreen, and other
21 skincare products. The application of seed oils was found to promote hydration and prevent
22 transdermal water loss, normalize the sebaceous glands, and enhance UV protection to
23 prevent photoaging (Lin et al., 2017; Michalak & Kiełtyka-Dadasiewicz, 2018). There were
24 several types of seed oil discussed in this article that showed significant unsaturated fatty
25 acids (Table 1), tocol content (Table 2), and phytosterols (Table 3). The seed oils found to

1 contribute in the major molecular pathway to protect the skin against oxidative stress by UV
2 radiation were also summarized in Table 4. Therefore, the utilization of seed oils with
3 alternative medication effects are promising in sunscreen formulation by providing additional
4 beneficial properties in skin beauty.

5 *2.1. Pomegranate seed oil*

6 Pomegranate (*Punica granatum* L.) is an important fruit crop that is extensively cultivated in
7 Asia, North Africa, the Mediterranean, and the Middle East and became popular due to its
8 nutritious properties. The seed contained 17.5-35.1 % oil, which is light with a thin
9 consistency (Çavdar et al., 2017). The seed oil contained high amount of unsaturated fatty
10 acids, mainly isomer punicic acid (75.2-82.3 %) as shown in Table 1 (Boroushaki et al.,
11 2016). The total unsaturated fatty acid content including punicic acid reported in the study of
12 Çavdar et al. (2017) was higher than in the papers of Melo et al. (2016) and Khoddami et al.
13 (2014). The differences in pomegranate seed lipid profile might be related to the differences
14 of cultivar, environmental growth conditions, and its ripening stage (Çavdar et al., 2017).
15 Punicic acid is an omega-5 fatty acid which is known as trichosanic acid. It is an isomer of
16 conjugated α -linolenic acid with structural similarities to conjugated linoleic acid. Punicic
17 acid has increasingly attracted scientific interest and gained wide attention for their
18 therapeutic potential due to its several potential health benefits, including antioxidant,
19 antidiabetic, neurodegenerative prevention, and serum lipid-lowering activities (Melo et al.
20 2014; Mirmiran et al., 2016; Shabbir et al. 2017).

21 Apart from the unique lipid composition of pomegranate seed oil, it was found to have high
22 amount of skin beneficial tocopherols such as α and γ -tocopherol and phytosterols such as β -
23 sitosterol, campesterol, stigmasterol as shown in Table 2 and Table 3 (Melo et al., 2016). The
24 phytochemical composition of pomegranate seed oil and their nutraceutical effects made it an

1 attractive ingredient in the cosmetic application (Khoddami et al., 2014; Boroushaki et al.,
2 2016). According to previous studies, pomegranate seed oil has been reported to have skin
3 beneficial effects in epidermal tissue regeneration and UV protection enhancement
4 (Zarfeshany et al., 2014; Montenegro & Santagati, 2019). The study from Baccarin et al.
5 (2015) suggested the effect of cell DNA protection against UVB-induced damage exhibited
6 by pomegranate seed oil nanoemulsion with pomegranate peel polyphenol-rich extract
7 encapsulation. In addition, Afaq et al. (2009) reported the photo-chemopreventive effects of
8 pomegranate derivatives, including juice, extract, and oil that inhibited UVB-mediated DNA
9 and protein damage tested in human skin model. The results suggested the effect of
10 pomegranate derivatives against UVB-mediated damages to human skin (Afaq et al. 2009).
11 Besides that, pomegranate extract was found to have a protective effect in the normal human
12 epidermal keratinocytes cell line against UVB-induced oxidative stress and able to
13 downregulate the expression of biomarkers for photoaging (Zaid et al. 2007). Therefore, the
14 nutraceutical properties of pomegranate suggested it could be a useful supplement in a
15 sunscreen formulation.

16 *2.2. Castor oil*

17 Castor oil obtained from castor (*Ricinus communis* L.) plant. Castor oil is the major industrial
18 crop in India but it also cultivated in Brazil, China, Africa, and South America (Patel et al.,
19 2016). The seeds contain 34.6-56.6 % oil, which is viscous and pale yellow. The oil yields
20 vary according to the plant variety and the solvent extraction (Sbihi et al., 2018). The study
21 from Sbihi et al. (2018) reported the seed oil yield and phytosterol content were higher in
22 ethanolic extraction and higher tocol content in hexane extraction. As stated in Table 1, castor
23 oil is rich in high content of unsaturated fatty acid, mostly ricinoleic acid ranged from 75.8 to
24 94.6 % (Ndiaye et al., 2006; Patel et al., 2016; Sbihi et al., 2018). Ricinoleic acid is a hydroxy
25 monounsaturated fatty acid that is widely applied in the chemical industry. It shows

1 antimicrobial effect and prevents the growth of virus (Prasad & Rao, 2017). Ricinoleic acid
2 acts as a humectant to provide skin moisturizing effect and improves various skin conditions
3 such as rough skin (Patel et al., 2016). Besides, ricinoleic acid also used as skin-conditioning
4 agents, emulsion stabilisers, and surfactants in cosmetics (Patel et al., 2016). With high
5 ricinoleic acid, castor oil and the hydrogenated castor oil and/or its esters are produced and
6 applied in automobiles, cosmetic, hair, and skincare as emollient and are useful for cleansing
7 and conditioning the skin (Patel et al., 2016).

8 Furthermore, it was found to have high amount of phytosterols, tocopherol, and tocotrienol.
9 According to the industry reports from the Food and Drug Administration (FDA) 2002, castor
10 oil was applied in 769 cosmetic products and its hydrogenated oil was used in 202 cosmetic
11 products (Johnson, 2007). Topical application of castor oil showed significant effect in
12 improving the signs and symptoms in patients with chronic inflammation of the eyelid tissues
13 and ocular surface (Muntz et al., 2020). With high ricinoleic acid and bioactive compounds
14 with proven anti-inflammatory, antimicrobial, and moisturizing properties in castor oil, thus
15 contributed to the improvement of the sign of ocular surface diseases (Muntz et al., 2020).
16 Besides that, Shobha, et al. (2018) reported the utilization of castor seed extract to synthesize
17 zinc oxide nanoparticle with distinctive anticancer, antibacterial, and antioxidant activity.
18 This show the potential of castor plant in sunscreen development as zinc oxide is one of the
19 FDA approved sunscreen mineral UV filter.

20 *2.3. Cocoa butter*

21 Cocoa (*Theobroma cacao* L.) is the main source to make chocolate. Cocoa butter is the
22 creamy fat extracted from the cocoa bean. It is widely used as a base to produce functional
23 foods and skincare products. Table 1 showed the yield and fatty acid composition of cocoa
24 butter which made up mainly of palmitic, stearic, and oleic acids. Cocoa butter is a source of

1 natural antioxidant which is widely utilised as an emollient in cosmetic formulations
2 (Scapagnini et al., 2014). It is a common active ingredient in lotions, creams, and lip balms.
3 According to Scapagnini et al. (2014), the lipid of the cocoa butter benefits skin health
4 through dry skin alleviation and skin elasticity improvement. Besides that, it also plays an
5 important role in the pro-inflammatory cytokines downregulation thus result in its anti-
6 inflammatory effect (Scapagnini et al., 2014).

7 Cocoa contains bioactive compounds and polyphenols that function in inhibiting lipid
8 peroxidation and combating against ROS (Heinrich et al., 2006; Scapagnini et al., 2014).
9 Topical application of cocoa butter increases dermal antioxidant capacity and protects the
10 epidermis from oxidative stress and exogenous ROS which leads to antiaging properties
11 (Scapagnini et al., 2014). Based on the study from Heinrich et al. (2006), topical application
12 and oral intake of cocoa polyphenols, especially flavanols provide effective photoprotection
13 and anti-inflammation. Thus, it acts as a promising ingredient for further dermatological
14 applications, ranging from skincare regimen to photoprotection and photoaging prevention.

15 *2.4. Jojoba oil*

16 Jojoba (*Simmondsia chinensis*) is a desert shrub in the Sonoran desert and Baja California
17 regions of North America. The oil yield of jojoba seed is 48.7-54.6 %, which is in color- and
18 odor-free. Jojoba oil is a liquid wax ester which is similar to the sebum produced by the
19 human sebaceous gland (Matsumoto et al., 2019). It is suitable to be used as a natural
20 emollient to moisturize and soothe the skin. Jojoba oil is resistant to oxidation and rancidity
21 (Calka & Pawlica, 2019) and thus, can be used as a carrier oil for essential oil and active
22 substances that susceptible to degradation. With soothing and moisturizing effects, jojoba oil
23 not only applied as a humectant meanwhile also maintain the skin moisture (Calka &
24 Pawlica, 2019).

1 From the study conducted by Habashy et al. (2005), topical application of jojoba oil was
2 found to be effective in the reduction of edema in animal models with significant anti-
3 inflammatory properties. The oil revealed a significant anti-inflammatory, antioxidative, and
4 antibacterial properties. Besides that, *in vitro* wound healing effects of jojoba oil were studied
5 on human keratinocytes and human dermal fibroblasts that showed skin repair properties
6 (Ranzato et al. 2011). In addition, *in vivo* study from Matsumoto et al. (2019) with mice
7 models reported the beneficial properties of topical application of jojoba oil through
8 transdermal delivery that can increase the level of serum non-esterified fatty acid. The study
9 from Matsumoto et al. (2019) thus, concluded the beneficial effect of jojoba oil in enhancing
10 liver lipolysis and reducing the skin fatty acid trafficking. Apart from that, the addition of
11 jojoba oil was found to enhance the viscosity and stability of lubricants at high temperature
12 which is suitable to be utilized as a cosmetic ingredient (Alvarez & Rodríguez, 2000). Also, a
13 pilot study from Meier et al. (2012) with the application of jojoba oil in clay facial mask
14 preparation was found preliminary evidence of jojoba oil in the treatment of lesioned skin,
15 mild acne vulgaris, and improvement of overall skin condition. Floratech, a company that
16 produces and markets botanical-derived ingredients for personal care and cosmetic industry
17 has patented a lipid complex (L22[®]) produced from jojoba oil/macadamia seed oil esters,
18 squalene, phytosteryl macadamiate, phytosterols, and tocopherol. L22[®] was claimed to be
19 able to balance the changes of skin lipid components due to aging to maintain the same
20 balance as present on a healthy 22-year-old skin condition (Floratech, 2019). Besides that, the
21 company also formulated a day cream with sunscreen active by using L22[®] (formula L044)
22 with the proven of skin moisturization synergy observed when combining with Floraesters[®]
23 K-20W Jojoba and glycerin (Floratech, 2019). Overall, jojoba oil is useful in the preparation
24 of future skincare products with the lipid structure similar to human serum and its bioactive

1 compounds is an adding value to sunscreen formulation to reduce the effect of UV-induced
2 inflammation and free radical scavenging production.

3 *2.5. Rosehip oil*

4 The fruit of rosehip (*Rosa canina* L.) has been used as a herbal medicine for 2,000 years
5 (Winther et al. 2016). There are many studies suggested the plant contains health-promoting
6 properties. As shown in Table 1, the oil extracted from rosehip seed contains high amount of
7 polyunsaturated fatty acids followed by monounsaturated fatty acid (Szentmihalyi et al.,
8 2002; Marmol et al., 2017; Kulaitienė et al., 2020). With the high content of polyunsaturated
9 fatty acid, it acts as a potential source to prevent obesity and hyperlipidaemia. Besides,
10 rosehip oil also contains high phytosterols (β -sitosterol, stigmasterol, and campesterol) and
11 tocopherols (Ilyasoglu, 2014; Grajzer et al., 2015). The findings from Ilyasoglu (2014) and
12 Grajzer et al. (2015) indicated the presence of bioactive compounds as good sources of
13 phytonutrients in rosehip seed and seed oil. Rosehip oil with phytonutrients showed
14 therapeutic effects on the skin. The presence of tocopherols such as γ - and δ -tocopherol were
15 found to exhibit effective anti-inflammatory, cytotoxic, and anti-mutagenic effect in the
16 human body (Grajzer et al., 2015).

17 Moreover, rosehip oil was found to have high amount of carotene pigment up to 107.7 mg/kg
18 (Grajzer et al., 2015). The presence of carotenoid in rosehip oil provides skin moisturizing
19 properties and promotes skin cell regeneration to improve skin flexibility and permeability.
20 Overall, rosehip oil was rich in polyunsaturated fatty acids, phytosterols, and tocopherols
21 which could be proposed as an ingredient in cosmetic formulations that aid in reducing the
22 signs of photoaging and prevent sunburn (Marmol et al., 2017).

23 *2.6. Grapeseed oil*

1 Grapeseed oil is extracted from the seeds of grape (*Vitis vinifera* L.). Grapeseed is a by-
2 product of winemaking and contains 8-12 % oil (Garavaglia et al., 2016). There is a growing
3 interest in grapeseed consumption and application worldwide due to its nutritional value. The
4 high antioxidant potential of the oil benefits in modulating the antioxidant enzyme
5 expression, protecting against cellular oxidative damage, anti-atherosclerotic, anti-
6 inflammation, and some cancers (Puiggros et al., 2005; Perez et al., 2015). The lipid
7 composition of grapeseed oil consisted majority of polyunsaturated fatty acid followed by
8 monounsaturated fatty acid (Table 1) (Garavaglia et al., 2016). Due to its high content of
9 unsaturated fatty acids, dietary consumption of grapeseed oil showed health-promoting
10 effects in the prevention of cardiovascular diseases, diabetes, and obesity.

11 Grapeseed oil is common in the cosmetic industry as a raw material with softening, soothing,
12 antioxidant. and moisturizing effect. The oil with high unsaturated fatty acids and
13 antioxidants can be used in the therapy of psoriasis and skin chafe. Grapeseed oil showed a
14 high amount of omega-6 fatty acid that can prevent excessive water loss by forming a
15 protective barrier on the skin (Lin et al., 2017). Apart from that, with the high amount of
16 vitamin E, grapeseed oil is effective in aging prevention (Soto et al., 2015) benefits skin
17 health (Bail et al., 2018; Glampedaki & Dutschk, 2014). Besides that, grapeseed oil also
18 provides phenolic components like flavonoids, carotenoids, phenolic acids and tannins
19 (Puiggros et al., 2005; Perez et al., 2015) which are capable in improving UV protection and
20 epidermal antioxidant activity to delay premature aging and photoaging (Lorencini et al.,
21 2014). Therefore, grapeseed oil is suitable to be used in sunscreen formulation with added
22 ability to delay skin aging.

23 *2.7. Kenaf seed oil*

1 Kenaf (*Hibiscus cannabinus*) is a plant that received attention worldwide for its commercial
2 value as fiber applications. It is used in the production of twine, rope, pulp and paper (Cheng
3 et al., 2016). Kenaf seed is a by-product of kenaf, which is found to have a high content of
4 kenaf seed oil. The fatty acid composition of kenaf seed oil was shown in Table 1. At the
5 same time, it also consists of tocopherols, phytosterols, and polyphenols (Cheong et al., 2017;
6 Nyam et al., 2009; Omenna et al., 2017). It was proven to have high nutritional value and
7 significant antioxidant activity that showed nutraceutical properties to promote good health
8 (Cheong et al., 2017; Ryu et al., 2017).

9 The utilization of kenaf seed oil was proven to provide antioxidant activity to the formulation
10 and exhibit synergistic effects (Chu et al., 2019; Chu & Nyam, 2020). According to the
11 previous studies from Chu et al. (2019) and Lee et al. (2019), KSO was utilized as a
12 renewable source and potential ingredient to produce an innovative sunscreen formulation.
13 The utilization of kenaf seed oil in the lipid phase of nanostructured lipid carrier for UV filter
14 encapsulation was found to exhibit synergistic effect to boost up the photoprotective
15 properties of the formulation (Chu et al. 2019). Meanwhile, Chu & Nyam (2020) showed the
16 potential of kenaf seed oil application in cosmetic cream formulation fortified with palm-
17 based vitamin E with adding value to the antioxidant activity. Moreover, Chu et al. (2021)
18 reported the enhancement of photoprotection in term of the SPF value and UVA/UVB ratio
19 of the photoprotective prototype developed from kenaf seed oil and tocopherol. Therefore,
20 besides being an edible oil, kenaf seed oil can be applied in skincare and sunscreen
21 formulation with additional skin beneficial properties.

22 2.8. Pumpkin seed oil

23 Pumpkin (*Cucurbita sp.*) belongs to the family Cucurbitaceae. The seeds, skins, and leaves of
24 the pumpkin plant are used as functional food or traditional medicines (Ramak & Mahboubi,

1 2018). Among several species of pumpkin, *Cucurbita pepo*, *Cucurbita maxima* and
2 *Cucurbita moschata* are cultivated extensively worldwide. Pumpkin is a valuable vegetable
3 primarily due to its high carotenoid content and minerals with the low glycemic index (Dar et
4 al., 2017). Pumpkin seed oil is a dark greenish oil which is extracted from the seeds by
5 pressing or solvent extraction. From Table 1, the seed oil contains high amount of unsaturated
6 fatty acids. The unsaturated fatty acids in the oil predominant with oleic, linoleic, and
7 palmitic acids. Besides, it also rich in phytosterols, tocopherols, and squalene (Nyam et al.,
8 2009; Naziri et al. 2015). It was proven to have pharmacological activities in anti-diabetic,
9 anti-fungal, anti-bacterial, anti-inflammation, and antioxidant effects (Bardaa et al., 2016).

10 High bioactive compounds in pumpkin seed oil could provide high protection against
11 oxidative stress (Rezig et al., 2012) and photoprotection benefit, and anti-inflammation
12 (Bardaa et al., 2016). In addition, both Bardaa et al. (2016) and Rabrenovic et al. (2014)
13 confirmed the prevalence of α - and γ -tocopherol, phytosterols, and squalene content in the
14 seed oil that made it suitable to be used in topical application with medicinal proposes. The
15 study from Bardaa et al. (2016) showed significant wound healing effect of pumpkin seed oil
16 in animal assays through topical application. Apart from that, Chu et al. (2020) reported
17 pumpkin seed oil in nanostructured lipid carrier development for sunscreen formulation
18 development demonstrated the presence of synergistic effect between pumpkin seed oil and
19 synthetic UV filters. Pumpkin seed oil showed the effect in boosting the UV protection of a
20 sunscreen formulation (Chu et al., 2020). Overall, pumpkin seed oil with unique fatty acid
21 composition and high squalene content would be recommended in the nutritional, UV
22 protection, and medicinal purposes.

23 **3. Non-prescription over-the-counter (OTC) sunscreen drug and the role of seed oil in** 24 **sunscreen**

1 In the United States, sunscreen active ingredients are regulated by the U.S. Food and Drug
2 Administration (FDA) and pre-market registration is needed for sunscreen products. The
3 sunscreen active ingredients are recognised as non-prescription over-the-counter (OTC) drug
4 and the sunscreen with UV filters are regulated under Sunscreen Drug Products for Over-the-
5 Counter Human Use Monograph (21 CFR part 310, 352, 700) and The Sunscreen Innovation
6 Act to review on the safety and efficiency of the active ingredients (Federal Register, 2019).
7 However, in 2019, the FDA published a proposed update to the current sunscreen regulation
8 and highlighted the concerns on the safety and efficiency of the approved active ingredients.
9 Among the 16 approved UV filters, only 2 are proposed to be safe and effective to use and 2
10 are classified as non-safe (FDA, 2019). Due to the concern on the safety of synthetic UV
11 filters in sunscreen that lead to growing demand for natural cosmetic ingredients. Hence,
12 plant seed oils show high potential to be added to sunscreen formulation. The unique fatty
13 acid composition and bioactive compounds in seed oil add value to the topical
14 photoprotection formulation through two different pathways, which are function as an
15 antioxidant to scavenge the UV-induced free radicals and/or act as a UV filter to absorb the
16 harmful UV radiation from damaging the skin. The application of seed oils contributed to
17 synergistic effect to the sunscreen formulation, exhibit antiaging and anti-inflammation as
18 well as act as potential natural hormetins.

19 *3.1. Synergistic effect with antioxidants*

20 The presence of natural antioxidants from seed oil may be a promising option to enhance
21 sunscreen photostability, decrease skin damage caused by UV radiation (Baccarin et al.,
22 2015), and improve SPF value of the formulation without introducing additional UV active
23 ingredients (Afonso et al., 2014). The bioactive compounds such as carotenoids and phenolic
24 compounds are found to be able to absorb UV radiation that showed potential synergistic
25 effect with UV filters. Carotenoids are potent natural antioxidants and play important roles to

1 protect the plants from UV damage. According to Darvin et al. (2011), the presence of
2 carotenoids (α -, γ -, β -carotene, lutein, zeaxanthin, lycopene) and their isomers in human skin
3 can protect against oxidation. Due to the photoprotective role of carotenoids in plants, they
4 are applied as natural photoprotective agents in the treatment of human photosensitivity,
5 particularly mediated by porphyrins (Anstey, 2002). Stahl & Sies (2012) reported the effect
6 of β -carotene and lycopene dietary intake that provide protection against UV-induced skin
7 damage in humans. Mezzomo & Ferreira (2016) reported the function of carotenoids to
8 absorb harmful UV radiation and act as UV filters to protect the skin against photodamage.
9 Carotenoids like phytoene and phytofluene are precursor molecules of unsaturated
10 carotenoids contribute photoprotective effects with their absorption UVA and UVB spectra,
11 respectively (Melendez-Martinez, 2007). Due to the spectral properties in light absorption
12 (UVB and UVA range), they are expected to have skin beneficial properties by their natural
13 photoprotective effects (Fiedor & Burda, 2014). Moreover, the previous study also suggested
14 β -carotene supplementation protect against photodamage caused by visible and infrared
15 radiations in a time-dependent manner (Melendez-Martinez, 2007; 2019).

16 Apart from that, phenolic compounds also play vital roles in photoprotection. The findings
17 from Nichols & Katiyar, (2010) indicated the ability of tea polyphenols and pro-
18 anthocyanidins from grapeseeds in absorbing mainly in UVB and part of the UVA and UVC
19 wavelength. Moreover, Agati et al. (2013) reported the effect of flavonoids such as quercetin
20 and quercetin derivatives in UVB spectrum absorption activity. Therefore, antioxidants with
21 potential UV absorbing activity may be promising to be added in sunscreen formulation to
22 boost up the effect of UV filters. According to the previous studies, the findings indicated the
23 adding value of antioxidants in sunscreen development to enhance the photoprotective
24 properties while maintaining antioxidant capacity (Lacatusu et al., 2014; Chu et al., 2019;
25 Chu et al. 2020; Chu et al., 2021). Also, Chu et al. (2019) and Badea et al. (2016) claimed the

1 synergistic interaction that occurred among the sunscreen active compounds with different
2 seed oils to boost up the photoprotection. Hence, by applying renewable plant-based
3 resources such as seed oils, they showed the ability to manifest self-antioxidative properties
4 and have advantages by replacing a considerable amount of synthetic UV filters (Niculae et
5 al., 2014). The combination of biomedical featured seed oils with the unique properties of
6 lipid nanoparticles was found to be effective in producing a sunscreen formulation that
7 demonstrated the additional skin beneficial properties from the natural bioactive compounds
8 (Lacatusu et al., 2014; Baccarin et al., 2015; Chu et al., 2019; Badea et al., 2016; Niculae et
9 al., 2014). Therefore, the addition of seed oils showed the advantages in terms of minimizing
10 the side effects of synthetic ingredients with the presence of synergistic effect.

11 *3.2. Antiaging*

12 Premature skin aging is caused by UV radiation that damage the skin connective tissue. The
13 exposure of UV radiation initiates the production of ROS and cellular mechanism that
14 damages skin connective tissue and finally lead to photoaging (Figure 1). UV radiation
15 triggers the mitogen-activated protein kinase (MAPK) pathway. The activated kinases
16 upregulate expression and functional activation of the nuclear transcription factor, AP-1,
17 which then stimulates transcription of genes for matrix-degrading enzymes such as matrix
18 metalloproteinase (MMP) -1, -2, -3, -9 and -12 (Kwon et al., 2019; Freitas-Rodríguez et al.,
19 2017). Moreover, transcription factor AP-1 also causes skin aging through transforming
20 growth factor (TGF)- β 1 pathway inhibition followed by collagen gene expression (Kwon et
21 al., 2019). UV radiation triggers the production of ROS which will be quenched by the
22 antioxidant defences in the skin. If the antioxidant defence is overwhelmed that will cause
23 oxidative stress to damage skin cells and alter their gene expression. At last, it will lead to
24 photoaging and finally promoting skin cancers. Thus, topical application of antioxidant not
25 only to introduce the antioxidant compounds, in addition to direct chemical interference with

1 free radicals generated and thus interfere with UV-induced gene expression by multiple
2 pathways.

3 Seed oils with high antioxidants protect skin from oxidative stress and implement cellular
4 antioxidant level to promote skin health (Thring et al., 2009; Lin et al., 2017). Seed oils are
5 found in rich with carotenoids, phenolic compounds, phytosterols, and vitamin E which play
6 important roles in quenching the UV-induced ROS to prevent premature aging. Fiedor &
7 Burda (2014) reported the mechanism of carotenoids associated with epidermal and dermal
8 damage. Carotenoids show excellent singlet oxygen quenching and ROS scavenging
9 properties (Fiedor & Burda, 2014). Carotenoids act as antioxidants that provide radical
10 scavenging effect, inhibit lipid peroxidation, and protect the skin against ROS generated by
11 UV radiation (Mezzomo & Ferreira, 2016). Besides, they also found in inhibiting UV-
12 induced gene by downregulating the expression of metalloproteases which are responsible for
13 premature aging as well as modulate photoimmune system (Mezzomo & Ferreira, 2016).
14 According to Melendez-Martinez (2007), carotenoids triggered keratinocyte proliferation,
15 epidermal differentiation, and reduced inflammation that benefit skin health. Overall, the
16 reduction of the sign of photoaging (wrinkling, pigmentation, dryness, and loss of skin
17 elasticity) is closely associated with the beneficial role of carotenoids on the skin.

18 Besides that, the findings from Nichols & Katiyar, (2010) indicated the ability of tea
19 polyphenols and pro-anthocyanidins from grapeseeds in preventing UV-induced
20 inflammation, DNA damage, and oxidative stress which contributed to the antiaging effect.

21 Vitamin E with high antioxidant activity showed potential protection against UV-induced
22 skin photodamage (Krol et al., 2000). From Thiele et al. (2006), topical application of
23 vitamin E up to 1 % is considered safe and effective to improve the level of skin vitamin E.
24 According to Krol et al. (2000), topical application of α -tocopherol was found to inhibit the
25 formation of cyclobutane pyrimidine photoproducts in the animal model. Vitamin E protects

1 the skin from various deleterious effects mainly contributed to lipid peroxidation interacts
2 with enzymatic and nonenzymatic pathways of other antioxidant systems and acts as a free-
3 radical scavenger (Anstey, 2002; Ribeiro et al., 2015). The study from Maalouf et al. (2002)
4 indicated topical application of vitamin E protects against UVB-induced skin damage and
5 photoaging. In addition, the application of vitamin E on human keratinocyte cell line was
6 found to demonstrate some degree of protection against cell death after UVB irradiation
7 (Maalouf et al., 2002). On the other hand, vitamin E is a free radical scavenger that not only
8 to combat the free radicals produced from UV radiation but also act as a moisture barrier to
9 the skin that decelerates the aging process in return (Pinto et al., 2018; Muthukumarasamy &
10 Ideris. 2016). The study from Rekik et al. (2016) reported the beneficial properties from the
11 combination of polyphenols, carotenoids, vitamin E, and phytosterols in anti-inflammation
12 and antiaging by protecting the skin against free radicals and ensuring the stability and
13 integrity of the skin.

14 *3.3. Anti-inflammation*

15 UV radiation that causes inflammation has been well documented clinically and
16 histologically (Hruza & Pentland, 1993). Acute exposure of UV radiation results in sunburn,
17 followed by tanning and epidermal thickening. Meanwhile, chronic exposure can induce skin
18 aging and skin cancers. UV-induced inflammation also known as UV-induced erythema. It is
19 caused by UV radiation which triggers chemical reactions occurring in the skin. It activates
20 the transcription of pro-inflammatory cytokines such as IL-1 and IL-6 which lead to sunburn
21 or inflammation (Lin et al., 2017). The inflammatory cytokines contribute to tissue repair and
22 infection control. However, they also activate keratinocytes and immune cells to damage the
23 skin tissue through ROS production. ROS triggers MAPK pathway as indicated in Figure 1 to
24 cause the degradation of ECM which leads to skin aging. Therefore, the intensity of
25 inflammation resolution is critical to limit normal skin tissue damage. Topical application of

1 seed oils with mono- and polyunsaturated fatty acids may influence the inflammatory
2 responses. Due to its high composition of unsaturated fatty acids and antioxidants, seed oils
3 contain relatively high protection against inflammation and oxidative stress. According to the
4 literatures, pomegranate seed, rosehip, grapeseed, kenaf seed oil, and pumpkin seed oil were
5 found to prevent inflammation and contributed to wound healing effect (Lin et al., 2017;
6 Nyam et al. 2015; Bardaa et al., 2016; Rekik et al., 2016). Besides that, pumpkin seed oil
7 with relatively high squalene content is beneficial to skin health (Nyam et al. 2009). Squalene
8 is resistant to peroxidation to function as a ROS quencher, protect skin lipid peroxidation
9 against the exposure to UV radiation, and other sources of oxidative damage (Huang et al.,
10 2009). It functions in enhancing regeneration, nourishment, and protection of human skin as
11 well as in skin treatment from cracks, eczema, dermatitis, rashes, and so forth (Muller et al.,
12 2007). The presence of bioactive compounds and unique fatty acid composition in seed oils
13 are valuable in skin health to prevent UV-induced inflammation.

14 *3.4. Natural hormetin*

15 Hormesis is a biphasic dose response to an agent in which a low dose will cause beneficial
16 effects and a high dose will lead to toxic effects (Mattson 2009). In the biological and
17 medicinal field, hormesis is a phenomenon in which the cell and organism response to the
18 induction of mild stress (Mattson 2009). The examples of mild stress induction can be from
19 exercises, dietary intake, and phytonutrient exposure that results in cellular signalling
20 pathways to mediate hormetic responses. The application of seed oils could be a novel
21 biological hormetin in the cosmetic formulation due to their effect of certain phytochemicals
22 in hormesis. The presence of high content of bioactive compounds in the seed oil exhibit
23 direct free radical scavenging properties and responsible for the health benefits. However,
24 according to Mattson (2009) and Rattan (2015), the presence of some phytonutrients such as
25 polyphenols, flavonoids, and curcumin exert advantages in activating adaptive stress response

1 signalling pathways, leading to the production growth factors for cellular regeneration,
2 cytoprotective protein production, and protein repair.

3 Hormesis induced by mild stress benefit in aging due to the function to maintain and repair
4 the cells and proteins in the body (Rattan, 2004). Aging is caused by the failure of cellular
5 maintenance. Therefore, Rattan (2004) suggested the application of mild stress to trigger
6 hormesis could be a promising approach for modulating aging by mediating several stress-
7 induced gene expression to improve the cellular function. The previous study from Rattan et
8 al. (2012) showed beneficial effects of Chinese herb Sanchi (*Panax notoginseng*) extract in
9 skin health due to the production of stress-induced proteins involved in protein repair and
10 removal of abnormal proteins. Besides that, the clinical evaluation on Sanchi extract also
11 indicated significant positive effects against facial wrinkles and other symptoms of facial skin
12 aging (Rattan et al. 2012). The application of natural hormetins from seed oil could be a
13 promising approach to aging intervention. Seed oil can act as a free radical scavenging agent
14 to protect the skin against harmful UV radiation and at the same time trigger hormetic
15 responses to benefit skin health. Unfortunately, a more complete research should be carried
16 out in order to define the complete pathway of hormesis triggered by seed oils.

17 **4. Conclusion**

18 The review of seed oils in sunscreen development is valuable in the growing market of
19 natural cosmetics. Seed oils as sources of unsaturated fatty acids and bioactive compounds
20 play crucial roles in photoaging prevention. Numerous scientific studies have confirmed the
21 beneficial effects of seed oils on exhibiting synergistic effect with synthetic UV active
22 ingredients to improve skin health. The phytonutrients of seed oils play crucial roles to boost
23 up the photoprotection, promote skin health by their antioxidative activities, protect the skin
24 from UV-induced erythema, and trigger hormetic responses for protein repair. Therefore,

1 seed oils are beneficial in delaying aging process through antioxidant replenishment and skin
2 cell regeneration. Future studies should be conducted to verify the cellular pathway and
3 molecular mechanisms in dermatological treatments by the application of seed oils suggested
4 from pomegranate, castor, cocoa butter, jojoba, rosehip, grapeseed, kenaf, and pumpkin in
5 sunscreen products. Besides that, hormesis induced by seed oils and their beneficial effects in
6 UV protection should be defined. In principle, phytonutrients from plant seed oils can be a
7 propitious therapeutical strategy to develop novel cosmetic formulations.

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11 **Conflict of interest**

12 The authors declare no conflict of interest.

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1 **Table 1 Fatty acid composition of seed oils reported from the previous studies.**

Fatty acid (%)	Pomegranate seed oil	Castor oil	Cocoa butter	Jojoba oil	Rosehip oil	Grapeseed oil	Kenaf seed oil	Pumpkin seed oil
C12:0	-	-	-	-	0.01-0.03	-	-	-
C14:0	-	-	0.08-3.9	0.30-3.50	0.04-0.05	-	0.14-0.25	0.2
C16:0	2.4-4.6	0.3-5.0	22.5-26.6	3.10-9.00	2.73-3.65	7.1-7.8	19.3-23.3	14.8-19.1
C16:1	-	-	0.2-0.3	0.6-2.2	0.1-0.2	-	0.5-0.6	0.02-0.15
C17:1	-	-	0.2-0.2	-	0.04-0.06	-	0.2-0.3	0.08
C18:0	2.3-2.6	0.9-5.4	35.0-37.9	28.2-46.3	.1-2.8	2.5-4.7	3.8-4.6	6.7-7.4
C18:1	6.2-8.0	2.1-7.4	31.9-35.8	0.2-3.1	13.5-18.2	13.9-21.9	33.0-37.6	25.8-42.8
C18:2	5.5-8.7	1.8-10.4	2.7-3.3	0.2-3.1	47.4-54.3	66.0-75.3	31.7-36.5	30.4-50.9
C18:3	75.2-82.3	0.7-0.9	0.1-0.2	-	19.3-30.6	0.3-1.1	1.1-1.2	0.18
C18:1-OH	-	75.8-94.6	-	-	-	-	-	-
C20:0	0.2-0.5	-	1.0-1.1	0.4-3.8	0.7-1.0	0.1-0.2	0.6-0.7	0.4
C20:1	0.6-0.7	-	0.03-0.04	20.8-47.0	0.3-0.7	0.1-0.6	-	0.09
C20:5	-	-	-	-	0.01-0.1	-	-	-
C21:0	-	-	-	8.2-19.7	0.03-0.05	-	-	-
C22:0	-	-	0.1-0.2	-	0.2-0.4	-	0.3-0.4	0.06
C22:1	-	-	-	-	0.1-0.3	-	-	0.06
C24:0	-	-	0.05-0.1	1.4-4.4	0.1-0.2	-	0.2-0.4	-
C24:1	-	-	-	-	0.03-0.3	-	0.2-3.6	-
SFA	5.4-7.5	5.5-10.9	58.8-69.8	41.6-67.0	5.2-7.6	9.7-12.6	24.9-29.4	22.1-27.2

MUFA	6.8-8.7	78.3-84.8	32.4-36.3	21.6-52.3	14.7-18.9	14.5-22.2	37.1-41.9	26.1-43.2
PUFA	83.9-87.9	9.5-11.4	2.8-3.5	0.2-3.1	73.9-79.5	66.3-75.8	32.8-37.7	30.6-51.1
Oil yield (%)	17.5-35.1	34.6-56.6	34.8-41.8	48.7-54.6	4.9-16.1	8.0-12.0	2.1-24.8	49.1
References	Khoddami et al. (2014); Çavdar et al. (2017); Drinić et al. (2020)	Ndiaye et al. (2006); Sbihi et al. (2018)	Servent et al. (2018); Melo et al. (2020)	Agarwal et al. (2018)	Kulaitienė et al. (2020)	Lutterodt et al. (2011); Garavaglia et al. (2016)	Chew et al. (2016; 2018); Cheng et al. (2016)	Nyam <i>et al.</i> (2009); Bardaa et al. (2016)

1 SFA, Saturated fatty acids; MUFA, Monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids.

2

1 **Table 2 Tocopherol and tocotrienol content of seed oils reported from the previous studies.**

Tocopherol (mg/100 g oil)	Pomegranate seed oil	Castor oil	Cocoa butter	Jojoba oil	Rosehip oil	Grapeseed oil	Kenaf seed oil	Pumpkin seed oil
α	3.8-6.5	0.6-1.3	0.9-1.6	8.5	11.7-14.7	9.6	12.2-21.9	15.2-35.3
β	1.0	0.3-0.7	-	0.2	-	0.08	6.4-6.8	-
γ	153.2-382.7	30.9-46.5	17.9-25.8	33.0	63.0-77.7	3.4	17.8-27.2	61.3-77.5
δ	8.8-17.0	53.0-96.6	0.7-0.8	0.02	23.0-26.0	0.09	1.3-2.5	4.14
Tocotrienol (mg/100 g oil)								
α	0.07	0.2-0.4	-	-	-	34.5	2.2-3.7	-
β	-	-	-	-	-	0.3	-	-
γ	0.7	-	-	-	-	49.5	2.0-2.4	-
δ	-	0.5-0.6	-	-	-	-	3.0-6.0	-
Total (mg/100 g oil)	175.1-398.7	92.5-129.7	19.5-28.2	41.7	103.8-112.5	97.5	51.3-64.1	80.65-116.9
References	Górnaś et al. (2015); Melo et al. (2016)	Sbihi et al. (2018)	Oracz et al. (2014)	El-Mallah, M. H., & El- Shami (2009)	Grajzer et al. (2015)	Górnaś et al. (2015)	Chew et al. (2017)	Nyam et al. (2009); Naziri et al. (2015)

2

1 **Table 3 Phytosterols of seed oils reported from the previous studies.**

Phytosterol (mg/100 g oil)	Pomegranate seed oil	Castor oil	Cocoa butter	Jojoba oil	Rosehip oil	Grapeseed oil	Kenaf seed oil	Pumpkin seed oil
Campesterol	49.0	249.2-273.2	140.4-172.1	67.2	23.3	2.6-95.7	58.1-52.9	22.6
Stigmasterol	12.0	520.1-554.1	164.5-279.5	26.6	18.9	102.0-108.0	23.3-28.5	18.0
β -Sitosterol	374.0	1070.0-1192.0	191.1-203.0	278.0	544	666.0-674.0	289.9-468.0	211.0
Others	104.0	530.7-583.7	-	259.0	46.8	107.8-127.8	-	590.7 (squalene)
Total	539.0	2370.0-2603.0	496.0-644.1	397.7	663	878.4-1005.5	371.3-549.3	864.7
References	Melo et al. (2016)	Sbihi et al. (2018)	Mohamad et al. (2019)	Busson-Breyse et al. (1994)	Ilyasoglu (2014)	Garavaglia et al. (2016)	Nyam et al. (2009); Chew et al. (2018)	Nyam et al. (2009)

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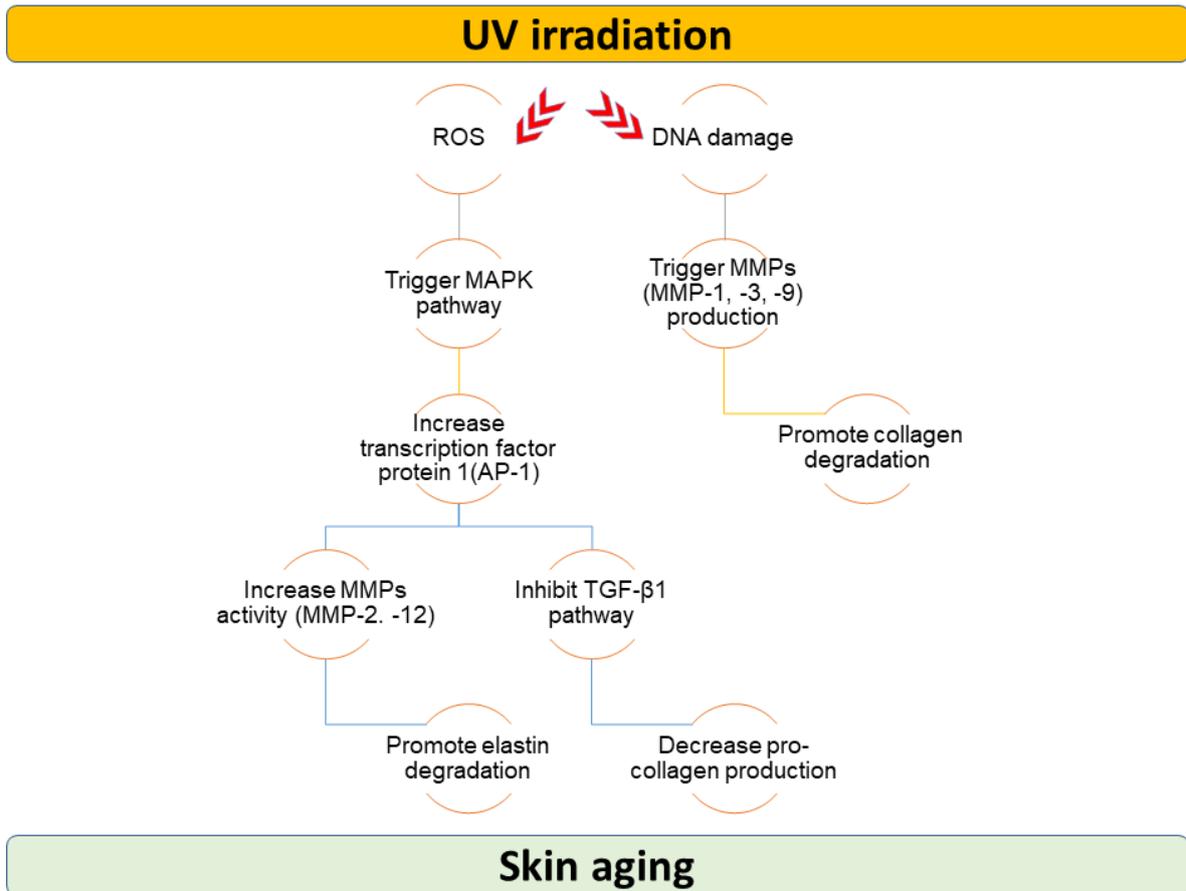
1 **Table 4 List of seed oils with major contributed compounds and molecular pathways that benefit in photoprotection.**

2

Seed oil	Effects in photoprotection	Major contributed compounds	Molecular pathways	References
Pomegranate seed oil	<ul style="list-style-type: none"> Inhibit UVB-induced protein oxidation and markers of DNA damage Prevent from photoaging UV filter booster 	<ul style="list-style-type: none"> Phytosterols Phenolic compounds 	AP-1 signalling pathway which regulates MMPs expression in human skin	Montenegro & Santegoti (2019); Afaq et al. (2009)
Castor oil	<ul style="list-style-type: none"> Protect from UV-induced damage Antioxidants 	Fatty acid composition	<ul style="list-style-type: none"> UV absorption 	Kaur & Saraf (2010)
Cocoa butter	<ul style="list-style-type: none"> Protect from ROS-induced damage Anti-inflammation Antioxidants 	<ul style="list-style-type: none"> Polyphenols 	<ul style="list-style-type: none"> Extracellular matrix (ECM) remodelling Downregulate pro-inflammatory cytokines 	Scapagnini et al. (2014); Heinrich et al. (2006)
Joboba oil	<ul style="list-style-type: none"> Prevent from photoaging Antioxidants Anti-inflammation 	<ul style="list-style-type: none"> Phytosterols Vitamin E Vitamin A 	<ul style="list-style-type: none"> UV absorption Reduced nitric oxide level and tumor necrosis factor-alpha (TNF-α) pathway 	Habashy et al. (2005); Calka & Pawlica (2019)
Rosehip oil	<ul style="list-style-type: none"> Inhibit ROS-induced damage Anti-inflammation 	<ul style="list-style-type: none"> β-carotene and lycopene Vitamin E 	<ul style="list-style-type: none"> MMPs gene expression pathway NF-κB activation pathway 	Marmol et al. (2017)
Grapeseed oil	<ul style="list-style-type: none"> Inhibit lipid oxidation Inhibit ROS-induced damage Anti-inflammation 	<ul style="list-style-type: none"> Phenolic compounds Vitamin E 	<ul style="list-style-type: none"> Glutathione related enzymes expression Inhibit the activity of arachidonic acid 	Garavaglia et al. (2016); Puiggros et al. (2005)

Kenaf seed oil	<ul style="list-style-type: none"> • UV filter booster • Antioxidants 	<ul style="list-style-type: none"> • Vitamin E • Carotenoids • Flavonoids 	No report	Lee et al. (2019); Chu et al., (2019; 2021); Yusri et al. (2012)
Pumpkin seed oil	<ul style="list-style-type: none"> • UV filter booster • Antioxidants • Anti-inflammation 	<ul style="list-style-type: none"> • Vitamin E • Squalene • β-carotene 	<ul style="list-style-type: none"> • Extracellular matrix (ECM) remodelling • Inhibit the activity of arachidonic acid 	Chu et al. (2020); Badae et al. (2016); Al-Okbi et al. (2017)

1



1

- 2 **Figure 1 UV-induced pathways that result in skin aging (Kwon et al., 2019; Freitas-**
- 3 **Rodríguez et al., 2017).**