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Avocado (*Persea americana* Mill.) bioactive compounds - extraction method, chemical compositions and cosmeceutical applications: A scoping review)

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Abstract

The cosmeceutical industry has been blooming over the years, necessitating a demand for safe and effective options. Fruit bioactive compounds are reported as safe for human health and broadly effective alternatives with less adverse effects. Avocado (*Persea americana* Mill.) is a tropical fruit rich in phytonutrients and lipid-soluble bioactive compounds. These compounds have been reported to have various potential health benefits, including improving skin health. This scoping review investigated the bioactive compounds of avocados that were reported to confer beneficial activities on the skin. Published data between August 1982 till February 2022 were extracted from Ovid Medline, Scopus, Pubmed, SciFinder and Web of Science. A total of 307 published articles were identified using the search terms, of which 31 full articles were reviewed and appraised in this synthesis. Results: This comprehensive scoping review examined the cosmeceutical activities of bioactive phytochemicals found in avocado (*Persea americana* Mill.) outlining their mechanisms of action. The review highlighted the antioxidant, antimicrobial, anti-inflammatory, wound healing, anti-tyrosinase, and anti-aging properties of avocado extracts. Acetone extracts, especially from seeds, showed the highest antioxidant capacity and were also effective in antimicrobial activities. Methanol extracts demonstrated significant anti-inflammatory effects. Furthermore, bioactive compounds from avocados were found to enhance wound healing and anti-aging effects, such as increasing collagen production and improving skin hydration and elasticity. This scoping review provides a comprehensive collection of evidence and critically appraises recent literature on bioactive compounds of Avocado and extraction solvents and potential cosmeceutical applications.

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Introduction

Cosmeceuticals are defined as cosmetics with active compounds that has positive therapeutic qualities on the skin (Husein El Hadmed & Castillo, 2016). These products aim to enhance skin appearance and health while protecting against environmental damage from UV radiation, pollution, and oxidative stress (Husein El Hadmed & Castillo, 2016). In recent years, the cosmeceutical sector has been experiencing significant growth, with an annual increase in consumer spending on cosmetics aimed at delaying or reversing skin aging. Research suggests that there has been a 33% rise in expenditure within the anti-aging industry every year. Notably, there has been a shift towards natural bioactive ingredients in the cosmeceutical business, largely due to concerns about the ineffectiveness of synthetic cosmetics. This trend reflects a growing interest in products that are perceived as more beneficial for skin health (Smit et al., 2009; Yon et al., 2023).

Plant-derived bioactive compounds, such as polyphenols, phytosterols, biogenic amines, and carotenoids (Samtiya et al., 2021), have been found to have cosmeceutical benefits including moisturizing, revitalizing, anti-aging, UV protection, and preventing skin-related disorders. These compounds are highly sought-after as active ingredients in the cosmeceuticals industry (Romes et al., 2021). The demand for plant-derived bioactive components is driven by their non-artificial synthetic chemical properties, which are known to be less irritating to the skin compared to synthetic chemicals (Lagoa et al., 2020; Puglia & Santonocito, 2019). Other examples such as butylated hydroxyanisole (BHT) and butylated hydroxytoluene (BHA) have been restricted due to potential carcinogenicity (Pandey & Kumar, 2021).

Research has indicated that consuming bioactive antioxidants through food can offer cosmeceutical advantages. These include safeguarding skin cells, defending against dryness and environmental harm, and maintaining adequate moisture levels for optimal function (Nilforoushzadeh et al., 2018). Studies have also emphasized the benefits of antioxidants in providing nutrients for healthy skin, reducing wrinkles, and enhancing skin brightness, texture, and tone (Thiyagarasaiyar et al., 2020).

Avocado, also known as *Persea americana* Mill., is a plant from the Lauraceae family (Lister et al., 2021). It is grown worldwide, primarily in tropical and subtropical regions with warm and moderate conditions (García-Villegas et al., 2022). There is a diverse variety of avocado species, which includes Hass, Fuerte, Gwen, Bacon, and Reed, among many others, which can be categorised into main groups of: West Indian, West Indian-Guatemalan hybrid, Guatemalan and Mexican (Melgar et al., 2018; Wang et al., 2010) .

Avocado has gained an increased worldwide interest in recent years due to its high nutritional value (Moldovan et al., 2021). It is a popular fruit known for its unique taste, year-round availability, and excellent source of nutrients such as saponins, alkaloids, polyphenols, tannins, and flavonoids found in the fruit, seeds, and leaves. These phytonutrients contribute to antioxidant, antimicrobial, anti-inflammatory, wound-healing, and anti-aging properties (Lister et al., 2021). Consumption of avocado has also been linked to improved skin health due to its high bioavailability of carotenoids, lutein, and zeaxanthin, which can help prevent damage to the skin from ultraviolet (UV) and visible radiation (Dreher & Davenport, 2013)

Different parts of the plant are reported to confer specific benefits. Avocado oil is known to be rich in unsaturated fatty acids, lecithin, minerals, β-sitosterol, β-carotene, and vitamins A, C, D, and E. This makes it an excellent choice for moisturizing the skin when used topically (Lin et al., 2017). Studies have shown that avocado oil may help in reducing wrinkles, stretch marks, promoting wound healing, and treating psoriasis by aiding in the regeneration of the epidermis (Ana Paula de Oliveira et al., 2013; Poljšak et al., 2020). Consequently, multiple studies have been conducted on avocados to support their use in cosmeceuticals (Lister et al., 2021).

This scoping review critically appraises and summarises the published data on avocado bioactive compounds and the solvents used for their extraction, exploring their potential applications in the cosmetics industry. Additionally, the review provided a critical assessment of various extraction solvents, including methanol, ethanol, hexane, chloroform, and others, utilized for isolating bioactive compounds from avocados.

Materials and methods

This scoping review aimed to evaluate the most recent and representative information on the bioactive phytochemicals of functional extracts from *Persea americana* Mill. This scoping review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Tricco et al., 2018) .

Search Strategy

The present scoping review was carried out using the electronic databases: Ovid MEDLINE, Scopus, Pubmed, SciFinder and Web of Science. We retrieved published data from August 1982 to January 2022. Specific keywords "avocado" OR "*Persea americana* Mill." AND "skin" AND "cosmetics" were used. The same strategy was used for all the databases with adaptations, as appropriate. Next, the list of studies was completed by searching the bibliographies of the selected publications and implementing the inclusion and exclusion criteria in each case. Results were limited to the English language. All the research articles had been published in peer-reviewed journals, and those with fully accessible texts were selected.

Inclusion Criteria

Studies reporting on 1) *Persea americana* Mill. parts, including leaves, pulp, seed, and peel, and 2) its nutrients or bio compounds were included.

Exclusion Criteria

The exclusion criteria were as follows: a) studies published in languages other than English were excluded, b) Patents, literature reviews, and systematic reviews, c) Data from non-open access journal articles or partially accessed (abstract only) articles.

Data Extraction

The two-steps selection was carried out: 1) non-eligible article were removed by screening the titles and abstract, and 2) three authors, XNL., LLY., and WYL., independently screened titles, abstracts, and full-text articles according to the stated inclusion criteria and data availability. The data were extracted from main articles and their supplementary materials into an excel spreadsheet. Two other authors (SM., BHG.) then review the selected data. Disagreements were resolved via discussion and consultation, which were then amended. The following data were extracted from each study: 1) Study characteristics: author name, year of publication, country of study, total phenolic content of extracts, total antioxidant capacity, wound healing properties, antibacterial activity, anti-tyrosinase activity and anti-inflammatory activities. A reference manager (EndNote X9, Thompson Reuters, Philadelphia, PA, USA) was used to import the list of references from all databases, where duplicates were then removed.

Study selection process

This review has extracted and summarised findings from published data on the cosmeceutical application of avocado and its bioactive compounds. A total of 307 published articles were identified through literature screening. The duplicates (n = 94) and articles that were not related to the subject of this review (n = 182) were removed, resulting in 31 articles remaining. Figure 1 is the illustrative flow chart showing article extraction and filtering.

Of the 31 studies included in this systematic review, 11 studies evaluated antioxidant capacity of avocado (Ekom & Kuete, 2022; Ferreira da Vinha et al., 2013; Forero-Doria et al., 2017; Hürkul et al., 2021; Kosińska et al., 2012; Melgar et al., 2018; Nguyen et al., 2021; Paoletti et al., 2010; Rodríguez-Carpena et al., 2011), five studies on antimicrobial activity (Donnarumma et al., 2007; Ekom & Kuete, 2022; Melgar et al., 2018; Nguyen et al., 2021; Paoletti et al., 2010; Rodríguez-Carpena et al., 2011), six on anti-inflammatory properties (Borghi et al., 2015; Hürkul et al., 2021; Rosenblat et al., 2011; Sharquie

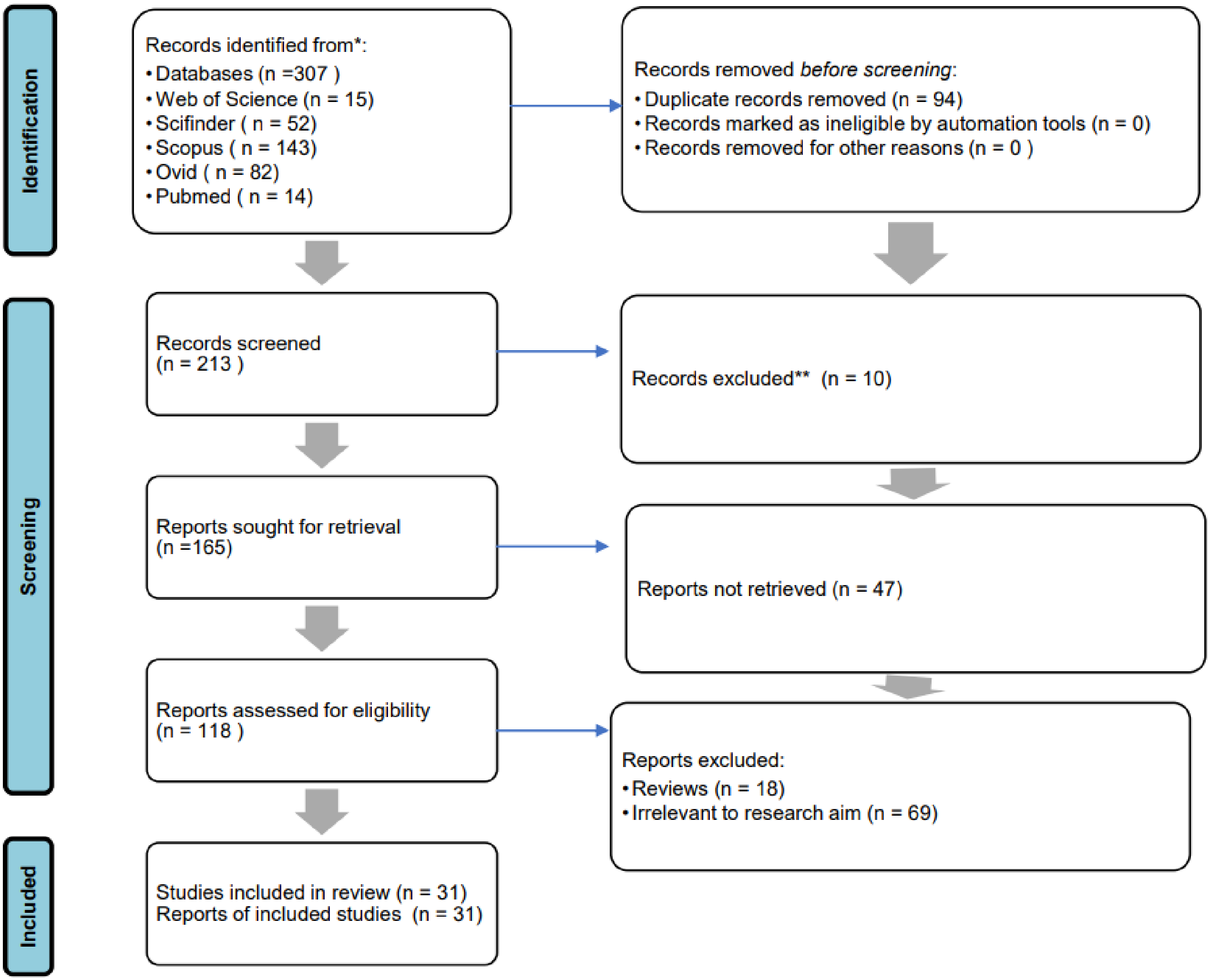

Fig. 1: Schematic illustration of article screening and filtering.

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et al., 2012) , six on wound healing properties (Alves et al., 2019; Ana Paula de Oliveira et al., 2013; Ekom & Kuete, 2022; Oryan et al., 2015; Sichani et al., 2021), two on anti-tyrosinase properties (Hürkul et al., 2021; Laksmiani et al., 2020) and four studies discussed its anti-ageing properties (Susanne M. Henning et al., 2022; Lister et al., 2021; Moldovan et al., 2021; Naeimifar et al., 2020). Figure 2 is an avocado fruit structure and its cosmeceutical benefits appraised in this review.

Results and discussion

This scoping review aimed to provide a complete description of the cosmeceutical's activities of bioactive phytochemicals of *Persea americana* Mill. The mechanisms of action through which these bioactive compounds or functional extracts exhibit cosmeceutical activities were defined.

After conducting an exhaustive screening, 31 selected articles were extracted and appraised. The findings were systematically categorized into three main areas: bioactive phytochemicals and their cosmeceutical benefits, extraction methods of bioactive phytochemicals, and in vitro and in vivo studies on these compounds.

The review highlights the cosmeceutical benefits of bioactive phytochemicals, including their antioxidant capacity, anti-inflammatory properties, wound-healing potential, anti-tyrosinase activity, and anti-ageing effects (Table 1).

Antioxidant capacity

The avocado's antioxidant capacity correlates with total phenolic content and procyanidins. Studies included in this synthesis showed that different extracts were used to obtain active phytochemicals of avocados (Table 1). Acetone extracts exhibited the most significant antioxidant capacity, followed by Methanol and ethyl acetate (Rodríguez-Carpena et al., 2011). Various assays were also used to obtain values to compare the antioxidant capacity among parts of the avocado or types of cultivars, mainly the DPPH, ORAC, ABTS and TBARS assays. Comparing IC50 and EC50 values from these assays showed that the Tonnage cultivar possesses the highest antioxidant activity, followed by Simmonds, Hass, Booth 8, Choquette, Booth 7, Loretta and Slimcado. In terms of avocado parts, seeds generally contribute the most to the antioxidant capacity compared to the peel and pulp.

According to a study by Melgar and colleagues (2018), the methanol extract of Hass avocado seeds demonstrated more significant antimicrobial activity compared to the acetone and diethyl ether extracts. The study found that avocado seeds exhibited higher antimicrobial activity than peels, as indicated by greater MIC values and lower MBC values in antibacterial and antifungal assays.

Additionally, Hurkul and colleagues (2021) reported that the HRBC membrane stabilization assay was the primary method used to evaluate the anti-inflammatory properties of avocado. The results indicated that methanol extract produced lower IC50 values than the N-hexane extract, suggesting greater anti-inflammatory activity. However, the study found contradictory results when comparing the anti-inflammatory activity of different parts of the avocado, such as peels, seeds, and pulp. The study also discussed the anti-tyrosinase capacity of avocado, noting that the highest anti-tyrosinase activity was associated with avocado peel extracted by N-hexane.

Different extraction solvents at various concentrations result in different extraction efficiencies where the composition of phenolic compounds responsible for antioxidant properties is affected (Table 1). Acetone extracts exhibited the most significant antioxidant capacity, followed by methanol and ethyl acetate (Rafique & Akhtar, 2018; Rodríguez-Carpena et al., 2011). The DPPH assay in Rodriguez-Carpena and colleagues (2011) showed that Hass avocado seeds extracted with acetone produced an In Vitro antioxidant activity of 130.26±36.80 mmol Trolox/g fresh matter. In contrast, methanol extract exhibited 66.24±24.84 mmol Trolox/g fresh matter, and ethyl acetate exhibited 17.78±4.34 mmol Trolox/g fresh matter.

Rafique and Akhtar (2018) state that acetone extracts are better antioxidants, with 80% activity in 60% acetone and 10% methanol compared to 70% methanol. However, the ratio of acetone has been shown to affect the antioxidant capacity of avocado extracts. 50% acetone extract will achieve a greater antioxidant capacity compared to 70% acetone due to the higher phenolic content achieved. DPPH and ABTS assays can be used to obtain IC50 values, where the lower the values, the greater the antioxidant capacity. Whereas another study comparing ultrasound-assisted batch extraction (UABE) and ultrasound-assisted continuous extraction (UACE) showed no significant differences in antioxidant capacity. Differences were only noticed in the extraction times where UACE reaches equilibrium up to 53% faster than UABE (Oryan et al., 2015)

The results obtained by Vinha and colleagues (2013) were in agreement with other studies, which stated that Hass avocado seeds exhibited the highest antioxidant capacity of 43%, followed by peels (35%) and pulp (23%). The study by Melger and colleagues (2018) reported that Bacon avocados' seeds, peels and pulps extracted with methanol solution and tested via DPPH and ABTS assay, showed IC50 values of seeds to be the lowest (4.17±0.04 mg/mL and 0.03±0.01 mg/mL) followed by peels (5.25±0.05 mg/mL and 0.06±0.02 mg/mL).

Pulps showed the highest values of 11.34±0.11 mg/mL and 0.65±0.08 mg/mL. Interestingly, the

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Antioxidant	Ethyl acetate	Hass	Seed	- TPC - Flavonols - Procyanidins - Catechins - OH-B - OH-C	N/A	CUPRAC	58.00 ±15.55	(Rodríguez-Carpena et al., 2011)
						DPPH	17.78 ± 4.34	
						ABTS	21.57 ± 7.51	
			Peel			CUPRAC	56.40 ± 21.19	
						DPPH	17.85 ± 7.07	
						ABTS	16.12 ± 6.98	
			Pulp			CUPRAC	2.48 ± 0.33	
						DPPH	0.37 ± 0.07	
						ABTS	0.64 ± 0.10	
		Fuerte	Seed			CUPRAC	96.09 ± 27.76	
						DPPH	27.80 ±10.16	
						ABTS	38.15 ±12.78	
			Peel			CUPRAC	103.68±26.69	
						DPPH	35.18 ± 12.56	
						ABTS	34.82 ±12.61	
			Pulp			CUPRAC	2.44 ± 0.65	
						DPPH	0.23 ± 0.07	
						ABTS	0.56 ± 0.11	

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Antioxidant	Acetone	Hass	Seed	- TPC - Flavonols - Procyanidins - Catechins - OH-B - OH-C	N/A	CUPRAC	275.36±59.09	(Rodríguez-Carpena et al., 2011)
						DPPH	130.26±36.80	
						ABTS	158.29±26.27	
			Peel			CUPRAC	218.04±42.42	
						DPPH	88.94±48.22	
						ABTS	103.75±44.49	
			Pulp			CUPRAC	1.63±0.39	
						DPPH	0.33±0.07	
						ABTS	0.84±0.24	
		Fuerte	Seed			CUPRAC	353.43±75.83	
						DPPH	167.50±42.08	
						ABTS	194.80±44.69	
			Peel			CUPRAC	456.24±77.07	
						DPPH	199.61±33.15	
						ABTS	242.26±28.31	
			Pulp			CUPRAC	2.04±0.32	
						DPPH	0.39±0.10	
						ABTS	0.91±0.12	

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Antioxidant	Methanol	Hass	Seed	- TPC - Flavonols - Procyanidins - Catechins - OH-B - OH-C	N/A	CUPRAC	141.67±41.24	(Rodríguez-Carpena et al., 2011)
						DPPH	66.24±24.84	
						ABTS	78.93±26.73	
			Peel			CUPRAC	145.98±69.25	
						DPPH	71.92±28.93	
						ABTS	74.06±23.17	
			Pulp			CUPRAC	1.33±0.43	
						DPPH	0.32±0.07	
						ABTS	0.94±0.23	
		Fuerte	Seed			CUPRAC	184.42±66.05	
						DPPH	94.27±30.47	
						ABTS	121.61±31.87	
			Peel			CUPRAC	330.75±62.57	
						DPPH	174.71±29.80	
						ABTS	185.87±26.91	
			Pulp			CUPRAC	1.64±0.44	
						DPPH	0.29±0.09	
						ABTS	0.78±0.17	

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Antioxidant	N/A	Hass	Seed			Disk diffusion assay	7.18-9.73	(Rodríguez-Carpena et al., 2011)
			Peel				4.95-6.20	
			Pulp				5.21-9.48	
		Fuerte	Seed				5.00-9.81	
			Peel				5.11-6.91	
			Pulp				5.11-13.00	
	Aqueous + Ultrasound-assisted batch extraction (UABE)	N/A	Seed	TPC	N/A	ORAC assay	Values presented in chart, no specific values stated	(Oryan et al., 2015)
	Aqueous + Ultrasound-assisted continuous extraction (UACE)							
	Methanol	N/A	Seed	TPC including: - Tannins - Flavonoids - Alkaloids - Polyphenols Not mentioned to be correlated to antioxidant: - Anthocyanins - Anthraquinones - Triterpenes - Steroids - Saponins	N/A	Antibacterial assay	64-128	(Ekom & Kuete, 2022)
							512->2048	
						DPPH assay	55.91 ± 2.12	
						FRAP assay	N/A	

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Antioxidant	80% Methanol	Hass	Peel	Seed: - 3-O-caffeoylquinic acid - 3-O-p-coumaroylquinic acid - Procyanidins - Catechin/epicatechins	N/A	ORAC assay	0.47 ± 0.036	(Kosińska et al., 2012)
Antimicrobial	Extracted twice with ethanol at 50°C for 1 h, followed by acetone extraction at 4°C overnight. Extract was dried and re-dissolved in 35 ml hexane and refrigerated at 4°C overnight prior to filtration.	Shepard	Seed Peel	Peel: - Quercetin - Glycosides - 5-O-caffeoylquinic acid - Catechins - Procyanidins	N/A	DPPH assay ORAC assay	0.358 0.21 ± 0.014	(Rosenblat et al., 2011)
						TEAC assay DPPH assay	0.094 ± 0.0007 0.920	
						ORAC assay	0.29 ± 0.020	
						TEAC assay	0.112 ± 0.0034	
						DPPH assay	0.927	

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Anti-ageing			Seed			ORAC assay TEAC assay DPPH assay	0.35 ± 0.021	(Ferreira da Vinha et al., 2013)
			Peel				0.091 ± 0.0047	
			Seed				0.776	
	Exracted with Hexane for 14 hours, cool crystallization and filtration	N/A	Seed	N/A	-1-acetoxy-2,4-dihydroxy-heptadec-16-ene - 1-acetoxy-2,4-dihydroxy-heptadec-16-yne	Keratinocyte survival assay	91.0 ± 10	(Rosenblat et al., 2011)
	Extracted twice with ethanol at 50°C for 1 h, followed by acetone extraction at 4°C overnight. Extract was dried and re-dissolved in 35 ml hexane and refrigerated at 4°C overnight prior to filtration.		Pulp			Measurement of amount of CPD in cellular DNA post UVB irradiation	37.5 ± 6.2	
							74.5 ± 41	
						ELISA assay	50	
							>5 µg/ml	
	Methanol, Hexane	Hass	Oil	Major phenolic compounds: - P-vanillin - Quercetin - Hydroxyphenylacetic acid - α-Tocopherol	N/A	DPPH assay	N/A	(Ferreira da Vinha et al., 2013)

Table 1: Summary of extraction of bioactive compounds and its cosmeceutical benefits of studies appraised in this review (cont.)

Properties	Extract	Cultivar	Part of Avocado	Active bioactive(s)		Assay(s)/ Test(s)	Values	Reference(s)
				Extract	Pure Compound(s)			
Anti-ageing	Methanol/Chloroform, Acetone	Margarida	Pulp	Phospholipids: - PE - PC - LPC - PI	N/A	Not conducted	N/A	(Züge et al., 2017)
	Acetone, Diethyl ether, Methanol	Maluma	Pulp	- TPC - Carotenoids - Chlorophyll	N/A	- ABTS - DPPH - FRAP	N/A	(Lister et al., 2021)
Anti-tyrosinase	Acetone Diethyl ether					Agar Well Diffusion Assay	5-17	(Hürkul et al., 2021)
						N/A	0-15	

study by Melgar and colleagues (2018) showed contradictory results; the analysis using four different assays, DPPH assay, reducing power, β-carotene bleaching inhibition, TBARS assay indicated that Hass avocado peels generate lower EC50 values compared to Hass avocado seeds. Lower EC50 values indicate greater potency of antioxidant compounds.

An *in-vitro* antimicrobial activity range of 5.00-13.00 mm is yielded via disk diffusion assay with avocado seed and pulp extract (Rodríguez-Carpena et al., 2011). Avocado pulp extracted with acetone, ether and methanol via agar well diffusion assay yielded an inhibitory diameter (mm) with a range of 0-28 (Nguyen et al., 2021). Avocado pulp slices which were dried, grounded and extracted in a water-alcoholic solution showed that 80% of the final product contained mannoheptulose and perseitol, which presents the antimicrobial activity of avocado via invasion assay (Donnarumma et al., 2007; Paoletti et al., 2010).

Anti-inflammatory

Methanol extract exhibits different anti-inflammatory activities with different parts of the avocado used via HRBC membrane stabilization assay (Table 2). Avocado seed, peel and pulp yielded an IC50 (mg/mL) value of 2.03±0.06, 2.01±0.06 and 2.22±0.15. Furthermore, N-hexane exhibits different anti-inflammatory activities with different parts of the avocado used via HRBC membrane stabilization assay. Avocado seed, peel and pulp yielded an IC50 (mg/mL) value of 7.73±0.09, 9.96±1.03 and 5.89±0.89 accordingly (Hürkul et al., 2021). Avocado pulp was extracted twice with ethanol (50°C for 1 h), followed by acetone extraction at 4°C overnight, and re-desolvation in 35 ml hexane and refrigerated using ELISA assay generated a secretion value of IL-6 (PFA: 0.5 μg/mL) of 50 mg/mL (Rosenblat et al., 2011).

Avocado also showed anti-inflammatory activity when *in-vivo*. The leaves of *Persea americana* Mill. (1%, 3% and 10%) yielded the effect of anti-inflammatory when used once daily for six days on adult male Swiss mice (Deuschle et al., 2019). The oil from avocado and soybean extracts cream showed an anti-inflammatory effect when consumed twice daily for 24 weeks. The avocado used as topical 5-alpha avocuta 2% creams also yielded an anti-inflammatory effect when used on human volunteers twice daily for 14 weeks. Furthermore, for eight weeks, rats fed on 10% (w/w) of avocado oils (C-RAO-C, E-URAO-I) also showed an anti-inflammatory effect.

The methanol extract and N-hexane of the avocado seed, peel, and pulp all yield-ed different IC50 values, suggesting that the anti-inflammatory activity may vary de-pending on the part of the plant used. The *in-vivo* studies also show promising results, with the leaves of *Persea americana* Mill. and avocado showing anti-inflammatory effects on mice and humans, respectively. The use of avocado oil in rats also yielded positive results. It would be worthwhile to conduct further research to investigate avocados' potential as an anti-inflammatory agent and determine the specific compounds responsible for these activities.

Wound healing

Avocado has shown significant benefits in wound healing. A study by Oryan and colleagues (2015), showed that an amount of 10mg/ml of Avocado/Soybean Unsaponifiable (ASU) applied to the wound area significantly increased collagen levels in comparison to control groups (P=0.001). Another study by Lamaud and colleagues (1982) on the production of collagen using programmed differential calorimetry reported that avocado and soya bean lipidic non-saponifiables (PIAS) reported a high score for thickness (1.25 ±0.02 N mm-2), elasticity (18.9±0.40 N mm-2), resistance to rupture (8.1±0.25 N mm-2) and elongation to rupture (60.9±1.07%) indicating a high collagen production. Hence, it is shown that avocados can increase the elasticity and reduce the size of the wound in a shorter period of time and in the zone of application, the thermal stability of collagen decreases.

Furthermore, oleic acid, also known as omega-9 fatty acid, was reported as the most prominent active ingredient, with the highest content of 47.20% (Sichani et al., 2021). Interestingly, oleic acid was also found in omega-50% SSFAO or avocado oil, which is used to apply on the wound. Studies have reported that it helps with the contraction of the wound by increasing the anti-inflammatory action with 50% SSFAO or in natural avocado oil (2.50 ± 0.15 cells, 2.71 ± 0.12 cells) in comparison with the EFA control (10.00 ± 0.41 cells) and petroleum jelly control (28.82 ± 1.70 cells). This could be due to the beneficial properties of the avocado such as polyunsaturated fatty acids (PUFA), mono-unsaturated fatty acids (MUFA), beta-sitosterol, beta-carotene, lecithin, minerals, vitamin A, C, D, E, linoleic acid and linolenic acid that allows better wound healing (Sichani et al., 2021).

Anti-tyrosinase

Tyrosinase is an enzyme that initiates the production of melanin, resulting in a darker skin tone (Hürkul et al., 2021). However, constant exposure to UV lights will instantly activate the production of melanin, protecting the skin and thus causing a darker skin tone (Alves et al., 2019). Several studies have investigated the potential of avocado bioactive compounds as skin whitening agents, particularly due to their ability to inhibit the activity of tyrosinase, the enzyme responsible for melanin production.

Catechins structure is reported to enhance the inhibition of tyrosinase activity and in the avocado, it is reported as an effective skin-whitening agent (Laksmiani et al., 2020). The ethyl acetate extract of avocado seeds (25.5%) showed the most catechins compared to ethanol extract (20.87%) and acetone extract (14.48%). The optimal extract that can be used in dermatological applications is n-hexane extracts on exocarp and seeds.

Laksmiani and colleagues (2020) found that avocado fruit extract could effectively inhibit tyrosinase activity and reduce melanin production in human melanoma cells. This study suggests that avocado fruit extract could be used as a natural skin-whitening agent. Another study by Nazir and colleagues (2018) investigated the skin-whitening potential of avocado seed extracts. The study found that the ethyl acetate extract of avocado seeds had the highest concentration of catechins, which are known to inhibit tyrosinase activity. The n-hexane extract of avocado seeds also had skin-whitening properties.

In addition to inhibiting tyrosinase activity, avocado bioactive compounds also protect the skin from UV-induced damage, which can cause hyperpigmentation. The antioxidant properties of avocado, particularly the presence of carotenoids and poly-phenols, can provide photoprotective effects and prevent skin damage caused by UV radiation.

Anti-aging

Anti-ageing studies have also shown that Avocado contains essential fatty acids such as linoleic acid, oleic acid, and linolenic acid, which contribute to hydration, elasticity and firmness of the skin. These properties play major roles in preventing and reducing wrinkles and fine lines. The study by Putri and colleagues (2018) focused on the anti-oxidant capacity of avocado oil topical application, showing that topical application of avocado oil results in smoother skin texture (Putri et al., 2018). Furthermore, Avocado unsaponifiable can be incorporated into topical creams and has been found to be effective as an alternative in treating dermatological conditions such as vulvar lichen sclerosus (VLS) (Felmingham et al., 2020).

Polyhydroxylated fatty alcohols (PFA), specifically 1-acetoxy-2,4-dihydroxy-heptadec-16-ene (Kosińska et al., 2012) and 1-acetoxy-2,4-dihydroxy-heptadec-16-yne (Ferreira da Vinha et al., 2013) have been extracted from avocado seed and pulp with hexane, ethanol and acetone. These two compounds exhibited photo-protective properties, which can slow down the process of skin ageing. The cell viability of keratinocytes treated with PFA of 0.5 μg/ml was 91.0 ± 10% after exposure to UVB irradiation at a dose of 20 mJ/cm (Table 1). The cell viability of PFA-treated samples was much higher than non-PFA-treated samples, with cell viability of 61.0 ± 3%, suggesting that PFA reduces UVB-induced cell death. PFA was also reported to enhance DNA repair in UVB-irradiated keratinocytes (Rosenblat et al., 2011). In another study, Mwinga and colleagues (2019) showed that avocado leaves and pulp had been used topically for anti-ageing purposes such as improving skin complexion, sunlight protection, removing pigmentation and making the skin soft- over the years.

Avocado oil is rich in essential fatty acids such as linoleic acid, oleic acid, palmitic acid and omega fatty acids such as triglycerides and phytosterol. These compounds contribute to skin moisturization by restoring the hydro-lipid shielding skin barrier (Naeimifar et al., 2020). A study on topical cream application with 2% avocado oil twice daily for 4 weeks showed an increase in hydration and an improvement in skin barrier function leading to better skin appearance (Moldovan et al., 2021). Another study was carried out for 12 weeks and reported that wrinkles were reduced from 9.50 ± 1.19 (baseline) to 9.35 ± 1.42 and the volume of nasolabial folds dropped (from 4.68 ± 1.83 (baseline) to 4.33 ± 1.77). These properties can be attributed to polyphenols, triglycerides, proteins, and vitamins A, D, and E (Naeimifar et al., 2020).

In the study by Lister and colleagues (2021), ointments containing different avocado peel extracts were applied twice daily for four weeks on rat skins, which showed higher avocado concentrations of peel extract lead to a higher percentage of hydration, elasticity and collagen levels. Oral consumption of an avocado has also been proven to increase the firmness and elasticity of the skin (Susanne M Henning et al., 2022).

Another study by Naeimifar and colleagues (2020) investigated the effect of avocado oil on skin hydration and elasticity. The research revealed that applying avocado oil topically can notably enhance skin hydration and boost skin elasticity, suggesting its potential as an ingredient in anti-aging products. Moreover, regular consumption of avocado may result in improved elasticity and firmness of facial skin among healthy women (Henning et al., 2022).

Moreover, the phytosterols found in avocado, such as beta-sitosterol, have been shown to have anti-aging properties. These compounds can improve skin texture, reduce the appearance of age spots, and promote collagen production, which can lead to firmer and more youthful-looking skin.

The polyhydroxylated fatty alcohols (PFA) found in avocado seed and pulp showed photo-protective properties; enhancing DNA repair in UVB-irradiated keratinocytes, which can prevent skin damage and premature ageing. The essential fatty acids and phytosterols in avocado oil contribute to skin moisturization and improve skin barrier function, leading to better skin appearance. The consumption of avocados can enhance the firmness and elasticity of the skin.

Bioactive compound extraction methods

Table 1 also lists various extraction techniques used on different parts of the avocado (*Persea americana* Mill), highlighting the resulting bioactive compounds and their potential benefits in cosmetics. Ethyl acetate extracts from the seeds, peel, and pulp of Hass and Fuerte cultivars contain bioactive such as TPC, flavanols, procyanidins, catechins, OH-B, and OH-C, which exhibit strong antioxidant properties (Rodríguez-Carpena et al., 2011). These antioxidants can reduce oxidative stress and mitigate signs of ageing. Similarly, acetone extracts from these parts are rich in antioxidants, further enhancing their anti-ageing potential. Methanol extracts, particularly from the seeds of both cultivars, yield significant quantities of tannins, flavonoids, alkaloids, and polyphenols, all of which contribute to skin protection and rejuvenation (Ekom & Kuete, 2022). Additionally, aqueous and methanol extracts, including ultrasound-assisted techniques, effectively extract high levels of polyphenols and other phytochemicals, which offer broad-spectrum antimicrobial and anti-inflammatory benefits essential for wound healing and skin health. Thus, the extraction technique and avocado part significantly influence the presence and concentration of bioactive compounds, determining their specific cosmetic applications.

Acetone extracts have been found to exhibit the greatest antioxidant capacity, followed by methanol and ethyl acetate, and the ratio of acetone has also been shown to affect the antioxidant capacity of avocado extracts. Overall, the varying levels of antioxidant capacity exhibited by different avocado cultivars and plant parts highlight the importance of an appropriate extraction method and solvent.

Methanol extracts produce the highest MIC (μg/mL) value presented by its MIC (μg/mL) of 64-128 and MBC (μg/mL) of 512->2048 via antimicrobial assay when extracting avocado seed (Lin et al., 2017). Whereas avocado peel extracted with 80% ethanol via antibacterial assay produces a MIC (mg/ml) of 0.015-0.030 and MBC (mg/mL) of 0.030-0.450. Furthermore, when the avocado seed was extracted with 80% ethanol via antibacterial assay, a MIC (mg/mL) of 0.020-0.150 and MBC (mg/mL) of 0.030-0.300 was detected. Whereas extraction via antifungal assay showed a MIC (mg/mL) of 0.020-0.300.

In-vitro and in-vivo studies on bioactive compounds of avocado

In-vivo studies revealed that the application of bio-active compounds from avocados accelerates the wound-healing process by promoting epithelialization and wound contraction, while also reducing inflammatory cells (Table 2).

Table 2 summarizes a comparison of the antioxidant properties of avocado extracts from different cultivars, using various solvents and extraction techniques. Ethyl acetate extraction demonstrated moderate antioxidant activity in CUPRAC assays (seeds: 58.00 ± 15.55, peels: 56.40 ± 21.19), but relatively lower activity in DPPH assays (seeds: 17.78 ± 4.34, peels: 17.85 ± 7.07) and ABTS assays (seeds: 21.57 ± 7.51, peels: 16.12 ± 6.98). This method effectively extracts phenolic compounds such as flavonols, procyanidins, and catechins, but results in lower antioxidant activities compared to other solvents due to limited solubility of specific bioactive compounds.

On the other hand, acetone extraction demonstrated significantly higher antioxidant activities across all assays, particularly in the CUPRAC (Hass seed: 275.36 ± 59.09, peel: 218.04 ± 42.42; Fuerte seed: 353.43 ± 75.83, peel: 456.24 ± 77.07) and DPPH assays (Hass seed: 130.26 ± 36.80). The high efficacy of acetone extraction can be attributed to its ability to dissolve a wider range of antioxidant compounds. However, it may also extract non-target substances, which complicates the extraction process.

Each extraction method has its advantages and disadvantages, with ethyl acetate offering specificity for certain phenolics, and acetone providing higher overall antioxidant yields, but with the potential for extracting a broader range of compounds.

In-vivo studies suggest that avocado bioactive compounds may aid in wound healing and have anti-aging effects on the skin (Susanne M. Henning et al., 2022)

The inclusion of *in vivo* and *in vitro* studies provides a more comprehensive understanding of the potential benefits of these compounds, however, there are still several limitations to consider. One limitation is the wide variety of sample sizes and study designs of studies included in this review; making it difficult to compare and generalize the results, as different sample sizes and types may produce different out-comes. The use of animal models in vivo studies may not accurately reflect the out-comes of cosmeceutical actions on human skin due to differences in skin structures. Another limitation is excluding studies published in languages other than English, which may result in selection bias, potentially limiting the scope of the review, as important studies published in other languages may have been missed.

Conclusion

To conclude, review summarizes the antioxidant, antimicrobial, anti-inflammatory, wound healing, anti-ageing and anti-tyrosinase properties activities of *Persea americana* Mill. and its potential application in cosmeceuticals. It is clear that there is growing interest in the potential benefits of avocado bioactive compounds, including their antioxidant, antimicrobial, anti-inflammatory, wound healing, anti-aging, and anti-tyrosinase properties. The review also highlights the importance of considering the different bioactive compound extraction solvents and methods used, as this can have a significant impact on the effectiveness of these compounds. However, further research is needed to understand better the mechanisms by which these compounds act on the skin and to optimize extraction methods to improve the yield.

Table 2: *In-vivo* studies on cosmeceutical activities of avocado

Cosmeceutical Action	Mechanism of action	Compound used	Part of avocado	Amount	Duration	Sample	Compound	References
Wound healing	Increase rate of wound contraction and epithelialization	Avocado/soybean unsaponifiables (ASU) topical cream with a ratio of 1:2.	Avocado unsaponifiables	1mL ASU/cream (10mg ASU/ml cream)	10 days	Adult male Wistar rats	- Polyunsaturated fatty acids (PUFA) - Monounsaturated fatty acids (MUFA) - β-sitosterol - β-carotene - Lecithin - Minerals - Vitamins A, C, D, and E - Oleic acid - Linoleic acid - Linolenic acid	(Oryan et al., 2015)
	Promote increased collagen synthesis and decreased numbers of inflammatory cells	Semisolid formulation of Avocado Oil (SSFAO 50%)	NA	±100 mg once daily	14 days	64 adult Wistar rats, male and female, with ages between 3-4 months and weighing 200–250g	- Flavonoids - Polyphenols - Tannins	(A. P. de Oliveira et al., 2013)
	- Increase the rate of wound contraction and epithelialization - Reduce the number of Colony Forming Units (CFU) of S. aureus at the infection site	Carbopol (1%) gels containing 1%, 5% and 10% MeOH extract of P. americana.	Seed	Once daily	20 days	63 male Wistar albino rats aged 8-10 weeks (150–200g)	- Unsaturated fatty acids (PUFAs) - Linoleic acid - Linolenic acids - Unsaturated fatty acids (MUFAs) - Oleic acid - Beta-sitosterol - Beta-carotene - Lecithin - Minerals - Vitamins A, C, D, and E. - Fatty acids (oleic, linoleic, and linolenic acids	(Ekom & Kuete, 2022)

Table 2: *In-vivo* studies on cosmeceutical activities of avocado (cont.)

Cosmeceutical Action	**Mechanism of action**	**Compound used**	**Part of avocado**	**Amount**	**Duration**	**Sample**	**Compound**	**References**
Wound healing	Increase collagen synthesis, reduce the number of inflammatory cells, accelerate the process of coagulation and accelerate the regeneration of epithelium thus help increase the wound healing process	Avocado Oil derived from squeezing avocado paste (Iran)	Oil	Twice daily	14 days	30 Winstar Rats (divided into 3 groups, 10 each)	- Fatty essentials acids like linoleic (6 - 30%), linolenic (0.4 - 4%) acids, and oleic acid (31 - 70%) - β-sitosterol - β-carotene - Lecithin - Minerals - Vitamins A, C, D and E	(Sichani et al., 2021)
Anti-aging	- Repair dry, damaged or chapped skin - Increase hydration - Improve or restore skin barrier function - Improve skin appearance	O/W and W/O creams containing 2% of avocado oil	Oil	Twice a day	4 weeks	O/W - 4 volunteers (23-50 years old) W/O - Volunteers (35-55 years old)	- Oleic acid - Linoleic acid - Palmitic acid - Phytosterols - Polyphenols - Triglycerides - Proteins - Vitamin A, D, E	(Moldovan et al., 2021)
	- Promotes firmness and elasticity that helps to reduce wrinkles without altering the hydration index	Topical Cream (O/W) - Avocado Oil, Saffron extract and honey fragrance obtained from Barij Essence Company	Oil	Apply ONE fingertip unit of cream on the face once daily	12 weeks	20 participants of both genders	- Alkaloids - Tannins - Phenols - Flavonoids - Glycosides	(Naeimifar et al., 2020)
	Increase average hydration, elasticity, and collagen levels of skin	Avocado Peel Extract Ointment 2.5%, 5%, 7.5%, 10%	Peel	Twice daily	4 weeks	25 male rats	- Lutein - Zeaxanthin	(Lister et al., 2021)

Table 2: *In-vivo* studies on cosmeceutical activities of avocado (cont.)

Cosmeceutical Action	**Mechanism of action**	**Compound used**	**Part of avocado**	**Amount**	**Duration**	**Sample**	**Compound**	**References**
Anti-aging	Increased firmness and elasticity of the forehead and reduced tiring of repeat stretching of the forehead skin	*Persea Americana* oral consumption	Fruit	One avocado once daily	8 weeks	39 female participants with Fitzpatrick skin type II-IV	- Phenolic compounds such as caffeic, ferulic, vanillic, and hydroxybenzoic acids and flavonoids such as quercetin, and kaempferol - Catechin - Chlorogenic acid - Rutin	(Susanne M Henning et al., 2022)
Anti-inflammatory	- Prevent UVB-induced mechanical allodynia - Antinociceptive - Anti-inflammatory	*Persea Americana* (1%, 3%, 10%)	Leaves	Once daily	6 days	Adult male Swiss mice (25–30 g)	ASE cream: - Hyaluronic acid - Vitamin E - Sodium carboxymethyl beta glucan - dimethylmethoxy chromanol - trimethylglycine ASE supplement: - Vitamin E - Para-aminobenzoic acid (PABA) - Phytosterols	(Deuschle et al., 2019)
	- Anti-fibrotic, emollient, lenitive actions - Effective alternatives in the treatment of symptoms and signs of mild to moderate vulvar lichen sclerosus (VLS)	Avocado and soybean extracts (ASE) cream and dietary supplements	Oil	Twice daily	24 weeks; 12 weeks	23 participants	Five-Alpha Avocuta	(Borghi et al., 2015)

Authors contributions

Conceptualization, G.B.H; methodology, S.M; formal analysis, Y.L.L, L.X.N., L.W.Y.; data curation, Y.L.L, L.X.N., L.W.Y writing—original draft preparation, Y.L.L, L.X.N., L.W.Y.; writing—review and editing, S.M., G.B.H.; supervision, G.B.H. All authors have read and agreed to the published version of the manuscript. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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