Persea americana

Subjects: Biology

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Persea americana, commonly known as avocado, has recently gained substantial popularity and is often marketed as a "superfood" because of its unique nutritional composition, antioxidant content, and biochemical profile. However, the term "superfood" can be vague and misleading, as it is often associated with unrealistic health claims. This article provides a comprehensive summary and assessment of the studies performed in the literature to understand the nutritional and therapeutic properties of avocado and its bioactive compounds.

avocado | Persea americana | metabolites | antioxidants | anticancer | antimicrobial | anti-inflammatory | diabetes | cardiovascular diseases (CVD) | bioavailability and pharmacokinetic

1. Introduction

Persea americana (commonly known as avocado, avocado pear, or alligator pear) is native to Mexico and Central America, and a member of the flowering plant family Lauraceae [1][2]. Botanically, avocado fruit is a berry with a single large seed [3]. Mexico is the leading producer of avocados worldwide [2]. The term "superfood" refers to foods that are beneficial to human health due to their high levels of nutrients and/or bioactive phytochemicals such as antioxidants [4]. In particular, avocado has recently gained dramatic popularity [5] and is often referred to as a "superfood" because of its unique nutritional and phytochemical composition compared to other fruits. This has led to an exponential increase in avocado consumption from 2.23 pounds per capita in 2000 to 7.1 pounds per capita in 2016 in the United States [6]. However, the term "superfood" has been used ambiguously in popular media, and often marketed with misleading health claims of preventing and curing ailments. Considering their immense popularity and diverse biochemical content, avocados have also been extensively used in the food, nutraceutical, pharmaceutical, and cosmetic industries. In addition, their health-benefiting properties have been investigated in a number of preclinical and clinical studies in the last few decades. The present review article is focused on the comprehensive summary and assessment of research performed to understand the role of avocado and its bioactive compounds in the prevention and treatment of various ailments, including cancer, microbial, inflammatory, diabetes and cardiovascular diseases. The studies emphasizing the nutritional composition of avocado, its major metabolites, and their pharmacokinetic properties are also reviewed and summarized. Furthermore, this review highlights several interesting aspects for future research on avocados.

2. The Vast Array of Secondary Metabolites of Avocado and Their Biological Significance

Using "Avocado" and "*Persea*" as search descriptors with a focus for pharmacologically active metabolites, various avocado metabolites were retrieved from Combined Chemical Dictionary v23.1 (CCD) [7] and The Human Metabolite Database (HMDB) [8]. In addition to the *P. americana*, the search strategy also covered other *Persea* species such as *P. mexicana, P. indica, P. gratissima, P. obovatifolia*, and *P. borbonia* (**Table 1**). As per the literature, most bioactive compounds were isolated predominantly from *P. americana.* Other synonyms of *P. americana* are *P. gratissima, Laurus persea, P. drymifolia*, and *P. nubigena* [9]. The metabolite arsenal can be classified chemically into eight main classes, including fatty alcohols, furan derivatives, carotenoids, carbohydrate, diterpenoids, lignan derivatives, and miscellaneous compounds, as shown in **Figure**

1, **Figure 2**, **Figure 3**, **Figure 4**, **Figure 5**, **Figure 6**, **Figure 7** and **Figure 8**, and **Table 1**. In brief, fatty alcohols isolated from avocado showed different degrees of unsaturation and alkyl chain length with several levels of hydroxylation and subsequent acetylation (**Figure 1**). These fatty alcohols have been reported to exhibit antiviral, cytotoxic, antifungal, trypanocidal, and antioxidant activity [10][11][12][13][14][15][16][17][18][19][20][21]. Phenolic compounds (**Figure 2**, and **Table 1**) of different chemical classes from simple organic acids such as gallic acid to larger flavonoids, anthocyanidins, and tocopherols were isolated from *Persea* species with significant antioxidant, neuroprotective and cardioprotective activities [22][23][24][25][26][27][28]. The antioxidant properties of avocados were also ascribed to their carotenoid content in many studies [24][28][29][30] (**Figure 3**). Moreover, sugar alcohol and ketoses with variable carbon chain length were isolated from avocado (**Figure 4**). Notable insecticidal, cytotoxic, and antifungal activities were also reported for the furan and furanone derivatives isolated from *Persea* species [18][31][32][33][34][35][36][37] (**Figure 5**), where the saturation of the furan ring was detrimental for the insecticidal activity [38]. The insecticidal activity of the furan derivatives was augmented by the diterpenoids compounds [39][40][41][42][43], especially in *P. indica* (**Figure 6**). Overall, avocado contains a vast array of secondary metabolites of different chemical classes which may attribute to its diverse biological activities.

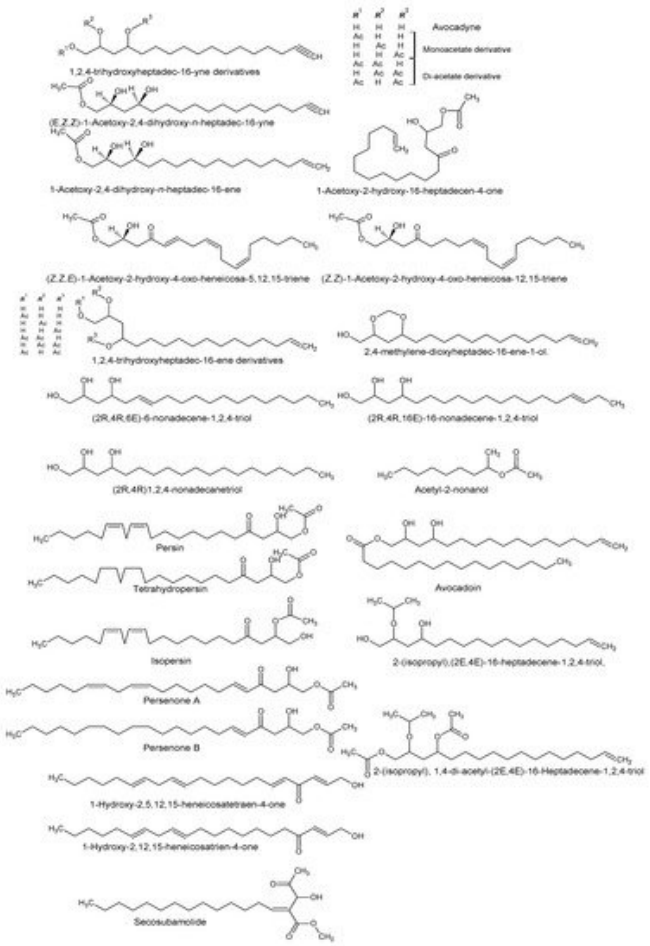

Figure 1. Fatty alcohols isolated from avocado.

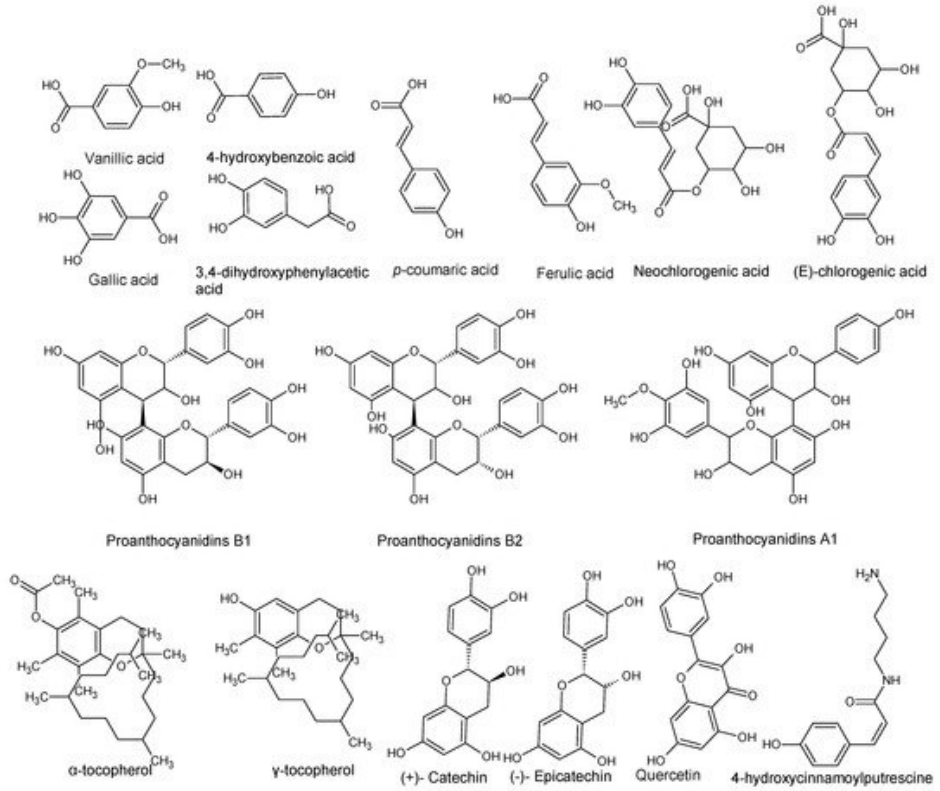

Figure 2. Phenolic compounds isolated from avocado.

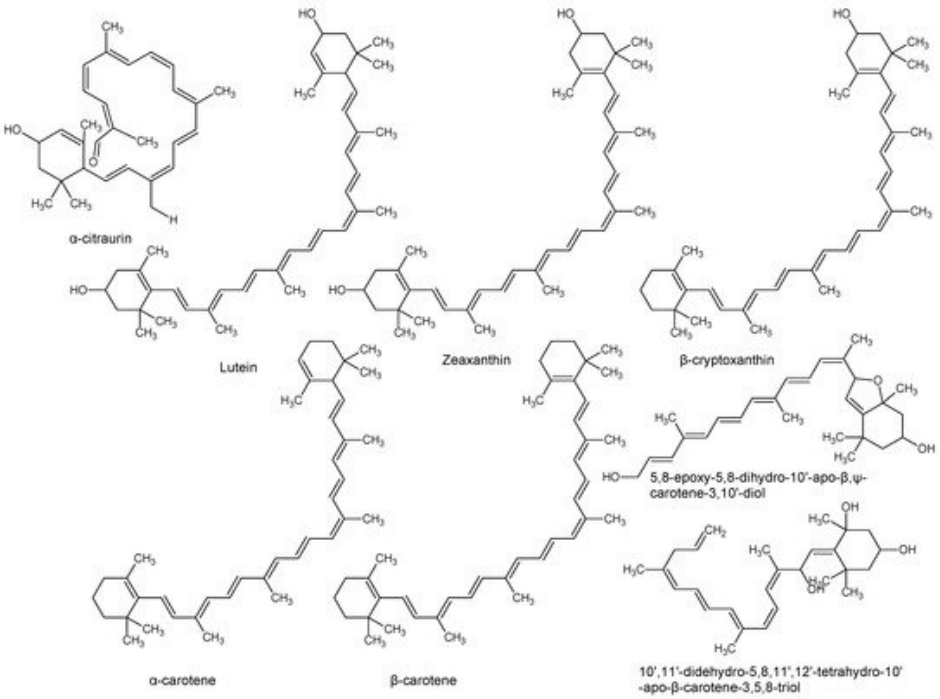

Figure 3. Carotenoids isolated from avocado.

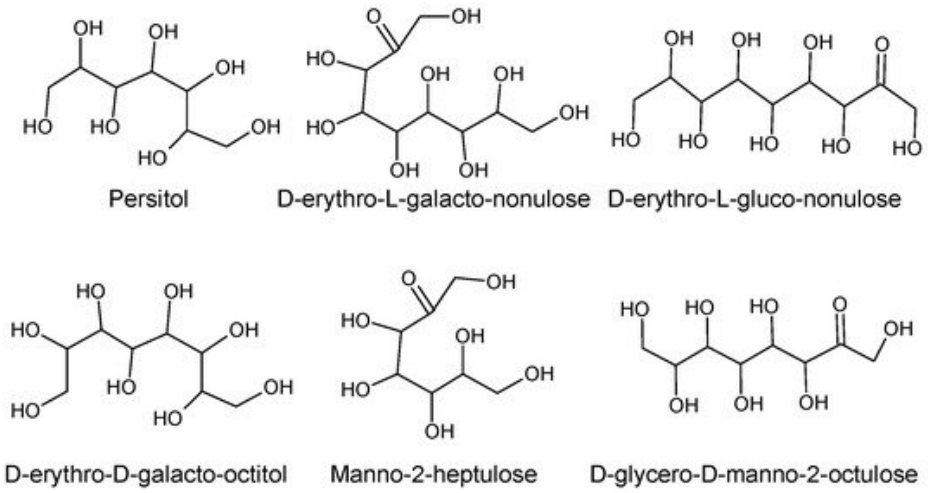

Figure 4. Sugars and sugar alcohol isolated from avocado.

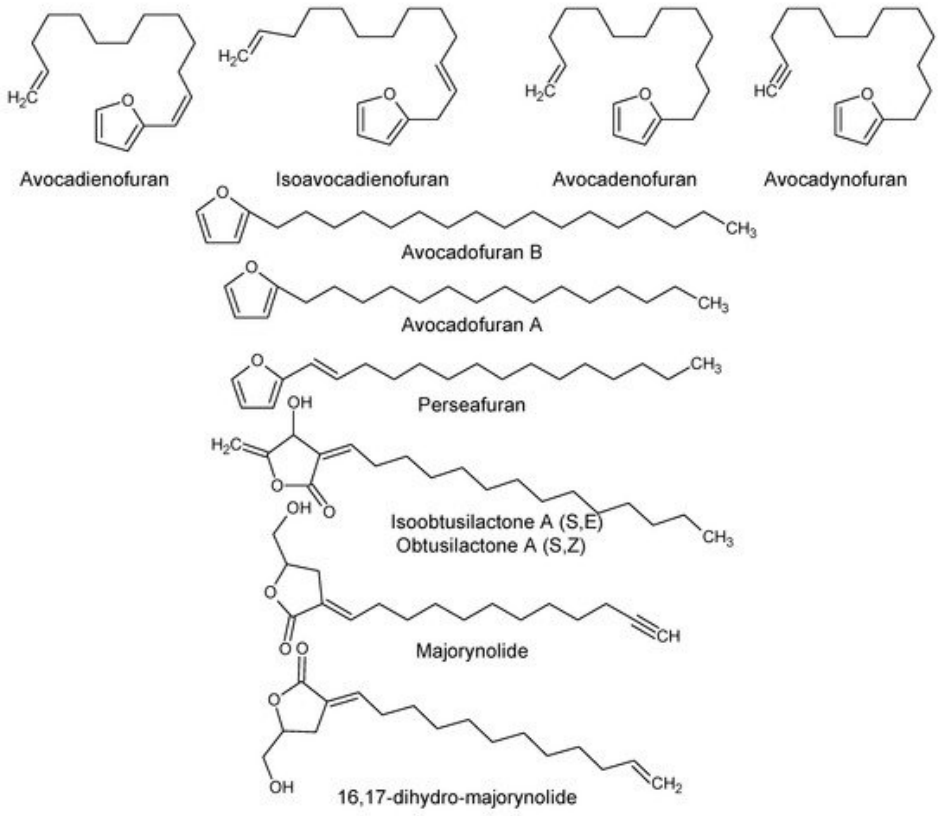

Figure 5. Furan and furanone derivatives isolated from avocado.

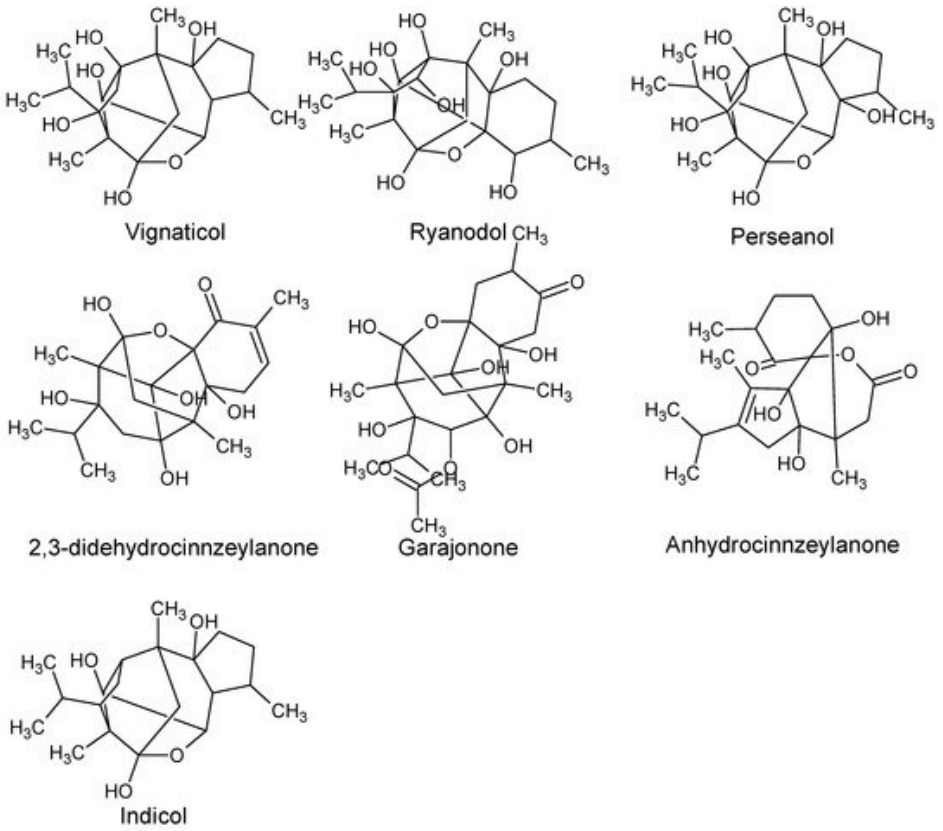

Figure 6. Diterpenoids isolated from avocado.

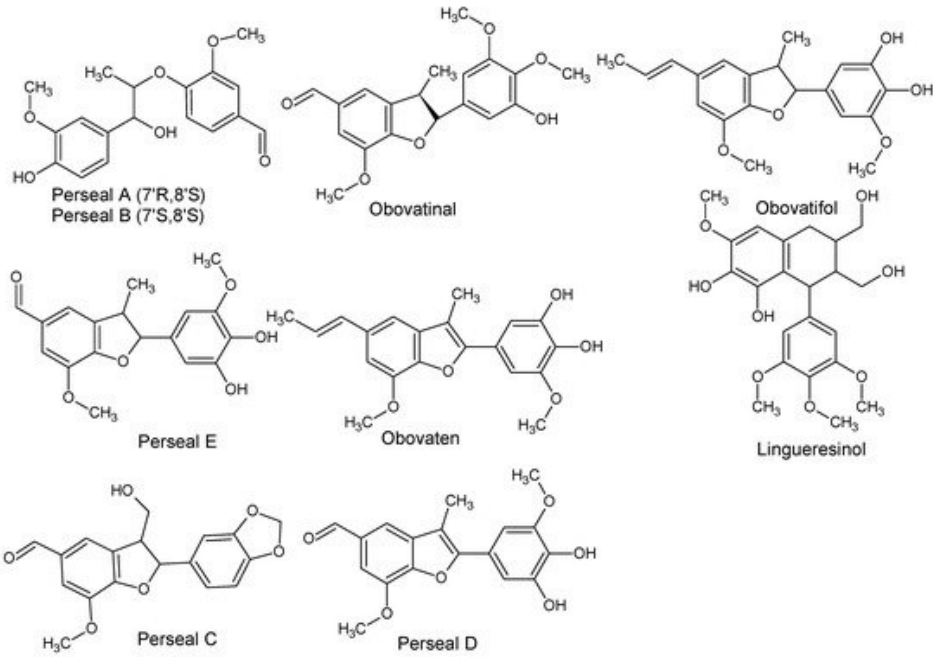

Figure 7. Norlignans, neolignans, and lignans isolated from avocado.

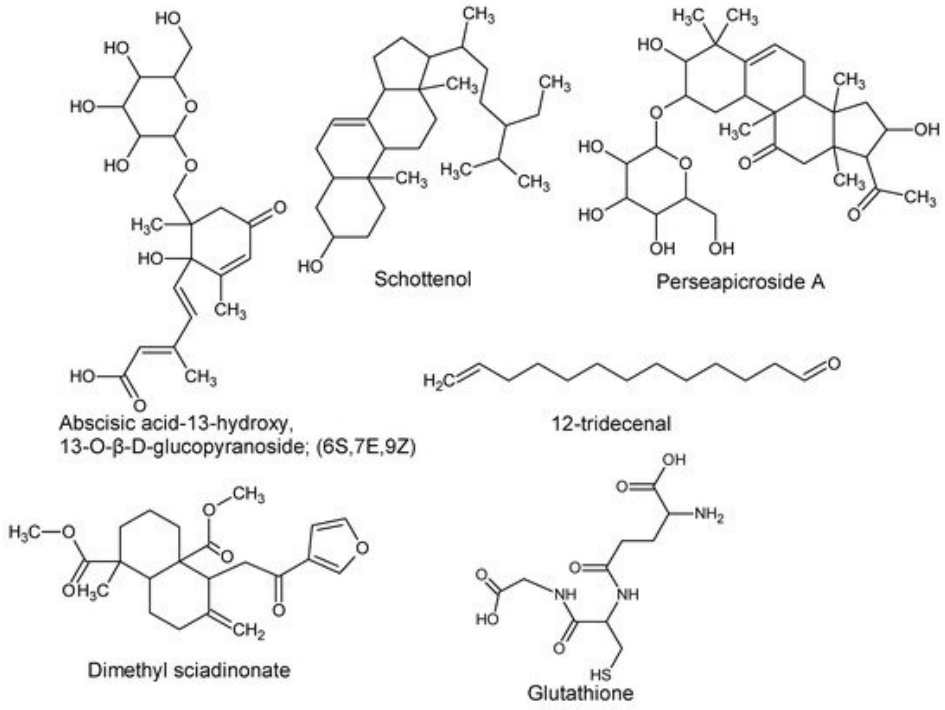

Figure 8. Miscellaneous compounds isolated from avocado.

Table 1. Metabolites isolated from *Persea* species.

Compound Name and Synonyms	Source	Extracts of Different Parts Used	Biological Significance	Reference
Fatty alcohols				
(2R,4R)-1,2,4-trihydroxyheptadec-16-yne [Avocadyne] 1,2,4-trihydroxyheptadec-16-ene 2,4-methylene-dioxyheptadec-16-ene-1-ol 1-acetoxy-2,4-dihydroxyheptadec-16-yne (2R,4R)1,2,4-Nonadecanetriol. (2R,4R,6E)-6-Nonadecene-1,2,4-triol (2R,4R,16E)-16-Nonadecene-1,2,4-triol [Avocadenol D]	*P. americana*	Pulp and seeds	Inhibition of the dengue virus replication. Cytotoxic, insecticidal, antimycobacterial, and trypanocidal activity.	[10][11][12][13][21]
(Z,Z)-1-Acetoxy-2-hydroxy-4-oxo-heneicosa-12,15-triene (Z,Z,E)-1-Acetoxy-2-hydroxy-4-oxo-heneicosa-5,12,15-triene 1,2,4-trihydroxyheptadec-16-ene	*P. americana*	Idioblast cells of pulp	Antifungal activity	[14]
(2R,4R)16-Heptadecene-1,2,4-triol and the following derivatives: 1,2, or 4 acetate (1,2), (1,4) or (2,4) di acetate 1-hexadecanolyl derivative (Avocadoin)	*P. americana*	Peel, idioblast cell, and leaves	Antifungal, cytotoxic, and insecticidal activity.	[11][14][15]
2-(isopropyl)-(2E,4E)-16-Heptadecene-1,2,4-triol 2-(isopropyl), 1,4-di-acetyl-(2E,4E)-16-Heptadecene-1,2,4-triol	*P. gratissima*	Leaves	-	[7]

Compound Name and Synonyms	Source	Extracts of Different Parts Used	Biological Significance	Reference
(2E,5E,12Z,15Z) 1-Hydroxy-2,5,12,15-heneicosatetraen-4-one 1-Hydroxy-2,12,15-heneicosatrien-4-one	*P. americana*	-	-	[7]
Acetyl-2-nonanol	*P. gratissima*	Leaves	-	[7]
Persin Tetrahydropersin Isopersin Tetrahydropersin	*P. americana*	Idioblast oil cells	Surfactant and emulsifier, nutrient, membrane stabilizer, energy source, and energy storage.	[8][16][17]
1-Acetoxy-2-hydroxy-16-heptadecen-4-one	*P. americana*	Pulp		[18]
Persenone A and B	*P. americana*	Pulp	Nitric oxide and superoxide generation inhibitors.	[19]
Secosubamolide	*P. americana*	Bark	Cytotoxic activity	[20]
Phenolics				
Gallic acid 3,4-Dihydroxyphenylacetic acid 4-Hydroxybenzoic acid Vanillic acid p-Coumaric acid Ferulic acid Quercetin	*P. americana*	Pulp oil and varied by ripening and peeling	Antioxidant activity	[28]
(+)-Catechin (−)-Epicatechin Neochlorogenic acid procyanidins	*P. americana*	By-products	Antioxidant and neuroprotective activity.	[22]
Proanthocyanidins B1, B2 and A-type trimer	*P. americana*	Seeds	Cytotoxic to HaCat cells.	[23]
Tocopherols (Vitamin E) α-tocopherol γ-tocopherol	*P. americana*	Pulp and pulp oil varied by ripening and peeling	Antioxidant activity	[24][28]
(*E*)-Chlorogenic acid (Caffeylquinic acid, Caffetannic acid, Helianthic acid, Igasuric acid)	*P. americana*	-	Antioxidant, antimicrobial (antibacterial and antiviral) hepatoprotective, cardioprotective, anti-hypertension, anti-obesity, anti-inflammatory,	[7][25]

Compound Name and Synonyms	Source	Extracts of Different Parts Used	Biological Significance	Reference
			antipyretic, neuroprotective, central nervous system stimulator.	
Scopoletin	*P. americana*	-	Anti-oncogenic and antioxidant activity.	[7][26]
4-Hydroxycinnamoylputrescine (4-Coumaroylputresine)	*P. gratissima*	-	Nutrient, promotes cell multiplication of tobacco explants.	[7][27]
Carotenoids				
Lutein zeaxanthin β-cryptoxanthin α-carotene β-carotene (pro-vitamin A, retinol)	*P. americana*	Pulp and pulp oil varied by ripening and peeling	Cytotoxic to prostate cancer cell lines, antioxidant, reduces the photosensitivity reactions in erythropoietic protoporphyria patients.	[24][28]
10',11'-Didehydro-5,8,11',12'-tetrahydro-10'-apo-β-carotene-3,5,8-triol 5,8-Epoxy-5,8-dihydro-10'-apo-β,ψ-carotene-3,10'-diol	*P. americana*	Pulp	Surfactant and emulsifier, nutrient, membrane stabilizer, energy source and energy storage.	[8][29]
α-Citraurin (3-Hydroxy-8'-apo-ε-caroten-8'-al)	*P. americana*	Pulp		[30]
Carbohydrates				
Perseulose	*P. gratissima*	Leaves, fruit, and seeds	Nutrient, membrane stabilizer, energy source and energy storage.	[44]
d-erythro-l-galacto-Nonulose	*P. americana*	Pulp		[45]
d-erythro-l-gluco-Nonulose	*P. americana*	Pulp		[46]
d-erythro-d-galacto-Octitol	*P. gratissima*	Pulp		[47]
d-manno-2-Heptulose	*P. gratissima* *P. americana*	Pulp		[7][47]
d-glycero-d-manno-2-Octulose	*P. gratissima*	Pulp		[47]
Furan derivatives				
Avocadofuran B (2-Heptadecylfuran)		Pulp	Insecticidal activity	[31][32]

Compound Name and Synonyms	Source	Extracts of Different Parts Used	Biological Significance	Reference
P. americana				
Avocadofuran A (2-Pentadecylfuran)	*P. americana*	Idioblast oil cells		
Avocadienofuran	*P. americana* *P. indica*	Seed oil pulp	-	[33][34]
Perseafuran [*(E)*-2-(1-Pentadecenyl) furan]				
Isoavocadienofuran		Seeds		
Avocadenofuran	*P. americana*	Pulp		[18]
Avocadynofuran	*P. americana* and *P. indica*	Pulp		[18][33]
Furanone derivatives				
Obtusilactone A (Borbonol)	*P. americana, P. borbonia* and other *Persea spp.*	Idioblast oil cells	Antifungal and anticancer activity.	[35][36]
Isoobtusilactone A (Borbonol 2)	*Persea spp*	Idioblast cell oil of pulp	Antifungal and anticancer activity.	[35][37]
Majorynolide	*P. major*	-	Cytotoxic, weak antimycobacterial activity.	[33]
16,17-Dihydro-Majorynolide	*P. major* and *P. indica*	-		
Diterpenoids				
Perseanol Vignaticol Indicol	*P. indica*	Branches	Insecticidal and antifeedant activity.	[39][40]
Ryanodol 2,3-DidehydrocinnzeylanoneAnhydrocinnzeylanoneGarajonone			Insecticidal and toxic to mice.	[41][42][43]
Norlignans/Neolignans/Lignans				
Perseal A ((7'R,8'S)4',7'-Dihydroxy-3,3'-dimethoxy-8,9-dinor-4,8'-oxylignan-7-al) Perseal B ((7'S,8'S) 4',7'-Dihydroxy-3,3'-dimethoxy-8,9-dinor-4,8'-oxylignan-7-al) Obovatinal	[61]			[48][49][50]

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Nutritional Composition	Unit	Value Per 100 g	1 Fruit 136 g	1 Serving 30 g
1. Proximate				
Water	g	72.3	98.4	21.7
Energy	kcal	167	227	50
Energy (insoluble fiber adjusted)	kcal	148	201	44
Protein	g	1.96	2.67	0.59
Total lipid (fat)	g	15.41	21	4.62
Ash	g	1.66	2.26	0.5

Nutritional Composition	Unit	Value Per 100 g	1 Fruit 136 g	1 Serving 30 g
Carbohydrate	g	8.64	11.8	2.59
Fiber	g	6.8	9.2	2
Sugars	g	0.3	0.41	0.09
Starch	g	0.11	0.15	0.03
2. Minerals				
Calcium	mg	13	18	4
Iron	mg	0.61	0.83	0.18
Magnesium	mg	29	39	9
Phosphorus	mg	54	73	16
Potassium	mg	507	690	152
Sodium	mg	8	11	2
Zinc	mg	0.68	0.92	0.2
Copper	mg	0.17	0.23	0.05
Manganese	mg	0.15	0.2	0.05
Selenium	ug	0.4	0.5	0.1
3. Vitamins and Phytochemicals				
Vitamin C	mg	8.8	12	2.6
Thiamine	mg	0.08	0.1	0.02
Riboflavin	mg	0.14	0.19	0.04
Niacin	mg	1.91	2.6	0.57
Pantothenic acid	mg	1.46	2	0.44
Vitamin B-6	mg	0.29	0.39	0.09
Folate, dietary folate equivalents	µg	89	121	27
Choline total	mg	14.2	19.3	4.3
Betaine	mg	0.7	1	0.2
Vitamin B-12	µg	0	0	0
Vitamin A	µg	7	10	2
β-Carotene	µg	63	86	19
α-Carotene	µg	24	33	7
β-Cryptoxanthin	µg	27	37	8

Nutritional Composition	Unit	Value Per 100 g	1 Fruit 136 g	1 Serving 30 g
Lutein + zeaxanthin	µg	271	369	81
Vitamin E (α-tocopherol)	mg	1.97	2.68	0.59
Tocopherol β	mg	0.04	0.05	0.01
Tocopherol γ	mg	0.32	0.44	0.1
Tocopherol δ	mg	0.02	0.03	0.01
Vitamin K1 (phylloquinone)	µg	21	28.6	6.3
4. Lipids				
Fatty acids, total monounsaturated	g	9.799	13.3	2.94
16:1	g	0.698		
17:1	g	0.01		
18:1	g	9.066		
20:1	g	0.025		
Fatty acids, total saturated	g	2.126	2.9	0.64
8:0	g	0.001		
16:0	g	2.075		
18:0	g	0.049		
Fatty acids, total polyunsaturated	g	1.816	2.47	0.55
18:2	g	1.674		
18:3	g	0.125		
18:3 n-3 c,c,c (ALA)	g	0.111		
18:3 n-6 c,c,c	g	0.015		
20:3	g	0.016		
[3] Cholesterol	mg	0	0	0 [64]
Stigmasterol	mg	2	3	1
Campesterol [65]	mg	5	7	2
β-sitosterol	mg	76	103	23 [66]

Fat contributes to most of the calories in an avocado. A 1000-kJ portion of avocado contains about 25 g of fat, most of which are healthier monounsaturated fatty acids (MUFA) [64]. The lipid content in avocados is higher than in other fruits. Most lipids found in avocados are polar lipids (glycolipids and phospholipids), which play a fundamental role in various cellular processes such as the functioning of the cell membranes as second messengers [67]. These lipids are also used to make emulsions of water and lipids, and have a wide variety of applications in food, pharmaceuticals, and cosmetics industries [68]. Compared to other vegetable oils, avocado oils are high in MUFA (oleic and palmitoleic acids) and low in polyunsaturated fatty acids (linoleic acid and linolenic acid) [3]. Oleic acid is the principal fatty acid in avocado, comprising 45% of its total fatty acids [69], and during the ripening process, palmitic acid content decreases and oleic acid content increases [70]. In terms of its total fat

content and fatty acid composition, avocado oil is considered to be similar to olive oil [71]. Other fatty acids present include palmitic and palmitoleic acids with smaller [64] amounts of myristic, stearic, cinolenic, and arachidonic acids [62]. However, the compositions of these fatty acids largely depend on the cultivars, stage of maturity, and part of the fruit and geographic location of plant growth [62]. Avocado spread instead of other fatty alternatives such as butter, cream cheese, and mayonnaise on sandwiches can help significantly reduce the intake of calories, saturated fat, sodium, and cholesterol.

Avocados are notable for their potassium content (>500 mg/100 g of fresh weight), and it provides 60% more than an equal serving of banana [72]. Potassium intake helps to maintain cardiovascular health and muscle function by regulating blood pressure through the modulation of liquid retention in the body [65]. In addition, potassium regulates the electrolyte balance in the body, which is important for the conduction of electrical signals in the heart (i.e., a steady, healthy heart rate) [65]. The high potassium and low sodium contents in the diet are shown to protect against cardiovascular diseases [3]. Moreover, avocados contain a number of other minerals, including phosphorus, magnesium, calcium, sodium, iron, and zinc (<1 mg/g of fresh weight) [73].

Vitamins such as β-carotene, tocopherol, retinol, ascorbic acid, thiamine, riboflavin, niacin, pyridoxine, and folic acid are also abundantly found in avocado, which are of great importance for overall health and well-being (**Table 2**) [62][74]. Carotenoids, including lutein, zeaxanthin, and α- and β-carotene found in the pulp of the avocado are potent free radical scavengers [65][74]. The lutein content of avocado is higher than any other fruit, which comprises about 70% of its total carotenoid content [65]. The colour of avocado pulp is predominantly attributed to the higher content of xanthophylls (lutein and zeaxanthin). Seasonal variations in the phytochemical profile of avocado especially carotenoids, tocopherol, and fatty acid content have also been reported [65]. Due to their fat-soluble nature, these bioactive compounds have been shown to promote vascular health [65]. Xanthophylls suppress the damage of blood vessels by decreasing the amount of oxidized low-density lipoproteins (LDL) [75]. Additionally, lutein and zeaxanthin have been reported to slow down the progression of age-related macular degeneration, cataracts, and cartilage deterioration [74][76]. Carotenoids in general were demonstrated to protect the skin from ultraviolet radiation-associated oxidation and inflammation [62]. Furthermore, a 68 g serving of Hass avocado contains about 57 mg of phytosterols, which is significantly higher compared to other fruits (about 3 mg per serving) [65]. Avocado phytosterols have been reported to reduce the risks of coronary heart disease [65]. The American Heart Association recommends the consumption of 2–3 g of sterols and stanols per day to promote heart health [65][77]. They are the plant analogues of cholesterol and can be classified into three major groups consisting of β-sitosterol, campesterol, and stigmasterol [78]. The most abundant phytosterol present in avocado is β-sitosterol (76.4 mg/100g), followed by campesterol (5.1 mg/100g) and stigmasterol (<3 mg/100g) [79]. In addition to its cholesterol-lowering activity, β-sitosterol has been demonstrated to inhibit the production of carcinogenic compounds, alleviate symptoms associated with benign prostatic hyperplasia, and strengthen the immune system [79]. In summary, these compounds have been hypothesized to work in conjunction in the prevention of oxidative stress and age-related degenerative diseases [80].

4. Antioxidant Properties of *P. americana*

Considering the health risks associated with synthetic antioxidants, the extraction, isolation, and identification of antioxidants from natural sources have become primary research focuses of the food, nutraceutical, and pharmaceutical industries in recent years [81][82][83]. Annually, over three million tons of avocados are produced worldwide, with only the pulp being used, while the seeds and peel are discarded [2]. Waste utilization by exploiting the phytochemical content of avocado by-products such as seeds and peels will add more value to the avocado industry and may lead to novel product development [84]. **Table 3** represents the studies currently available in the literature emphasizing the role of *P. Americana* plant as the source of potent antioxidants. Different parts of the plant, including the leaf, fruit pulp, peel, and seed have been widely studied for their antioxidant properties using conventional spectroscopic assays such as 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid diammonium salt (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH), oxygen radical absorbance capacity (ORAC), cupric-

reducing antioxidant capacity (CUPRAC), and ferric reducing ability of plasma (FRAP) as well as more sensitive analytical techniques including high-performance liquid chromatography (HPLC), high-performance liquid chromatography-mass spectrometry (HPLC-MS), gas chromatography-mass spectrometry (GC-MS) and gas chromatography-flame ionization detector (GC-FID). Hass is the most explored avocado variety in terms of its antioxidant properties, which can perhaps be attributed to the popularity and easier availability of this variety. It is evident from the studies performed so far that phenolic compounds (including phenolic and hydroxycinnamic acids, flavonoids, and condensed tannins), carotenoids, α, β, γ, and δ-tocopherols, acetogenins, monounsaturated and polyunsaturated fatty acids are the key antioxidants found in avocado. Moreover, most of these studies have reported significant positive correlations between the phenolic compounds and antioxidant capacity of avocado extracts [84][85][86][87][88]. Phenolic compounds found in avocado were shown to reduce oxidation, inflammation, and platelet aggregation [65]. Several studies have reported that different parts of the avocado plants contain potent phenolic antioxidants such as chlorogenic-, quinic-, succinic-, pantothenic-, abscisic-, ferulic-, gallic-, sinapinic-, *p*-coumaric-, gentisic-, protocatechuic-, 4-hydroxybenzoic-, and benzoic- acids, quercetin, quercetin-3-glucoside, quercetin-3-rhamnoside, vanillin, *p*-coumaroyl-D-glucose, catechins, (−)-epicatechin, and procyanidins (**Table 3**) [2][28][84][89][90][91][92][93][94][95][96][97]. Among the different parts of avocado investigated in several studies, leaf, peel, and seed extracts have shown consistently greater antioxidant capacity compared to that of the pulp [84][91][94][96][97][98][99][100][101][102][103][104][105][106]. Due to the presence of higher catechin, epicatechin, leucoanthocyanidin, triterpenes, furoic acid, and proanthocyanidin contents, avocado seed extracts have been reported to display greater antioxidant capacity [62][74]. Additionally, the ripening process was also shown to influence the phenolic contents of different parts of the avocado plant [96][107][108]. For example, a study by López-Cobo et al. [96] found a higher content of phenolics in the pulp and seed extracts of overripe avocados compared to their optimally ripe counterparts. It was hypothesized that the increase in the total phenolic content in the overripe fruit was mediated by higher phenylalanine ammonia-lyase activity associated with the ripening process [96]. They also observed an increased concentration of procyanidins in the overripe parts of the avocado, which was probably a result of the hydrolysis of complex tannins after ripening. Avocado peel, seed, and leaf, as the major by-products of the avocado industry, have been demonstrated as rich sources of polyphenolics and antioxidants. More studies of developing robust, green, and economical extraction techniques are fundamental to obtain greater yields of potent antioxidants. In vivo and clinical studies to understand the bioavailability of these antioxidants and their potential toxicity are also crucial.

Table 3. Antioxidant properties of *Persea Americana* (avocado).

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
Hass	Pulp and peel + pulp	Expeller pressed oils	ABTS and HPLC-PDA	Higher antioxidant capacity, α-tocopherol and β-carotene content were observed in oils from the unpeeled microwave-dried pulp of ripe and unripe avocado.	Oils from the pulp of ripe unpeeled microwave-dried avocado had significantly greater phenolic acid and quercetin contents.	[28]
Hass	Peel	50% (*v*/*v*) ethanol using accelerated solvent extraction	HPLC coupled to ultra-high-definition accurate-mass-QTOF	Sixty-one compounds belonging to 11 families were identified.	Procyanidins, flavonols, hydroxybenzoic, and hydroxycinnamic acids.	[90]
Hass	Seeds and	Accelerated solvent extraction	DPPH, TEAC, ORAC, HPLC-DAD-ESI-QTOF-MS	Significant antioxidant activity was observed in	Condensed tannins, phenolic acids, and flavonoids.	[91]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
	seed coat			both seed and seed coat extracts. A total of 84 compounds were identified, among which 45 were phenolic compounds.		
Hass	Pulp	Oil extracted with or without ultrasound	HPLC	Similar quantities of α, β, γ, and δ-tocopherols and phenolic compounds were detected both with and without ultrasound extractions.	Tocopherols and phenols.	[109]
Hass	Seeds	Methanol and 50% (*v/v*) ethanol	HPLC, ABTS, FRAP, ORAC and methoxy radical scavenging activity by EPR	50% (*v/v*) ethanol extract displayed greater antioxidant capacity in the ORAC, FRAP, and ABTS assays.	Chlorogenic acid, (−)-epicatechin, catechins and procyanidins.	[2]
Hass	Peel and seeds	Aqueous extract	ORAC	Peel extract showed higher antioxidant capacity than seed extract.	Epicatechin and chlorogenic acid were found in both extracts.	[101]
Hass	Pulp, peel, and seeds	Hexane to eliminate lipids and 80% methanol for phenolic extraction	HPLC-DAD-ESI-QTOF-MS	Higher concentrations of phenolic compounds were detected in the pulp and seed extract of overripe than in pulp and seed of optimally ripe fruit. The concentration of procyanidins increased after ripening.	Nine compounds in pulp, three in peel and three in seed. Procyanidins to degree of polymerization 2 to 6, and 13 were identified and quantified.	[96]
Hass	Peel, pulp, and seeds	Ultrasonic extraction with 80% (*v/v*) ethanol	DPPH, and ABTS	Seed and peel extracts exhibited greater antioxidant values and phenolic content than the pulp extract.	-	[102]
Hass	Peel, pulp, and seeds	Different solvents for different assays	DPPH and spectroscopic	All extracts exhibited significant antioxidant capacity. The seed extract had the greatest antioxidant activity, total	Carotenoids, phenolic compounds, flavonoids, vitamin c and tocopheryl acetate were detected in all extracts.	[106]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
				phenolic content, and flavonoids compared to that of peel and pulp.		
Hass	Pulp	Aqueous and ethanolic	FRAP and DPPH	Harvesting seasons affected the antioxidant capacity.	Positive correlations between FRAP and total phenolics, DPPH and total phenolics	[85]
Hass	Pulp	Hydrophilic and lipophilic extracts	DPPH, TEAC and ORAC	Higher antioxidant capacity values were obtained from lipophilic extracts compared to hydrophilic extracts.	A positive correlation was observed between DPPH/TEAC assays with palmitoleic, oleic, linoleic, α-linolenic acids.	[108]
Hass	Pulp	Acetone with 2,6-ditert-butyl-4-methylphenol, sodium carbonate, and sodium sulfate	HPLC-PDA	Seasonal variations in carotenoid were observed and α-tocopherol was detected.	Carotenoid such as: All-trans-neoxanthin; all-trans-violaxanthin; all-transneochrome; 9-cis-neoxanthin; all-trans-lutein-5,6-epoxide; chrysanthemaxanthin; lutein; zeaxanthin; β-cryptoxanthin; α-carotene; β-carotene were identified along with α-tocopherol.	[110]
Hass	Pulp	Tetrahydrofuran	DPPH	Low antioxidant activity.	A slight positive correlation against stearic acid content.	[111]
Hass	Leaves, pulp, peel, and seeds	Freeze-dried samples	FRAP, 4-dinitrophenylhydrazine and HPLC	The leaf, peel, and seed extracts had greater antioxidant capacity than that the pulp extracts. C7 sugars such as mannoheptulose and perseitol contributed to the antioxidant capacity of the pulp.	Vitamin C, anthocyanin, and C7 sugars.	[100]
Hass and Fuerte	Peel and seeds	80% (*v*/*v*) ethanol with ultrasonic extraction	ABTS, DPPH, FRAP, and HPLC-ABTS	Peel extracts of both varieties displayed higher antioxidant capacity in the ABTS and FRAP assays compared to their seed extracts, whereas in the DPPH assay, seed	Peel: procyanidin B2 and epicatechin Seed: trans-5-*O*-caffeoyl-D-quinic acid, procyanidin B1, catechin, and epicatechin.	[97]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
				extracts showed greater antioxidant activity.		
Hass and Fuerte	Pulp, peel, and seeds	Ethyl acetate, 70% (*v/v*) acetone, and 70% (*v/v*) methanol	CUPRAC, DPPH, and ABTS	Acetone (70% *v/v*) was found to be the most effective solvent for extracting antioxidants. Peel and seed extracts exhibited greater antioxidant values in all three assays compared to pulp.	Peels and seeds: catechins, procyanidins, and hydroxycinnamic acids Pulp: hydroxybenzoic and hydroxycinnamic acids and procyanidin.	[104]
Hass and Shepard	Seeds and peel	80% (*v/v*) methanol	HPLC-PAD, HPLC-ESI-MS, DPPH, ABTS and ORAC	The peel extracts displayed a higher total phenolic compound content and antioxidant activity in comparison to the seed extracts. Hass variety had a higher antioxidant capacity, which might be attributed to its procyanidin dimers and catechins than the Shepard variety.	Seed and peel extracts contained flavanol monomers, proanthocyanidins, and hydroxycinnamic acids. In addition, flavonol glycosides were detected in seed extracts.	[94]
Hass, Lamb-Hass, and Rugoro	Pulp	Methanol, ethanol, acetone, and ethyl acetate	HPLC-DAD-ESI-TOF	Seventeen compounds were identified using standards. Twenty-five compounds were tentatively identified.	Quinic acid, succinic acid, pantothenic acid, *p*-coumaroyl-D-glucose, abscisic acid, pentadecylfuran, avocado furan, and oleic acid were the most common compounds among the three avocado varieties.	[92]
Hass, Quintal, Margarida, and Fortuna	Peel, pulp, and seeds	Ethanol	ABTS, DPPH, FRAP	Peel extract of the Quintal variety showed the highest antioxidant capacity in all three assays. A similar trend was observed in terms of total phenolic and flavonoid contents.	Phenolics and flavonoids might contribute to the antioxidant capacity.	[99]
Hass, Bacon,	Pulp	Methanol	UHPLC-HE-MS	Pulp extracts had 19 individual	Gallic acid, sinapinic acid, vanillin, *p*-	[89]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
Fuerte, Pinkerton, Rincon, and Orotawa				phenolic compounds. A decrease in concentration of epicatechin concentration was observed with fruit ripening.	coumaric acid, gentisic acid, protocatechuic acid, 4-hydroxybenzoic acid, chlorogenic acid, and benzoic acid.	
Hass, Hass Motril, ColinV 33, Gem, Harvest, Jiménez 1, Jiménez 2, Lamb Hass, Marvel, Nobel, Pinkerton, Sir Prize and Tacambaro	Pulp	Methanol	GC coupled to APCI-TOF MS and FID	Twenty-seven compounds were quantified by GC-APCI-MS. Seven compounds are quantified by GC-FID. The concentration of organic acids, flavonoids, and vitamins decreased, whereas phenolic acids, ferulic acids, or *p*-coumaric acids increased with the ripening process.	Quinic, ferulic, chlorogenic and *p*-coumaric acids, epicatechin, and quercetin.	[93]
Booth 7	Pulp	Sodium acetate	ABTS	Total antioxidant capacity gradually increased with the ripening process. Treatment with aqueous 1-methylcyclopropene (1-MCP) significantly delayed the accumulation of total soluble phenolics, flavonoids, and total antioxidant capacity.	-	[112]
Collinson	Pulp	80% methanol and acetone	ABTS, DPPH, and FRAP	Lipophilic extracts displayed greater antioxidant capacity in the ABTS and DPPH assays compared to hydrophilic extracts. The opposite trend was observed in the FRAP assay.	-	[113]
Fortuna	Fresh and dried seeds	Water, 70% (*v*/*v*) ethanol, 70% (*v*/*v*) methanol, and	Spectroscopic and HPLC	Ethanol extract of dried seed showed 50, 38, and 24 mg/g of dry matter	Epicatechin, rutin, chlorogenic acid, quercetin.	[114]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
		partition with n-hexane chloroform, ethyl acetate, and n-butanol		of total phenol, condensed tannins, and flavonoid contents, respectively. HPLC study revealed epicatechin (4.7 µg/mL), rutin (2.8 µg/mL), and chlorogenic acid (1.4 µg/mL) and quercetin in the extract.		
Fortuna	Pulp	Oil extracted with SCO_2 and compressed LPG	DPPH	The SCO_2-extracted oil displayed higher antioxidant activity in the range of 17.4–82.5% compared to LPG-compressed oil.	-	[115]
Fortuna	Pulp	Lyophilized and cold pressed oil	GC-FID and GC-MS	A greater concentration of α-tocopherol and squalene were achieved with cold pressing.	α-tocopherol and squalene.	[116]
Fuerte	Pulp	Different solvents	FRAP, SOD and HPLC	Increase in the total antioxidant activity, SOD activity, and α-tocopherol content was observed in the presence of 1-MCP and low O_2.	-	[117]
Lula	Pulp	Oil extracted with water at high temperatures	HPLC and spectroscopic assays	Greater quantity of α-tocopherol was detected compared to β, γ, and δ-tocopherols. In addition, sterols and carotenoids were also reported.	Tocopherols, sterols, and carotenoids were potent antioxidants.	[118]
Mexican landrace	Peel	Methanol	DPPH	Antioxidant values in the range of 53.31–307.33 mmol trolox equivalents/fresh weight were reported.	Activity can be attributed to anthocyanins.	[119]
Slimcado, Booth 7, Booth 8, Choquette,	Pulp, peel, and seeds	Acetone, water, acetic acid	HPLC-MS, ORAC and DPPH	Seed extracts exerted the highest antioxidant activity, phenolic content,	Catechin, epicatechin, A- and B-type dimers, A- and B-type trimers,	[84]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
Loretta, Simmonds, and Tonnage				and procyanidins followed by peel and pulp. Significant correlations were observed among antioxidant capacities, phenolic contents, and procyanidins. Antioxidant activity can be attributed to the procyanidin content.	tetramers, pentamers and hexamers were identified in peels and seeds.	
-	Pulp	Supercritical CO_2/ ethanol extracts	HPLC	Supercritical CO_2 + ethanol at 200 bar and at 40 °C and 60 °C yielded significantly higher α-tocopherol content.	α-tocopherol	[120]
-	Seeds and pulp	Lipid	ABTS and DPPH	Seed extracts exhibited significantly greater antioxidant activity in both assays. Dose-dependent antioxidant activity was observed for both extracts.	-	[98]
-	Pulp	Oil extracted with mechanical pressing	DPPH	Greater antioxidant values were observed when the avocado pulp was dried at 60 °C under ventilation, and mechanical pressing was used for the oil extraction compared to vacuum oven and Soxhlet extraction.	α-tocopherol, phenolic compounds, carotenoids.	[121]
-	Seeds	Ultrasonic extraction with water	ORAC	Total antioxidant capacity increased with an increase in ultrasonic power. Positive correlation was observed between total polyphenolic content and antioxidant capacity.	-	[86]

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
-	Pulp	Acetone and its fractions	ORAC, HPLC-PDA/MS-TOF	Fractions with lipophilic acetogenins exhibited the highest antioxidant capacity.	1-acetoxy-2,4-dihydroxy-n-heptadeca-16-ene; Persediene; Persenone-C; Persenone-A; Persenone-B; Persin, and 1-acetoxy-2,4-dihydroxy-heneicosa-12,15-diene.	[122]
-	Leaves	50% ethanol extract	Spectroscopic, LC–ESI-MS, LCMS-IT-TOF	Glycosylated flavonoids were detected. [132][135]	Quercetin-3-glucoside and quercetin-3-rhamnoside.	[95]
-	Seeds	Different concentrations of ethanol	ORAC	The antioxidant values increased with temperature. However, it was negatively impacted by ethanol concentration.	-	[123]
-	Leaves, pulp, peel, and seeds	1M HCL and methanol	DPPH and FRAP	Greater DPPH radical scavenging activity, total phenol and flavonoid content were observed in leaf extracts. The peel extract showed the greatest FRAP value.	[84][137] -	[103]
[26][138][139][140][141][142][143][144][145]						
0 - 1	Pulp and seeds	50% (*v*/*v*) ethanol	DPPH and FRAP	Seeds extracts showed significantly greater antioxidant values compared to that of pulp in both assays. Similar trend was observed for total phenolic content. [140]	-	[105]
-	Peel	Different concentrations of ethanol [24]	DPPH	Maximum antioxidant activity when extraction was performed with 48% (*v*/*v*) ethanol under agitation for 20 min at 70 °C and solvent-to-solid ratio (*v*/*w*) 20.	Positive correlation was observed between total phenolic content and antioxidants.	[88] 2
-	Seeds	Different concentrations of ethanol	DPPH	Extraction for 60 min with 30% (*v*/*v*) ethanol at 70 °C with a solvent to-	Positive correlation was observed between total	[87]

etes combined [131]. es of cancer, late therapies [132][133]. eases to treat [133]. 1981–2010 [134]. In emo and radiation r alternatives to be ch [136]. The in vitro iver, lungs, larynx,). These properties dies have not only **4** depicts the major y of avocados. The depending on the vity of avocado did lass is perhaps the ines have reported apoptosis and the **ure 9**, **Table 4**) [24] ol extract of Hass nd cell cycle arrest lated the cyclin D1 by Lee et al. [144] in ds and peel. They t al. [138] found out or p53, caspase-3, larization in Jurkat thin, α-carotene, β- phase and increase e to the cumulative nd phenolics were a [48][49][50][51][52][53].

Variety	Part Studied	Types of Extract	Detection Assays	Major Findings	Type of Antioxidants	References
				solid material ratio of 8 yielded the maximum antioxidant capacity.	phenolic content and antioxidants.	
-	Leaves	Methanol, ethanol, cold and hot water	DPPH, FRAP, and hydroxyl radical scavenging ability	Significant antioxidant activity was observed in all three assays.	Antioxidant activity might be contributed by the phenolics and flavonoids.	[124]
-	Pulp	Oils extracted using Soxhlet, subcritical CO_2 (SCO_2) and ultrasound	ABTS, FRAP, and β-carotene bleaching	SCO_2-extracted oil displayed significantly greater ($p < 0.05$) antioxidant capacity in all three assays compared to Soxhlet or ultrasound-extracted oils.	Strong positive correlations ($p < 0.01$) were found between α and γ tocopherols and antioxidant activity.	[125]
-	Leaves	Powdered leaves	Spectroscopic	Vitamin C, tannins, alkaloids and phenolic content were reported.	-	[126]
-	Pulp	Lipid-soluble bioactive	DPPH, reducing power, metal chelating, nitric oxide scavenging, hydrogen peroxide scavenging, hemoglobin-induced linoleic acid system	Exhibited lower antioxidant properties compared to vitamin C.	-	[127]
-	Pulp	Methanol + water	ABTS and TBARS	Lower antioxidant activity was reported compared to other fruits tested in the study.	-	[128]

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Preclinical Studies

Variety	Parts	Type of Extracts	Bioactive Compounds	Type of Cell Lines	Major Findings and Molecular Mechanisms of Action	References
Hass	Seeds	Methanol	-	MCF-7 breast, H1299 lung, HT29 colon, and LNCaP prostate cancer cells	Dose-dependent inhibition of all cells with IC_{50} values 19–132 µg/mL after 48 h of treatment. In LNCaP prostate cancer cells, the induction of caspase 3-mediated apoptosis, PARP cleavage, downregulation of cyclin D1 and E2, cell cycle arrest at G_0/G_1 phase and reduction of nuclear translocation of nuclear factor kappa B (NF-κB) were observed.	[140]
Hass	Seeds	High-speed countercurrent chromatographic fraction of methanol-water partition (M7)	Proanthocyanidins B1, B2 and A-type trimer. Traces of abscisic acid glucosides.	HaCaT immortalized nontumorigenic human epidermal cells	Significant inhibition of cell proliferation, increased LDH activity. Molecular mechanisms of action were not investigated.	[23]

Preclinical Studies						
Variety	**Parts**	**Type of Extracts**	**Bioactive Compounds**	**Type of Cell Lines**	**Major Findings and Molecular Mechanisms of Action**	**References**
Hass	Pulp	Chloroform-soluble	Two aliphatic acetogenins- (2S,4S)-2,4-dihydroxyheptadec 16-enyl acetate] and 2 [(2S,4S)-2,4-dihydroxyheptadec-16-ynyl acetate.	83–01-82CA human oral cancer cell line, MEK overexpressing cell line 83–01-82CA/MEKCA	The two aliphatic acetogenins targeted the EGFR/RAS/RAF/MEK/ERK1/2 cancer pathway by synergistically inhibiting c-RAF (Ser338) and ERK1/2 (Thr202/Tyr204) phosphorylation.	[146]
Hass	Pulp	Chloroform	-	83-01-82CA human oral cancer and TE1177 normal epithelial cell lines	In the oral cancer cells, the extract induced apoptosis by increasing the levels of reactive oxygen species by twofold to threefold. Apoptosis was not induced in the normal cell line.	[141][142]
Hass	Pulp	Acetone	Lutein, zeaxanthin, β-cryptoxanthin, α-carotene, and β-carotene, α-tocopherol and γ-tocopherol.	LNCaP androgen-dependent and PC-3 androgen-independent prostate cancer cell lines	Inhibited the growth of both the prostate cancer cell lines. Arrested PC-3 cells at the G_2/M phase and increased the expression of p27 protein.	[24]
Lulu	Unripe fruit pulp	95% (*v*/*v*) ethanol extracts and its fractions	1,2,4-Trihydroxynonadecane, 1,2,4-Trihydroxyheptadec-16-ene and 1,2,4-Trihydroxyheptadec-16-yne.	A-549 human lung, MCF-7 human breast, HT-29 human colon, A-498 human Kidney, MIA PaCa-2 human pancreatic carcinoma, PC-3 human prostate cancer cells	All three compounds were active against six human tumor cell lines and exhibited selectivity against PC-3 cells. Molecular mechanisms were not studied.	[21]
-	Seeds	Ethanol extract and its hexane and dichloromethane fractions	-	Lung A549 and gastric BGC823 cancer cells	Growth inhibition at 200 µg/mL. The IC_{50} values and molecular mechanisms of action were not investigated.	[147]
-	Pulp and seed extracts	Lipids	Fatty acids, hydrocarbon, and sterols.	HCT116 colon and HePG2 liver cancer cell lines	Seed extract showed greater activity against HCT116 (IC_{50} < 4 µg/mL) and HePG2 (IC_{50} < 20 µg/mL) cell lines compared to the pulp extract. Molecular mechanisms of action were not investigated.	[98]
-	Seeds	Chloroform extracts and its soluble methanol fraction (FML) and non-soluble methanol fraction (FTML).	-	MCF-7 breast cancer cell line	Chloroform extract, FML, and FTML inhibited cell growth in a dose-dependent manner and displayed IC_{50} values of 94.87, 34.52, and 66.03 µg/mL, respectively. FML induced apoptosis and arrested cells at the subG_1/G_0 phase.	[148]

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- GC-APCI-TOF-MS: Gas chromatography–atmospheric pressure chemical ionization–time-of-flight mass spectrometry.
- GC-APCI-TOF-FID: Gas chromatography–atmospheric pressure chemical ionization–time-of-flight–flame ionization detector.

Preclinical Studies						
Variety	**Parts**	**Type of Extracts**	**Bioactive Compounds**	**Type of Cell Lines**	**Major Findings and Molecular Mechanisms of Action**	**References**
-	Leaves	Silver nanoparticles		MCF-7 breast and HeLa cervical cancer cells	Dose-dependent cytotoxicity was observed at concentrations above 50 µM in MCF-7 but not in HeLa cells. Downregulation of p53 expression was observed in both cell lines.	[149]
-	Leaves	Aqueous-ethanol (5% v/v)	-	Larynx cancer tissue	Significant increase in adenosine deaminase activity in cancerous tissues derived from 13 patients who underwent surgery for larynx cancer (median age of 57 years) compared to noncancerous (r = 0.60, p = 0.029) tissues.	[150]
-	Seeds	Fraction of ethanol extract	Triterpenoid	MCF-7 breast and HepG2 liver cancer cells	Inhibited MCF-7 (IC_{50} = 62 µg/mL) and HepG2 (IC_{50} = 12 µg/mL) cells with no activity against normal cells. Molecular mechanisms of action were not investigated.	[151]
-	Pulp	Ethanol, chloroform, ethyl acetate, and petroleum.	-	Esophageal squamous cell carcinoma and colon adenocarcinoma cell line	Moderate activity. The IC_{50} values and molecular mechanisms of action were not investigated.	[152]
-	Pulp	Aqueous	-	A549 lung, HepG-2 liver, HT-29 colon, and MCF-7 breast cancer cells.	Exhibited LC_{50} values in the range of 13.3–54.5 µg/mL against the tested cell lines. Molecular mechanisms of action were not investigated.	[153]
-	Root bark	Methanol extract and its fractions.	4-hydroxy-5-methylene-3-undecyclidenedihydrofuran-2 (3H)-one	MCF-7 breast cancer cell line	Antiproliferative activity with an IC_{50} value of 20.48 µg/mL with induction of apoptosis.	[36]
-	Endocarp, whole seed, seed and leaves	Ethanol	-	Jurkat lymphoblastic leukemia cells	Induced significant oxidative stress-dependent apoptosis via mitochondrial membrane depolarization. Activated transcription factor p53, protease caspase-3, and apoptosis-inducing factor (APAF).	[138]
-	Pulp	50% (*v/v*) Methanol	-	Human lymphocyte cells	Chemoprotective against cyclophosphamide-induced chromosomal aberrations at 200 mg/kg body weight.	[154]

Preclinical Studies						
Variety	**Parts**	**Type of Extracts**	**Bioactive Compounds**	**Type of Cell Lines**	**Major Findings and Molecular Mechanisms of Action**	**References**
-	Seeds and peel	Methanol	-	MDA-MB-231 breast cancer cells	Apoptosis due to activation of caspase-3 and its target protein, PARP.	[144]
-	Leaves	-	Persin	In vitro: MDA-MB-231, MCF-7, and T-47D breast cancer cells In vivo: Quackenbush lactating mice	In vitro: Persin selectively arrested cells at the G_2/M phase and induced caspase-dependent apoptosis. Apoptosis was dependent on the expression of Bim protein, which also indicated the microtubule-stabilizing properties of persin. Overall, MCF-7 and T-47D cells were more sensitive to persin compared to MDA-MB-231. In vivo: Persin exerted cytotoxicity in the lactating mammary epithelium.	[139]
		[26]		MCF-7, T-47D, and SK-Br3 breast cancer and MCF-10A human mammary epithelial cells.	Synergistic interaction between tamoxifen and persin against the tested breast cancer cells was observed. Significant reduction of IC_{50} values of tamoxifen when combined with 13.8 µmol/L of persin. The synergistic cytotoxicity was Bim-dependent and mediated by the modulation of ceramide metabolism.	[155]
			[160]			
-	Fruit	-	Persenone A	[161][162] In vitro: RAW 264.7 mouse macrophage cells In vivo: Female ICR mice (7 weeks old)	Downregulated the expression of iNOS/COX-2 (nitric oxide synthase/cyclooxygenase-2) in macrophage cells. When applied topically, reduced the generation of H_2O_2 in mouse skin.	[156]
			[161]		[155]	
50			[155]			
-	Fruit	-	(2R)-(12Z,15Z)-2-hydroxy-4-oxoheneicosa-12,15-dien-1-yl acetate (1), persenone A (2) and B (3)	HL-60 acute myeloid leukemia and RAW 264.7 mouse macrophage cells.	Suppressed the growth of HL-60 cells (compound 1, IC_{50} = 33.7; compound 2, IC_{50} = 1.4; compound 33, IC_{50} = 1.8 µM). Inhibited nitric oxide generation induced by lipopolysaccharide in combination with interferon-γ in RAW 264.7 cells.	[19]
-	[143][145][157][158]		Scopoletin	In vivo: Skin papilloma in mice induced by 7,12-dimethylbenz(a)anthracene and croton oil [143][157]	Reduced carcinogen-induced toxicity and led to decrease in the size of skin papilloma. Downregulated AhR, CYP1A1, PCNA, stat-3,	[26]

[163][164]

and the size of skin and tumor invasion hrome P450 1A1), vin, MMP-2 (matrix the upregulation of d [26]. Of note, the poptosis, cell cycle nsecutively leads to een correlated with nergistic interaction t MCF-7 (Michigan uction of tamoxifen nd mediated by the eins that play a key rotubule-stabilizing s [139][165].

out in a number of aDef defensin was and MCF-7 breast ly demonstrated to have antimicrobial properties [166][167]. The induction of apoptosis and abrogation of the cell cycle were also observed earlier in the human breast, lung, ovarian, and colorectal cancer cells when treated with chemically synthesized avocado β-hydroxy-α,β-unsaturated ketones by Leon et al. [145]. Although many preclinical studies were performed to elucidate the cytotoxicity of extracts derived from different parts of the avocado plant and their components, very few of them have investigated their molecular mechanisms of action. Interestingly, contradicting information regarding avocado extract-induced genotoxicity is also available. For instance, Kulkarn et al. [168] found out that avocado fruit and leaf extracts can induce chromosomal aberrations in human peripheral lymphocytes, with leaf extract being more genotoxic. The same research group later reported that avocado fruit extract can reduce cyclophosphamide-mediated chromosomal aberrations in human lymphocytes [154], which was perhaps due to the antagonistic effects of the extract on cyclophosphamide.

Traditionally, an avocado leaf decoction is used for the treatment of tumours and tumour-related diseases in Nigeria [169]. Despite their health benefits highlighted in numerous reports, clinical studies examining the direct correlation between avocado consumption and the prevention and treatment of cancer are scarce. Only one case-control study involving 243 men with prostate cancer and 273 controls in Jamaica demonstrated that MUFA from avocado may reduce the risk of prostate

[159]

Preclinical Studies

Variety	Parts	Type of Extracts	Bioactive Compounds	Type of Cell Lines	Major Findings and Molecular Mechanisms of Action	References
					survivin, MMP-2, cyclin D1, and c-myc, and upregulated p53, caspase-3, and TIMP-2.	[170][171][172]

Chemical synthesis [62][65]		Type of cell lines	Major findings and molecular mechanisms of action	References
[57][58][59][173]		K562 chronic myeloid leukemia cells	Cytotoxic with an IC_{50} value of 97.3 µg/mL. Activated caspase-8 and induced the expression of TNF-α.	[157]
Antimicrobial peptide-PaDef defensin		MCF-7 breast cancer cell line	Inhibited the growth in a concentration-dependent manner (IC_{50} = 141.62 µg/mL). Induced cytochrome c, APAF-1, and the caspase 7 and 9 expressions, loss of mitochondrial Δψm and enhanced the phosphorylation of MAPK p38.	[143]
Persin and tetrahydropersin		Breast cancer: MCF-7, T-47D, MDA-MB-468, MDA-MB-157, SkBr3, Hs578T, MDA-MB-231 cells, normal mammary epithelial MCF-10A cells, Ovarian cancer: OVCAR3 and IGROV-1 cells Prostate cancer: PC-3 and LNCaP cells	Persin was more potent compared to tetrahydropersin against most of the tested cancer cell lines with IC_{50} values in the range 15.1 ± 1.3 to more than 39 µM. Molecular mechanisms of action was not studied.	[158]
		A2780 human ovarian, SW1573 lung, HBL-100 human	GI_{50} values in the range of 0.5–3.9 µM. Induced	

Bioactive Compounds	Type of Cancer	Type of Study	Major Findings	References
Carotenoids- α-carotene, β-cryptoxanthin, lycopene, and lutein/zeaxanthin	Breast cancer	A nested case-control study in women consisting of 604 breast cancer cases and 626 controls.	In women with high mammographic density, plasma levels of carotenoids reduced breast cancer risk significantly (40–50% reduction, $p < 0.05$).	[171]
		An ancillary study involving 207 women ages 18 to 70 years who had been successfully treated for early-stage breast cancer.	An inverse association between total plasma carotenoid concentrations and the oxidative stress biomarkers (urinary 8-hydroxy-2′-deoxyguanosine and 8-isoprostaglandin-F2α) was observed.	[172]
	Larynx, pharynx and oral cancers	The study population involving 52 patients curatively treated for early-stage larynx, pharynx or oral cavity during 1997–2001.	An inverse association was observed between individual/grouped xanthophylls and urinary F2-isoprostanes (F_2-IsoPs), a biomarker of oxidative stress. However, individual/grouped carotenes did not show such association with F_2-IsoPs.	[170]
Glutathione	Advanced colorectal carcinoma	A randomized, double blind, placebo-controlled trial in 52 patients.	Prevented of oxaliplatin-induced neuropathy without reducing the clinical efficacy of oxaliplatin.	[57]
	Ovarian cancer	A multicenter, randomized, double-blind, parallel group design with 51 women.	Reduced the cisplatin-associated toxicity and improved the quality of life.	[58]
	Oral cancer	A population-based case-control study	Reduced oral cancer risk was associated with glutathione when fruit	[59]

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Bioactive Compounds	Type of Cancer	Type of Study	Major Findings	References
		involving 1,830 Caucasian participants (855 cases and 975 controls) in during 1984–1985 in the United States.	and vegetable were commonly consumed raw.	

6. Antimicrobial Properties of *P. americana*

Currently, there is a growing interest in finding alternatives to the synthetic antimicrobial agents that are commonly used in the food and pharmaceutical industries. This is due to the concerns of the consumers regarding the safety of products containing synthetic chemicals and their associated health risks [174]. Seeds (endocarp) and peels (exocarp) being the by-products of the avocado industry are generally disposed of as wastes [175] and have been investigated for their antimicrobial properties. Most of the studies conducted thus far have noted the antimicrobial activity of the extracts derived from different avocado varieties [104][176][177][178], while only a few have reported insignificant antimicrobial activity [101][179]. The antimicrobial activity of avocado extracts might be influenced by (i) the variety of the avocado, (ii) the parts used for investigation (i.e., exocarp, endocarp, or mesocarp), (iii) the solvent type used for extraction, and iv) the bacterial species examined [104][176]. Raymond and Dykes [176] investigated the antimicrobial activity of ethanolic and aqueous extracts of seeds and peels of three different avocado varieties (**Table 6**). The authors reported that ethanolic extracts had antibacterial activity against both Gram-positive and Gram-negative bacteria (except for *Escherichia coli*) ranging from 104.2 to 416.7 µg/mL, while aqueous extracts exhibited activity against *Listeria monocytogenes* and *Staphylococcus epidermidis*. Rodriguez-Carpena et al. [104] investigated the antibacterial activity of the extracts derived from different avocado parts (peel, seed, and pulp) of a number of varieties against *Bacillus cereus*, *S. aureus*, *L. monocytogenes, E. coli*, *Pseudomonas spp*., and *Yarrowia lipolytica*. The highest inhibitory activity against the Gram-positive bacteria- *B. cereus* and *L. monocytogenes* was observed, while *E. coli* was the most sensitive among the tested Gram-negative bacterial species. The authors mentioned that all avocado parts had antimicrobial properties, with pulp (mesocarp) showing the highest activity. In addition, the authors reported that the Gram-positive bacteria were more sensitive in comparison to the Gram-negative bacteria [104]. The Gram-negative bacteria have an extra protective outer membrane, which makes them more resistant to antibacterial agents compared to the Gram-positive bacteria [104][180]. β-sitosterol in avocados was also shown to play a key role in strengthening the immune system and the suppression of human immunodeficiency virus and other infections [181]. In particular, it has been found to enhance the proliferation of lymphocytes and natural killer cell activity for invading pathogens [181]. Salinas-Salazar et al. [177] investigated the antimicrobial activity of seed extracts of avocado enriched with acetogenin against *L. monocytogenes* and reported growth inhibition at 37 °C and 4 °C with MIC (minimum inhibitory concentration) values of 15.6 and 7.8 mg/L, respectively. Acetogenins of avocados are fatty acid derivatives with a long unsaturated aliphatic chain (C19–C23) [182][183]. Owing to the structural similarities between acetogenins and fatty acids, authors hypothesized that acetogenins may penetrate the cell membranes of bacteria and physically disrupt their functionality [177]. Indeed, several compounds might be associated in the antimicrobial activity of avocado extracts. Polyphenols have been previously reported for their antimicrobial properties [184]. However, the contribution of the phenolic compounds toward the antimicrobial activity of avocado extracts needs to be investigated. Rodriguez-Carpena et al. [104] found that avocado pulp extract had a higher antimicrobial activity than peel and seed extracts, despite having lower polyphenol content. Future studies should be conducted to isolate individual phenolic compounds from different parts of avocado and investigate their antimicrobial properties.

Table 6. Summary of studies that have been conducted that investigated the antimicrobial activity of *Persea americana* (avocado).

Variety/ies	Bacteria	Highlights	Reference
Hass Shepard	*Listeria monocytogenes* *Staphylococcus epidermidis*	The antimicrobial activity of peel and seed extracts was evaluated.	[176]

Variety/ies	Bacteria	Highlights	Reference
Fuerte	*Staphylococcus aureus* *Enterococcus faecalis* *Escherichia coli* *Salmonella Enteritidis* *Citrobacter freundii* *Pseudomonas aeruginosa* *Salmonella Typhimurium* *Enterobacter aerogenes*	Ethanol extracts showed antimicrobial activity against both Gram-positive and Gram-negative bacteria (except *E. coli*). Aqueous extracts had antimicrobial activity against *L. monocytogenes* and *S. epidermidis*.	
Hass Fuerte	*Bacillus cereus* *S. aureus* *L. monocytogenes* *E. coli* *Pseudomonas spp.* *Yarrowia lipolytica*	All avocado parts had antimicrobial activities. Pulp showed the highest antimicrobial activity. Gram-positive bacteria were found to be more sensitive than Gram-negative bacteria.	[104]
Hass	*L. monocytogenes*	The antilisterial properties of an enriched acetogenin extract from avocado seed were determined. Seeds had higher acetogenin content than pulp. The antimicrobial effect was probably caused by increased membrane permeability.	[177]
Lorena Hass	*S. aureus* *E. coli*	Extracts did not have antimicrobial activity against *S. aureus* ATCC 29213 and *E. coli* ATCC 25922	[179]
Hass	*Listeria innocua* *E. coli* *Lactobacillus sakei* *Weissella viridescens* *Leuconostoc mesenteroides*	Peel and seed extracts did not present antimicrobial activity against any bacteria analyzed.	[101]

7. Anti-Inflammatory Properties of *P. americana*

Several studies have investigated the anti-inflammatory properties of avocados via modulation of inflammatory responses (**Figure 9**, **Table 7**). The aqueous extract of avocado leaves showed an anti-inflammatory effect in vivo by inhibiting carrageenan-induced rat paw oedema [185]. Persenone A, an active constituent of avocado, reduced inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in murine macrophages [156]. Similarly, (2*R*)-(12*Z*,15*Z*)-2-hydroxy-4-oxoheneicosa-12,15-dien-1-yl acetate, persenone A and B isolated from the avocado fruit, decreased the generation of nitric oxide in mouse macrophages [19]. Avocado oil contains a high amount of oleic acid and essential fatty acids. A study by [186] highlighted the wound-healing properties of avocado fruit oil by increasing collagen synthesis and decreasing inflammation in Wistar rats. They also reported that oleic acid was the predominant unsaturated fatty acid (47.20%) present in the fruit oil [186].

Table 7. Anti-inflammatory properties of *Persea americana* (avocado) extracts, compounds, and combinations.

Extracts and Compounds	Key Findings and Molecular Mechanism of Action	Reference
Leaf aqueous extract	Reduced carrageenan-induced rat paw oedema.	[185]
Persenone A	Reduced inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in activated murine macrophages.	[156]
Avacado oil	Promoted increased collagen synthesis and decreased inflammation in wound healing on incisional and excisional cutaneous wound models in Wistar rats.	[186]
(2*R*)-(12*Z*,15*Z*)-2-hydroxy-4-oxoheneicosa-12,15-dien-1-yl acetate, persenone A and B	Decreased nitric oxide generation in activated mouse macrophages.	[19]

Extracts and Compounds	Key Findings and Molecular Mechanism of Action	Reference
Avocado–Soybean Unsaponifiables (ASU)	Inhibited collagenase, stromelysin, IL-6, IL-8, and prostaglandin E_2 (PGE2) release in activated human articular chondrocytes.	[187]
	Stimulated glycosaminoglycan and hydroxyproline synthesis, and inhibited the production of hydroxyproline in the granulomatous tissue of mice model.	[188]
	Suppressed critical regulators of the inflammatory response such as PGE-2 and COX-2 in activated human chondrocytes.	[189]
	Decreased catabolic enzymes, matrix metalloproteinases-3 and -13 expressions via inactivating the expression of MAPKs (ERK 1/2) and nuclear factor kappa-B (NF-*κ*B) in activated mouse or human chondrocytes.	[190]
	Reduced pro-inflammatory cytokines such as TNF-α, IL-1β, and iNOS expression in activated chondrocytes and THP-1 monocyte and macrophages.	[191]
	Exhibited a promising result on the bone repair by modulating the molecular targets of *Rankl* and *Il1β*, *RANKL*, *TRAP* in rat model.	[192]
	Decreased pain symptoms in patients with osteoarthritis of the temporomandibular joint.	[193]
	Modulated the expression of TGF-β1, TGF-β2, and BMP-2 in activated human periodontal ligament and human alveolar bone cells.	[194]
ASU + Epigallocatechin gallate	Inhibited COX-2 expression and PGE_2 production in activated equine chondrocytes.	[195]
	Inhibited the gene expression of IL-1β, TNF-α, IL-6, COX-2, and IL-8 in activated equine chondrocytes.	[196]

nction and stability [197]. Even though osteoarthritis (OA) is considered a non-inflammatory disease, recent studies have shown that inflammation is a leading cause for the initiation and continuation of the disease process [198]. Non-pharmacological agents that modulate the expression of pro-inflammatory mediators are highly promising as safe and effective ways to treat OA [196]. Avocado–soybean unsaponifiable (ASU) combination represents one of the most commonly used treatments for symptomatic OA [190]. ASU is a combination of avocado oil and soybean oil, which has been accepted as a medication/food supplement in many countries [199]. Three ratios of avocado (A) and soybean (S) unsaponifiable combinations (A:S = 1:2, 2:1, and 1:1) were studied for their anti-inflammatory properties on chondrocyte cells [187]. All the ratios showed significant inhibition compared to the individual extracts on collagenase, stromelysin, interleukin 6 (IL-6), interleukin 8 (IL-8), and prostaglandin E_2 (PGE2) release. In particular, 1:2 was found to be the most effective combination that exhibited chondroprotective effects in vivo by stimulating glycosaminoglycan and hydroxyproline synthesis and inhibiting the production of hydroxyproline in the granulomatous tissue [187]. In another study, the unsaponifiables of avocado alone indicated a significant chondroprotective effect [188]. Several preclinical and clinical studies conducted in the last few decades have revealed the modulation of different pathways and molecular targets associated with OA pathogenesis by ASU [200]. For instance, the anti-OA properties of ASU are mediated via the suppression of critical regulators of the inflammatory response such as iNOS/COX-2, and PGE-2 [189], and the reduction of catabolic enzymes (matrix metalloproteinases-3 and -13) and [190][191]. Gabay et al. [190] demonstrated the inactivation of the mitogen-activated protein kinases such as the extracellular signal-regulated kinase (ERK 1/2) and NF-*κ*B as the molecular mechanism of action for the anti-inflammatory effects of ASU. A recent study showed the potential bone repair properties of ASU by the modulation of molecular targets *Rankl* and *Il1β*, *RANKL*, and *TRAP* using a rat model [192]. Sterols, the major bioactive components of ASU, have also shown anti-inflammatory activity in articular chondrocytes [201].

A significant reduction of articular cartilage erosion and synovial haemorrhage compared to placebo was observed in horses using ASU extracts [202]. However, the extracts did not reduce signs of pain or lameness in horses. In humans, NSAID

(nonsteroidal anti-inflammatory drugs) consumption was reduced in patients with lower limb OA after six weeks of ASU consumption [203]. Furthermore, ASU significantly reduced the progression of joint space loss in patients with hip OA [204]. Another study by Maheu et al. [205] demonstrated slow radiographic progression in hip OA using ASU treatment. They also reported that the treatment was well tolerated by patients, even though the clinical outcome did not change. Interestingly, a recent study showed that the intake of ASU extract decreased the pain symptoms and an improved the quality of life in patients with OA of the temporomandibular joint [193].

Other studies have combined ASU with bioactive compounds such as epigallocatechin gallate (EGCG), and α-lipoic acid (LA) [196][195][206]. Interestingly, contrary to previous research, Heinecke et al. [195] reported a slight inhibition of COX-2 expression and PGE_2 production in activated chondrocytes. However, when ASU was combined with EGCG, both mediators were more significantly inhibited than their mono treatments [195]. Another study by Ownby et al. demonstrated that this combination inhibited the gene expression of interleukin-1 beta (IL-1β), tumour necrosis factor- α (TNF-α), IL-6, COX-2, and IL-8 in activated chondrocytes [196]. The combination of ASU with LA showed more significant suppression of PGE_2 production in activated chondrocytes than ASU or LA alone [206].

The implementation of ASU in the treatment of other inflammatory diseases has also been explored. In particular, ASU has shown efficacy against periodontal disease by modulating the expression of transforming growth factor-beta 1 (TGF-β1), TGF-β2, and bone morphogenetic protein 2 (BMP-2) [194]. Additionally, a recent study demonstrated that ASU can repair periodontal disease within seven days [207]. These results underline the significant anti-inflammatory properties of avocado mediated via multiple signal transduction pathways and their role in the potential treatment of various inflammatory diseases.

8. Conclusions and Future Direction

Several preclinical studies performed in the last few decades lay emphasis on the unique nutritional and phytochemical composition of avocado and its potential in the treatment and prevention of different diseases. Some studies have underlined its importance as the source of lead molecules for drug discovery due to the abundance of novel chemical skeletons. The cumulative effects of avocado components in the prevention and treatment of oxidative stress and age-related degenerative diseases are also indicated in a few studies. However, more comprehensive in vitro, in vivo, and clinical investigations are fundamental to significantly expand the understanding of the molecular mechanisms of action of its phytochemicals for developing subsequent therapeutic and nutritional interventions against cancer, diabetes, inflammatory, microbial, and cardiovascular diseases. Interestingly, despite its popularity as a “superfood”, clinical studies evaluating the therapeutic potential of avocado for the prevention and management of different ailments are limited in the literature. More investigations to understand the bioavailability and pharmacokinetics of avocado phytochemicals and antioxidants are also crucial to determine their clinical efficacy and potential toxicity. Regardless of the recent food trends and marketing gimmicks of “superfoods”, variety is fundamental for a balanced healthy diet. As many studies have revealed the complex synergistic interactions among different phytochemicals present in food matrices, studies to understand the possible synergy between bioactive compounds from avocado and other fruit and vegetables will help formulate diet-based preventive strategies for many diseases. A few reports have indicated the role of avocado in improving the bioavailability of nutrients from other plant-based foods. Therefore, consuming avocados with other fruit and vegetables as a part of the diet can be beneficial to human health.

References

1. Bergh, B.; Ellstrand, N. Taxonomy of the avocado. Calif. Avocado Soc. Yearb. 1986, 70, 135–145.

2. Segovia, F.J.; Hidalgo, G.I.; Villasante, J.; Ramis, X.; Almajano, M.P. Avocado seed: A comparative study of antioxidant content and capacity in protecting oil models from oxidation. Molecules 2018, 23, 2421.
3. Cowan, A.K.; Wolstenholme, B.N. Avocado. In Encyclopedia of Food and Health; Caballero, B., Finglas, P.M., Toldrá, F., Eds.; Academic Press: Oxford, UK, 2016; pp. 294–300.
4. Taulavuori, K.; Julkunen-Tiitto, R.; Hyöky, V.; Taulavuori, E. Blue Mood for Superfood. Nat. Prod. Commun. 2013, 8, 1934578X1300800627.
5. Rahmani, G.; Martin-Smith, J.; Sullivan, P. The Avocado Hand. Ir. Med. J. 2017, 110, 658.
6. Agricultural Marketing Resource Center. Avocados; Iowa State University in Ames: Ames, IA, USA, 2018.
7. Combined Chemical Dictionary 23.1; CRC Press, Taylor & Francis Group: Boca Raton, FL, USA, 2019; Available online: http://ccd.chemnetbase.com/faces/chemical/ChemicalSearch.xhtml;jsessionid=7B7405700267BD91E58E52C6333BF (accessed on 1 August 2019).
8. The Human Metabolome Database. 2019. Available online: http://www.hmdb.ca/ (accessed on 1 August 2019).
9. Yasir, M.; Das, S.; Kharya, M.D. The phytochemical and pharmacological profile of Persea americana Mill. Pharmacogn. Rev. 2010, 4, 77–84.
10. Wu, Y.H.; Tseng, C.K.; Wu, H.C.; Wei, C.K.; Lin, C.K.; Chen, I.S.; Chang, H.S.; Lee, J.C. Avocado (Persea americana) fruit extract (2R,4R)-1,2,4-trihydroxyheptadec-16-yne inhibits dengue virus replication via upregulation of NF-kappaB-dependent induction of antiviral interferon responses. Sci. Rep. 2019, 9, 423.
11. Adikaram, N.K.B.; Ewing, D.F.; Karunaratne, A.M.; Wijeratne, E.M.K. Antifungal Compounds from Immature Avocado Fruit Peel. Phytochemistry 1992, 31, 93–96.
12. Abe, F.; Nagafuji, S.; Okawa, M.; Kinjo, J.; Akahane, H.; Ogura, T.; Martinez-Alfaro, M.A.; Reyes-Chilpa, R. Trypanocidal Constituents in Plants 5. Evaluation of some mexican plants for their trypanocidal activity and active constituents in the seeds of Persea americana. Biol. Pharm. Bull. 2005, 28, 1314–1317.
13. Lu, Y.C.; Chang, H.S.; Peng, C.F.; Lin, C.H.; Chen, I.S. Secondary metabolites from the unripe pulp of Persea americana and their antimycobacterial activities. Food Chem. 2012, 135, 2904–2909.
14. Domergue, F.; Helms, G.L.; Prusky, D.; Browse, J. Antifungal compounds from idioblast cells isolated from avocado fruits. Phytochemistry 2000, 54, 183–189.
15. Lee, T.-H.; Tsai, Y.-F.; Huang, T.-T.; Chen, P.-Y.; Liang, W.-L.; Lee, C.-K. Heptadecanols from the leaves of Persea americana var. americana. Food Chem. 2012, 132, 921–924.
16. Bull, S.D.; Carman, R.M. Synthesis of the Avocado Antifungal,(Z, Z)-2-Hydroxy-4-oxohenicosa-12, 15-dien-1-yl Acetate. Aust. J. Chem. 1994, 47, 1661–1672.
17. Rodriguez-Saona, C.; Millar, J.G.; Trumble, J.T. Isolation, Identification, and Biological Activity of Isopersin, a New Compound from Avocado Idioblast Oil Cells. J. Nat. Prod. 1998, 61, 1168–1170.
18. Kashman, Y.; Néeman, I.; Lifshitz, A. New compounds from avocado pear. Tetrahedron 1969, 25, 4617–4631.
19. Kim, O.K.; Murakami, A.; Nakamura, Y.; Takeda, N.; Yoshizumi, H.; Ohigashi, H. Novel Nitric Oxide and Superoxide Generation Inhibitors, Persenone A and B, from Avocado Fruit. J. Agric. Food Chem. 2000, 48,

1557–1563.

20. Chen, C.-Y.; Chen, C.-H.; Wong, C.-H.; Liu, Y.-W.; Lin, Y.-S.; Wang, Y.-D.; Hsui, Y.-R. Cytotoxic Constituents of the Stems of Cinnamomum subavenium. J. Nat. Prod. 2007, 70, 103–106.
21. Oberlies, N.H.; Rogers, L.L.; Martin, J.M.; McLaughlin, J.L. Cytotoxic and insecticidal constituents of the unripe fruit of Persea americana. J. Nat. Prod. 1998, 61, 781–785.
22. Ortega-Arellano, H.F.; Jimenez-Del-Rio, M.; Velez-Pardo, C. Neuroprotective effects of methanolic extract of avocado Persea americana (var. Colinred) peel on paraquat-induced locomotor impairment, lipid peroxidation and shortage of life span in transgenic knockdown parkin drosophila melanogaster. Neurochem. Res. 2019, 44, 1986–1998.
23. Ramos-Jerz Mdel, R.; Villanueva, S.; Jerz, G.; Winterhalter, P.; Deters, A.M. Persea americana Mill. Seed: Fractionation, Characterization, and Effects on Human Keratinocytes and Fibroblasts. Evid. Based Complement. Altern. Med. 2013, 2013, 391247.
24. Lu, Q.Y.; Arteaga, J.R.; Zhang, Q.; Huerta, S.; Go, V.L.; Heber, D. Inhibition of prostate cancer cell growth by an avocado extract: Role of lipid-soluble bioactive substances. J. Nutr. Biochem. 2005, 16, 23–30.
25. Naveed, M.; Hejazi, V.; Abbas, M.; Kamboh, A.A.; Khan, G.J.; Shumzaid, M.; Ahmad, F.; Babazadeh, D.; FangFang, X.; Modarresi-Ghazani, F.; et al. Chlorogenic acid (CGA): A pharmacological review and call for further research. Biomed. Pharmacother. 2018, 97, 67–74.
26. Bhattacharyya, S.S.; Paul, S.; Dutta, S.; Boujedaini, N.; Khuda-Bukhsh, A.R. Anti-oncogenic potentials of a plant coumarin (7-hydroxy-6-methoxy coumarin) against 7,12-dimethylbenz [a] anthracene-induced skin papilloma in mice: The possible role of several key signal proteins. Chin. J. Integr. Med. 2010, 8, 645–654.
27. Martin, C.; Kunesch, G.; Martin-Tanguy, J.; Negrel, J.; Paynot, M.; Carre, M. Effect of cinnamoyl putrescines on in vitro cell multiplication and differentiation of tobacco explants. Plant Cell. Rep. 1985, 4, 158–160.
28. Santana, I.; Castelo-Branco, V.N.; Guimarães, B.M.; Silva, L.d.O.; Peixoto, V.O.D.S.; Cabral, L.M.C.; Freitas, S.P.; Torres, A.G. Hass avocado (Persea americana Mill.) oil enriched in phenolic compounds and tocopherols by expeller-pressing the unpeeled microwave dried fruit. Food Chem. 2019, 286, 354–361.
29. Gross, J.; Gabai, M.; Lifshitz, A.; Sklarz, B. Structures of some carotenoids from the pulp of Persea americana. Phytochemistry 1974, 13, 1917–1921.
30. Gross, J.; Gabai, M.; Lifshitz, A.; Sklarz, B. Carotenoids in pulp, peel and leaves of Persea americana. Phytochemistry 1973, 12, 2259–2263.
31. Rodriguez-Saona, C.R.; Maynard, D.F.; Phillips, S.; Trumble, J.T. Alkylfurans: Effects of Alkyl Side-Chain Length on Insecticidal Activity. J. Nat. Prod. 1999, 62, 191–193.
32. Rodriguez-Saona, C.; Millar, J.G.; Maynard, D.F.; Trumble, J.T. Novel Antifeedant and Insecticidal Compounds from Avocado Idioblast Cell Oil. J. Chem. Ecol. 1998, 24, 867–889.
33. Fraga, B.M.; Terrero, D. Alkene-γ-lactones and avocadofurans from Persea indica: A revision of the structure of majorenolide and related lactones. Phytochemistry 1996, 41, 229–232.
34. Rosenblat, G.; Kagan, H.M.; Shah, M.A.; Spiteller, G.; Neeman, I. Chemical characterization of lysyl oxidase inhibitor from avocado seed oil. J. Am. Oil Chem. Soc. 1995, 72, 225–229.

35. Zaki, A.; Zentmyer, G.; Pettus, J.; Sills, J.; Keen, N.; Sing, V. Borbonol from Persea spp.-chemical properties and antifungal activity against Phytophthora cinnamomi. Physiol. Plant Pathol. 1980, 16, 205–212.
36. Falodun, A.; Engel, N.; Kragl, U.; Nebe, B.; Langer, P. Novel anticancer alkene lactone from Persea americana. Pharm. Biol. 2013, 51, 700–706.
37. Chen, C.-Y.; Chen, C.-H.; Lo, Y.-C.; Wu, B.-N.; Wang, H.-M.; Lo, W.-L.; Yen, C.-M.; Lin, R.-J. Anticancer Activity of Isoobtusilactone A from Cinnamomum kotoense: Involvement of Apoptosis, Cell-Cycle Dysregulation, Mitochondria Regulation, and Reactive Oxygen Species. J. Nat. Prod. 2008, 71, 933–940.
38. Rodriguez-Saona, C.; Maynard, D.F.; Phillips, S.; Trumble, J.T. Avocadofurans and their tetrahydrofuran analogues: Comparison of growth inhibitory and insecticidal activity. J. Agric. Food Chem. 2000, 48, 3642–3645.
39. Fraga, B.M.; González-Coloma, A.; Gutiérrez, C.; Terrero, D. Insect Antifeedant Isoryanodane Diterpenes from Persea indica. J. Nat. Prod. 1997, 60, 880–883.
40. Han, A.; Tao, Y.; Reisman, S.E. 16-Step Synthesis of the Isoryanodane Diterpene (+)-Perseanol. ChemRxiv. Preprint. 2019, in press.
41. Gonzalez-Coloma, A.; Hernandez, M.G.; Perales, A.; Fraga, B.M. Chemical ecology of canarian laurel forest: Toxic diterpenes from Persea indica (Lauraceae). J. Chem. Ecol. 1990, 16, 2723–2733.
42. Fraga, B.M.; Terrero, D.; Gutiérrez, C.; González-Coloma, A. Minor diterpenes from Persea indica: Their antifeedant activity. Phytochemistry 2001, 56, 315–320.
43. GonzÍez-Coloma, A.; Cabrera, R.; Socorro Monzón, A.R.; Frag, B.M. Persea indica as a natural source of the insecticide ryanodol. Phytochemistry 1993, 34, 397–400.
44. Hann, R.M.; Hudson, C.S. Proof of the Structure and Configuration of Perseulose (L-Galaheptulose). J. Am. Chem. Soc. 1939, 61, 336–340.
45. Sephton, H.H.; Richtmyer, N.K. The isolation of D-erythro-L-galacto-nonulose from the avocado, together with its synthesis and proof of structure through reduction to D-arabino-D-manno-nonitol and D-arabino-D-gluco-nonitol. Carbohyd. Res. 1966, 2, 289–300.
46. Sephton, H.H.; Richtmyer, N.K. Isolation of D-erythro-L-gluco-Nonulose from the Avocado1. J. Org. Chem. 1963, 28, 2388–2390.
47. Charlson, A.J.; Richtmyer, N.K. The Isolation of an octulose and an octitol from natural sources: D-glycero-D-manno-Octulose and D-erythro-D-galacto-octitol from the avocado and D-glycero-D-manno-octulose from Sedum species1,2. J. Am. Chem. Soc. 1960, 82, 3428–3434.
48. Ian-Lih, T.; Chih-Feng, H.; Chang-Yih, D.; Ih-Sheng, C. Cytotoxic neolignans from Persea obovatifolia. Phytochemistry 1996, 43, 1261–1263.
49. Xia, Y.; Wang, W. Asymmetric synthesis of machilin C and its analogue. Chem. Pap. 2010, 64, 630–636.
50. Ward, R.S. Lignans neolignans, and related compounds. Nat. Prod. Rep. 1993, 10, 1–28.
51. Tsai, I.-L.; Hsieh, C.-F.; Duh, C.-Y.; Chen, I.-S. Further study on the chemical constituents and their cytotoxicity from the leaves of Persea obovatifolia. Chin. Pharm. J. 1999, 51, 335–346.

52. Tsai, I.-L.; Hsieh, C.-F.; Duh, C.-Y. Additional cytotoxic neolignans from Persea obovatifolia. Phytochemistry 1998, 48, 1371–1375.
53. Sepulveda-Boza, S.; Delhvi, S.; Cassels, B.K. An aryltetralin lignan from Persea lingue. Phytochemistry 1990, 29, 2357–2358.
54. Chang, C.-F.; Isogai, A.; Kamikado, T.; Murakoshi, S.; Sakurai, A.; Tamura, S. Isolation and structure elucidation of growth inhibitors for silkworm larvae from avocado leaves. Agric. Biol. Chem. 1975, 39, 1167–1168.
55. El Kharrassi, Y.; Samadi, M.; Lopez, T.; Nury, T.; El Kebbaj, R.; Andreoletti, P.; El Hajj, H.I.; Vamecq, J.; Moustaid, K.; Latruffe, N.; et al. Biological activities of Schottenol and Spinasterol, two natural phytosterols present in argan oil and in cactus pear seed oil, on murine miroglial BV2 cells. Biochem. Biophys. Res. Commun. 2014, 446, 798–804.
56. Ohsaki, A.; Kubota, T.; Asaka, Y. Perseapicroside A, hexanorcucurbitacin-type glucopyranoside from Persea mexicana. Phytochemistry 1990, 29, 1330–1332.
57. Cascinu, S.; Catalano, V.; Cordella, L.; Labianca, R.; Giordani, P.; Baldelli, A.M.; Beretta, G.D.; Ubiali, E.; Catalano, G. Neuroprotective effect of reduced glutathione on oxaliplatin-based chemotherapy in advanced colorectal cancer: A randomized, double-blind, placebo-controlled trial. J. Clin. Oncol. 2002, 20, 3478–3483.
58. Smyth, J.F.; Bowman, A.; Perren, T.; Wilkinson, P.; Prescott, R.J.; Quinn, K.J.; Tedeschi, M. Glutathione reduces the toxicity and improves quality of life of women diagnosed with ovarian cancer treated with cisplatin: Results of a double-blind, randomised trial. Ann. Oncol. 1997, 8, 569–573.
59. Flagg, E.W.; Coates, R.J.; Jones, D.P.; Byers, T.E.; Greenberg, R.S.; Gridley, G.; McLaughlin, J.K.; Blot, W.J.; Haber, M.; Preston-Martin, S.; et al. Dietary Glutathione Intake and the Risk of Oral and Pharyngeal Cancer. Am. J. Epidemiol. 1994, 139, 453–465.
60. Choudhury, S.; Vajczikova, I. Variations in the essential oil composition of Persea bombycina (King ex Hook. f.) Kost and its effect on muga silkworm (Antheraea assama Ww)—A new report. Indian J. Chem. B 2003, 42B, 641–647.
61. U.S. Department of Agriculture, Agricultural Research Service. Avocados, Raw, California. FoodData Central. 2019. Available online: https://fdc.nal.usda.gov/fdc-app.html#/food-details/171706/nutrients (accessed on 22 September 2019).
62. Duarte, P.F.; Chaves, M.A.; Borges, C.D.; Mendonça, C.R.B. Avocado: Characteristics, health benefits and uses. Cienc. Rural 2016, 46, 747–754.
63. Duester, K.C. Avocados a look beyond basic nutrition for one of nature's whole foods. Nutr. Today 2000, 35, 151–157.
64. Bao, J.; Atkinson, F.; Petocz, P.; Willett, W.C.; Brand-Miller, J.C. Prediction of postprandial glycemia and insulinemia in lean, young, healthy adults: Glycemic load compared with carbohydrate content alone. Am. J. Clin. Nutr. 2011, 93, 984–996.
65. Dreher, M.L.; Davenport, A.J. Hass avocado composition and potential health effects. Crit. Rev. Food Sci. Nutr. 2013, 53, 738–750.
66. Landahl, S.; Meyer, M.D.; Terry, L.A. Spatial and temporal analysis of textural and biochemical changes of imported avocado cv. Hass during fruit ripening. J. Agric. Food Chem. 2009, 57, 7039–7047.

67. Wang, L.; Bordi, P.L.; Fleming, J.A.; Hill, A.M.; Kris-Etherton, P.M. Effect of a moderate fat diet with and without avocados on lipoprotein particle number, size and subclasses in overweight and obese adults: A randomized, controlled trial. J. Am. Heart Assoc. 2015, 4, e001355.
68. Ranade, S.S.; Thiagarajan, P. A review on Persea americana Mill.(avocado)-its fruits and oil. Int. J. Pharmtech Res. 2015, 8, 72–77.
69. de Melo, M.F.F.T.; Pereira, D.E.; Moura, R.d.L.; da Silva, E.B.; de Melo, F.A.L.T.; Dias, C.d.C.Q.; Silva, M.d.C.A.; de Oliveira, M.E.G.; Viera, V.B.; Pintado, M.M.E.; et al. Maternal supplementation with avocado (Persea americana Mill.) pulp and oil alters reflex maturation, physical development, and offspring memory in rats. Front. Neurosci. 2019, 13, 9.
70. Carvalho, C.P.; Bernal, E.J.; Velásquez, M.A.; Cartagena, V.J.R. Fatty acid content of avocados (Persea americana Mill. cv. Hass) in relation to orchard altitude and fruit maturity stage. Agron. Colomb. 2015, 33, 220–227.
71. Swisher, H.E. Avocado oil. J. Am. Oil Chem. Soc. 1988, 65, 1704–1706.
72. Murray, M.T.; Pizzorno, J. The Encyclopedia of Healing Foods; Simon and Schuster: NewYork, NY, USA, 2010.
73. Lidia, D.-A.; Alicia, O.-M.; Felipe, G.-O. Avocado. In Tropical and Subtropical Fruits; Muhammad, S., Ed.; Wiley: Hoboken, NJ, USA, 2012; Volume 1, pp. 435–454.
74. Dabas, D.; Shegog, R.M.; Ziegler, G.R.; Lambert, J.D. Avocado (Persea americana) seed as a source of bioactive phytochemicals. Curr. Pharm. Des. 2013, 19, 6133–6140.
75. Bauman, H.; Moyer, T. Food as Medicine: Avocado (Persea americana, Lauraceae). In HerbalEGram; American Botanical Council: Austin, TX, USA, 2017; Volume 14.
76. Eisenhauer, B.; Natoli, S.; Liew, G.; Flood, V.M. Lutein and Zeaxanthin-Food Sources, Bioavailability and Dietary Variety in Age-Related Macular Degeneration Protection. Nutrients 2017, 9, 120.
77. Lichtenstein Alice, H.; Deckelbaum Richard, J. Stanol/Sterol Ester–Containing Foods and Blood Cholesterol Levels. Circulation 2001, 103, 1177–1179.
78. Weihrauch, J.L.; Gardner, J.M. Sterol content of foods of plant origin. J. Am. Diet. Assoc. 1978, 73, 39–47.
79. Duester, K.C. Avocado fruit is a rich source of beta-sitosterol. J. Am. Diet. Assoc. 2001, 101, 404–405.
80. Honarbakhsh, S.; Schachter, M. Vitamins and cardiovascular disease. Br. J. Nutr. 2009, 101, 1113–1131.
81. Bhuyan, D.J.; Vuong, Q.V.; Chalmers, A.C.; van Altena, I.A.; Bowyer, M.C.; Scarlett, C.J. Investigation of phytochemicals and antioxidant capacity of selected Eucalyptus species using conventional extraction. Chem. Pap. 2016, 70, 567–575.
82. Fu, L.; Xu, B.T.; Xu, X.R.; Qin, X.S.; Gan, R.Y.; Li, H.B. Antioxidant capacities and total phenolic contents of 56 wild fruits from South China. Molecules 2010, 15, 8602–8617.
83. Vázquez, G.; Santos, J.; Freire, M.S.; Antorrena, G.; González-Álvarez, J. Extraction of antioxidants from eucalyptus (Eucalyptus globulus) bark. Wood Sci. Technol. 2012, 46, 443–457.
84. Wang, W.; Bostic, T.R.; Gu, L. Antioxidant capacities, procyanidins and pigments in avocados of different strains and cultivars. Food Chem. 2010, 122, 1193–1198.

85. Wang, M.; Zheng, Y.; Khuong, T.; Lovatt, C.J. Effect of harvest date on the nutritional quality and antioxidant capacity in ‘Hass’ avocado during storage. Food Chem. 2012, 135, 694–698.
86. Segovia, F.J.; Corral-Pérez, J.J.; Almajano, M.P. Avocado seed: Modeling extraction of bioactive compounds. Ind. Crop. Prod. 2016, 85, 213–220.
87. Boyadzhieva, S.; Georgieva, S.; Angelov, G. Optimization of the extraction of natural antioxidants from avocado seeds. Bulg. Chem. Commun. 2018, 50, 80–84.
88. Boyadzhieva, S.; Georgieva, S.; Angelov, G. Recovery of antioxidant phenolic compounds from avocado peels by solvent extraction. Bulg. Chem. Commun. 2018, 50, 83–89.
89. Di Stefano, V.; Avellone, G.; Bongiorno, D.; Indelicato, S.; Massenti, R.; Lo Bianco, R. Quantitative evaluation of the phenolic profile in fruits of six avocado (Persea americana) cultivars by ultra-high-performance liquid chromatography-heated electrospray-mass spectrometry. Int. J. Food Prop. 2017, 20, 1302–1312.
90. Figueroa, J.G.; Borrás-Linares, I.; Lozano-Sánchez, J.; Segura-Carretero, A. Comprehensive identification of bioactive compounds of avocado peel by liquid chromatography coupled to ultra-high-definition accurate-mass Q-TOF. Food Chem. 2018, 245, 707–716.
91. Figueroa, J.G.; Borrás-Linares, I.; Lozano-Sánchez, J.; Segura-Carretero, A. Comprehensive characterization of phenolic and other polar compounds in the seed and seed coat of avocado by HPLC-DAD-ESI-QTOF-MS. Food Res. Int. 2018, 105, 752–763.
92. Hurtado-Fernandez, E.; Carrasco-Pancorbo, A.; Fernandez-Gutierrez, A. Profiling LC-DAD-ESI-TOF MS method for the determination of phenolic metabolites from avocado (Persea americana). J. Agric. Food Chem. 2011, 59, 2255–2267.
93. Hurtado-Fernández, E.; Pacchiarotta, T.; Mayboroda, O.A.; Fernández-Gutiérrez, A.; Carrasco-Pancorbo, A. Quantitative characterization of important metabolites of avocado fruit by gas chromatography coupled to different detectors (APCI-TOF MS and FID). Food Res. Int. 2014, 62, 801–811.
94. Kosińska, A.; Karamać, M.; Estrella, I.; Hernández, T.; Bartolomé, B.; Dykes, G.A. Phenolic Compound Profiles and Antioxidant Capacity of Persea americana Mill. Peels and Seeds of Two Varieties. J. Agric. Food Chem. 2012, 60, 4613–4619.
95. Lima, C.R.; Vasconcelos, C.F.; Costa-Silva, J.H.; Maranhao, C.A.; Costa, J.; Batista, T.M.; Carneiro, E.M.; Soares, L.A.; Ferreira, F.; Wanderley, A.G. Anti-diabetic activity of extract from Persea americana Mill. leaf via the activation of protein kinase B (PKB/Akt) in streptozotocin-induced diabetic rats. J. Ethnopharmacol. 2012, 141, 517–525.
96. López-Cobo, A.; Gómez-Caravaca, A.M.; Pasini, F.; Caboni, M.F.; Segura-Carretero, A.; Fernández-Gutiérrez, A. HPLC-DAD-ESI-QTOF-MS and HPLC-FLD-MS as valuable tools for the determination of phenolic and other polar compounds in the edible part and by-products of avocado. Lwt Food Sci. Technol. 2016, 73, 505–513.
97. Tremocoldi, M.A.; Rosalen, P.L.; Franchin, M.; Massarioli, A.P.; Denny, C.; Daiuto, É.R.; Paschoal, J.A.R.; Melo, P.S.; Alencar, S.M.d. Exploration of avocado by-products as natural sources of bioactive compounds. PLoS ONE 2018, 13, e0192577.
98. Alkhalf, M.I.; Alansari, W.S.; Ibrahim, E.A.; Elhalwagy, M.E.A. Anti-oxidant, anti-inflammatory and anti-cancer activities of avocado (Persea americana) fruit and seed extract. J. King Saud Univ. Sci. 2018.

99. Amado, D.A.V.; Helmann, G.A.B.; Detoni, A.M.; Carvalho, S.L.C.D.; Aguiar, C.M.D.; Martin, C.A.; Tiuman, T.S.; Cottica, S.M. Antioxidant and antibacterial activity and preliminary toxicity analysis of four varieties of avocado (Persea americana Mill.). Braz. J. Food Technol. 2019, 22.
100. Bertling, I.; Tesfay, S.; Bower, J. Antioxidants in ‘Hass’ avocado. South Afr. Avocado Grow. Assoc. Yearb. 2007, 30, 17–19.
101. Calderón-Oliver, M.; Escalona-Buendía, H.B.; Medina-Campos, O.N.; Pedraza-Chaverri, J.; Pedroza-Islas, R.; Ponce-Alquicira, E. Optimization of the antioxidant and antimicrobial response of the combined effect of nisin and avocado byproducts. Lwt-Food Sci. Technol. 2016, 65, 46–52.
102. Daiuto, É.R.; Tremocoldi, M.A.; Alencar, S.M.D.; Vieites, R.L.; Minarelli, P.H. Composição química e atividade antioxidante da polpa e resíduos de abacate ‘Hass’. Rev. Bras. Frutic. 2014, 36, 417–424.
103. Oboh, G.; Adelusi, T.; Akinyemi, A. Inhibitory effect of phenolic extract from leaf and fruit of avocado pear (Persea americana) on Fe2+ induced lipid peroxidation in rats’pancreas in vitro. Futa J. Res. Sci. 2013, 2, 276–286.
104. Rodriguez-Carpena, J.G.; Morcuende, D.; Andrade, M.J.; Kylli, P.; Estevez, M. Avocado (Persea americana Mill.) phenolics, in vitro antioxidant and antimicrobial activities, and inhibition of lipid and protein oxidation in porcine patties. J. Agric. Food Chem. 2011, 59, 5625–5635.
105. Soong, Y.-Y.; Barlow, P.J. Antioxidant activity and phenolic content of selected fruit seeds. Food Chem. 2004, 88, 411–417.
106. Vinha, A.F.; Moreira, J.; Barreira, S.V. Physicochemical parameters, phytochemical composition and antioxidant activity of the algarvian avocado (Persea americana Mill.). J. Agric. Sci. 2013, 5, 100.
107. Hurtado-Fernández, E.; Pacchiarotta, T.; Gómez-Romero, M.; Schoenmaker, B.; Derks, R.; Deelder, A.M.; Mayboroda, O.A.; Carrasco-Pancorbo, A.; Fernández-Gutiérrez, A. Ultra high performance liquid chromatography-time of flight mass spectrometry for analysis of avocado fruit metabolites: Method evaluation and applicability to the analysis of ripening degrees. J. Chromatogr. A 2011, 1218, 7723–7738.
108. Villa-Rodríguez, J.A.; Molina-Corral, F.J.; Ayala-Zavala, J.F.; Olivas, G.I.; González-Aguilar, G.A. Effect of maturity stage on the content of fatty acids and antioxidant activity of ‘Hass’ avocado. Food Res. Int. 2011, 44, 1231–1237.
109. Segura, N.; Amarillo, M.; Martinez, N.; Grompone, M. Improvement in the extraction of Hass avocado virgin oil by ultrasound application. J. Food Res. 2018, 7, 106–113.
110. Lu, Q.Y.; Zhang, Y.; Wang, Y.; Wang, D.; Lee, R.P.; Gao, K.; Byrns, R.; Heber, D. California Hass avocado: Profiling of carotenoids, tocopherol, fatty acid, and fat content during maturation and from different growing areas. J. Agric. Food Chem. 2009, 57, 10408–10413.
111. Plaza, L.; Sánchez-Moreno, C.; de Pascual-Teresa, S.; de Ancos, B.; Cano, M.P. Fatty Acids, Sterols, and Antioxidant Activity in Minimally Processed Avocados during Refrigerated Storage. J. Agric. Food Chem. 2009, 57, 3204–3209.
112. Zhang, Z.; Huber, D.J.; Rao, J. Antioxidant systems of ripening avocado (Persea americana Mill.) fruit following treatment at the preclimacteric stage with aqueous 1-methylcyclopropene. Postharvest Biol. Technol. 2013, 76, 58–64.
113. Souza, D.S.; Marques, L.G.; Gomes, E.d.B.; Narain, N. Lyophilization of Avocado (Persea americana Mill.): Effect of Freezing and Lyophilization Pressure on Antioxidant Activity, Texture, and Browning of Pulp. Dry.

Technol. 2015, 33, 194–204.

114. Soldera-Silva, A.; Seyfried, M.; Campestrini, L.H.; Zawadzki-Baggio, S.F.; Minho, A.P.; Molento, M.B.; Maurer, J.B.B. Assessment of anthelmintic activity and bio-guided chemical analysis of Persea americana seed extracts. Vet. Parasitol. 2018, 251, 34–43.
115. Abaide, E.R.; Zabot, G.L.; Tres, M.V.; Martins, R.F.; Fagundez, J.L.; Nunes, L.F.; Druzian, S.; Soares, J.F.; Dal Prá, V.; Silva, J.R.F.; et al. Yield, composition, and antioxidant activity of avocado pulp oil extracted by pressurized fluids. Food Bioprod. Process. 2017, 102, 289–298.
116. dos Santos, M.A.Z.; Alicieo, T.V.R.; Pereira, C.M.P.; Ramis-Ramos, G.; Mendonça, C.R.B. Profile of Bioactive Compounds in Avocado Pulp Oil: Influence of the Drying Processes and Extraction Methods. J. Am. Oil Chem. Soc. 2014, 91, 19–27.
117. Prabath Pathirana, U.; Sekozawa, Y.; Sugaya, S.; Gemma, H. Changes in lipid oxidation stability and antioxidant properties of avocado in response to 1-MCP and low oxygen treatment under low-temperature storage. Int. Food Res. J. 2013, 20, 1065–1075.
118. Foudjo, B.U.S.; Kansci, G.; Fokou, E.; Genot, C. Prediction of critical times for water-extracted avocado oil heated at high temperatures. Int. J.Biol. Chem. Sci. 2018, 12, 2053–2064.
119. Corrales-García, J.E.; del Rosario García-Mateos, M.; Martínez-López, E.; Barrientos-Priego, A.F.; Ybarra-Moncada, M.C.; Ibarra-Estrada, E.; Méndez-Zúñiga, S.M.; Becerra-Morales, D. Anthocyanin and Oil Contents, Fatty Acids Profiles and Antioxidant Activity of Mexican Landrace Avocado Fruits. Plant Foods Hum. Nutr. 2019, 74, 210–215.
120. Corzzini, S.C.S.; Barros, H.D.F.Q.; Grimaldi, R.; Cabral, F.A. Extraction of edible avocado oil using supercritical CO2 and a CO2/ethanol mixture as solvents. J. Food Eng. 2017, 194, 40–45.
121. Krumreich, F.D.; Borges, C.D.; Mendonça, C.R.B.; Jansen-Alves, C.; Zambiazi, R.C. Bioactive compounds and quality parameters of avocado oil obtained by different processes. Food Chem. 2018, 257, 376–381.
122. Rodriguez-Sanchez, D.; Silva-Platas, C.; Rojo, R.P.; Garcia, N.; Cisneros-Zevallos, L.; Garcia-Rivas, G.; Hernandez-Brenes, C. Activity-guided identification of acetogenins as novel lipophilic antioxidants present in avocado pulp (Persea americana). J. Chromatogr. B 2013, 942–943, 37–45.
123. Gómez, F.S.; Sánchez, S.P.; Iradi, M.G.G.; Azman, N.A.M.; Almajano, M.P. Avocado Seeds: Extraction Optimization and Possible Use as Antioxidant in Food. Antioxidants 2014, 3, 439–454.
124. Kingne, F.K.; Tsafack, H.D.; Boungo, G.T.; Mboukap, A.; Azia, A. Phenolic Content and Antioxidant Activity of Young and Mature Mango (Mangifera indica) and Avocado (Persea americana) Leaves Extracts. J. Food. Stab. 2018, 1, 14–27.
125. Tan, C.X.; Chong, G.H.; Hamzah, H.; Ghazali, H.M. Characterization of Virgin Avocado Oil Obtained via Advanced Green Techniques. Eur. J. Lipid Sci. Technol. 2018, 120, 1800170.
126. Princwill-Ogbonna, I.; Ogbonna, P.; Ogujiofor, I. Proximate Composition, Vitamin, Mineral and biologically Active Compounds Levels in Leaves of Mangifera indica (Mango), Persea americana (Avocado pea), and Annona muricata (Sour sop). J. Appl. Sci.Environ. Manag. 2019, 23, 65–74.
127. Nabavi, S.F.; Nabavi, S.M.N.; Setzer, W.; Nabavi, S.A.; Nabavi, S.A.; Ebrahimzadeh, M.A. Antioxidant and antihemolytic activity of lipid-soluble bioactive substances in avocado fruits. Fruits 2013, 68, 185–193.

128. Garcia-Alonso, M.; de Pascual-Teresa, S.; Santos-Buelga, C.; Rivas-Gonzalo, J.C. Evaluation of the antioxidant properties of fruits. Food Chem. 2004, 84, 13–18.
129. Oboh, G.; Odubanjo, V.O.; Bello, F.; Ademosun, A.O.; Oyeleye, S.I.; Nwanna, E.E.; Ademiluyi, A.O. Aqueous extracts of avocado pear (Persea americana Mill.) leaves and seeds exhibit anti-cholinesterases and antioxidant activities in vitro. J. Basic Clin. Physiol. Pharmacol. 2016, 27, 131–140.
130. Nagaraj, M.; Sandhya, V.; Supriya, G.; Manju, R.; Pranitha, K.; Shivaji, B.; Lalitha, V.; Kiran, B. Antioxidant and antibacterial activity of avocado (Persea gratissima Gaertner.) seed extract. World Appl. Sci. J. 2010, 9, 695–698.
131. Wang, C.Y.; Bai, X.Y.; Wang, C.H. Traditional Chinese medicine: A treasured natural resource of anticancer drug research and development. Am. J. Chin. Med. 2014, 42, 543–559.
132. Bhuyan, D.J.; Sakoff, J.; Bond, D.R.; Predebon, M.; Vuong, Q.V.; Chalmers, A.C.; van Altena, I.A.; Bowyer, M.C.; Scarlett, C.J. In vitro anticancer properties of selected Eucalyptus species. In Vitro Cell. Dev. Biol. Anim. 2017, 53, 604–615.
133. Zhang, Y.; Liang, Y.; He, C. Anticancer activities and mechanisms of heat-clearing and detoxicating traditional Chinese herbal medicine. Chin. Med. 2017, 12, 20.
134. Bhuyan, D.J.; Vuong, Q.V.; Chalmers, A.C.; Bowyer, M.C.; Scarlett, C.J. An array of bioactive compounds from Australian eucalypts and their relevance in pancreatic cancer therapeutics. Pancreas 2018, 47, 690–707.
135. Wang, H.; Khor, T.O.; Shu, L.; Su, Z.-Y.; Fuentes, F.; Lee, J.-H.; Kong, A.-N.T. Plants vs. cancer: A review on natural phytochemicals in preventing and treating cancers and their druggability. Anticancer Agents Med. Chem. 2012, 12, 1281–1305.
136. Bhuyan, D.J.; Vuong, Q.V.; Bond, D.R.; Chalmers, A.C.; Bowyer, M.C.; Scarlett, C.J. Eucalyptus microcorys leaf extract derived HPLC-fraction reduces the viability of MIA PaCa-2 cells by inducing apoptosis and arresting cell cycle. Biomed. Pharmacother. 2018, 105, 449–460.
137. Mooz, E.D.; Gaiano, N.M.; Shimano, M.Y.H.; Amancio, R.D.; Spoto, M.H.F. Physical and chemical characterization of the pulp of different varieties of avocado targeting oil extraction potential. Food Sci. Technol 2012, 32, 274–280.
138. Bonilla-Porras, A.R.; Salazar-Ospina, A.; Jimenez-Del-Rio, M.; Pereanez-Jimenez, A.; Velez-Pardo, C. Pro-apoptotic effect of Persea americana var. Hass (avocado) on Jurkat lymphoblastic leukemia cells. Pharm. Biol. 2013.
139. Butt, A.J.; Roberts, C.G.; Seawright, A.A.; Oelrichs, P.B.; MacLeod, J.K.; Liaw, T.Y.E.; Kavallaris, M.; Somers-Edgar, T.J.; Lehrbach, G.M.; Watts, C.K.; et al. A novel plant toxin, persin, with in vivo activity in the mammary gland, induces Bim-dependent apoptosis in human breast cancer cells. Mol. Cancer Ther. 2006, 5, 2300–2309.
140. Dabas, D.; Elias, R.J.; Ziegler, G.R.; Lambert, J.D. In Vitro Antioxidant and Cancer Inhibitory Activity of a Colored Avocado Seed Extract. Int. J. Food Sci. 2019, 2019, 7.
141. Ding, H.; Chin, Y.-W.; Kinghorn, A.D.; D'Ambrosio, S.M. Chemopreventive characteristics of avocado fruit. Semin. Cancer Biol. 2007, 17, 386–394.
142. Ding, H.; Han, C.; Guo, D.; Chin, Y.W.; Ding, Y.; Kinghorn, A.D.; D'Ambrosio, S.M. Selective induction of apoptosis of human oral cancer cell lines by avocado extracts via a ROS-mediated mechanism. Nutr.

Cancer 2009, 61, 348–356.

143. Guzman-Rodriguez, J.J.; Lopez-Gomez, R.; Salgado-Garciglia, R.; Ochoa-Zarzosa, A.; Lopez-Meza, J.E. The defensin from avocado (Persea americana var. drymifolia) PaDef induces apoptosis in the human breast cancer cell line MCF-7. Biomed. Pharmacother. 2016, 82, 620–627.
144. Lee, S.-G.; Yu, M.-H.; Lee, S.-P.; Lee, I.-S. Antioxidant activities and induction of apoptosis by methanol extracts from avocado. J. Korean Soc. Food Sci. Nutr. 2008, 37, 269–275.
145. Leon, L.G.; Carballo, R.M.; Vega-Hernandez, M.C.; Miranda, P.O.; Martin, V.S.; Padron, J.I.; Padron, J.M. β'-Hydroxy-alpha,β-unsaturated ketones: A new pharmacophore for the design of anticancer drugs. Part 2. ChemMedChem 2008, 3, 1740–1747.
146. D'Ambrosio, S.M.; Han, C.; Pan, L.; Kinghorn, A.D.; Ding, H. Aliphatic acetogenin constituents of avocado fruits inhibit human oral cancer cell proliferation by targeting the EGFR/RAS/RAF/MEK/ERK1/2 pathway. Biochem. Biophys. Res. Commun. 2011, 409, 465–469.
147. Vo, T.S.; Le, P.U. Free radical scavenging and anti-proliferative activities of avocado (Persea americana Mill.) seed extract. Asian Pac. J. Trop. Biomed. 2019, 9, 91.
148. Widiyastuti, Y.; Pratiwi, R.; Riyanto, S.; Wahyuono, S. Cytotoxic Activity and Apoptosis Induction of Avocado (Perseaamericana) Seed Extract on MCF-7 Cancer Cell Line. Indones. J. Biotechnol. 2018, 23, 61–67.
149. Salazar, L.; López, M.J.V.; Grijalva, M.; Castillo, L.; Maldonado, A. Biological Effect of Organically Coated Grias neuberthii and Persea americana Silver Nanoparticles on HeLa and MCF-7 Cancer Cell Lines. J. Nanotechnol. 2018, 2018, 11.
150. Ant, A.; Avcý, A.; Genç, M.; Ýnal, E.; Tunçel, Ü.; Þencan, Z. Avocado leaf extract activates Adenosine Deaminase (ADA) in Larynx cancer tissues. Acta Oncol. Tur. 2018, 51, 199–204.
151. Abubakar, A.N.F.; Achmadi, S.S.; Suparto, I.H. Triterpenoid of avocado (Persea americana) seed and its cytotoxic activity toward breast MCF-7 and liver HepG2 cancer cells. Asian Pac. J. Trop. Biomed. 2017, 7, 397–400.
152. Vahedi Larijani, L.; Ghasemi, M.; AbedianKenari, S.; Naghshvar, F. Evaluating the effect of four extracts of avocado fruit on esophageal squamous carcinoma and colon adenocarcinoma cell lines in comparison with peripheral blood mononuclear cells. Acta Med. Iran. 2014, 52, 201–205.
153. Khalifa, N.S.; Barakat, H.S.; Elhallouty, S.; Salem, D. Effect of the Water Extracts of Avocado Fruit and Cherimoya Leaf on Four Human Cancer Cell Lines and Vicia Faba Root Tip Cells. J. Agric. Sci. 2013, 5, 245.
154. Paul, R.; Kulkarni, P.; Ganesh, N. Avocado fruit (Persea americana Mill) exhibits chemo-protective potentiality against cyclophosphamide induced genotoxicity in human lymphocyte culture. J. Exp. Ther. Oncol. 2011, 9, 221–230.
155. Roberts, C.G.; Gurisik, E.; Biden, T.J.; Sutherland, R.L.; Butt, A.J. Synergistic cytotoxicity between tamoxifen and the plant toxin persin in human breast cancer cells is dependent on Bim expression and mediated by modulation of ceramide metabolism. Mol. Cancer Ther. 2007, 6, 2777–2785.
156. Kim, O.K.; Murakami, A.; Takahashi, D.; Nakamura, Y.; Torikai, K.; Kim, H.W.; Ohigashi, H. An avocado constituent, persenone A, suppresses expression of inducible forms of nitric oxide synthase and cyclooxygenase in macrophages, and hydrogen peroxide generation in mouse skin. Biosci. Biotechnol. Biochem. 2000, 64, 2504–2507.

157. Flores-Alvarez, L.J.; Guzman-Rodriguez, J.J.; Lopez-Gomez, R.; Salgado-Garciglia, R.; Ochoa-Zarzosa, A.; Lopez-Meza, J.E. PaDef defensin from avocado (Persea americana var. drymifolia) is cytotoxic to K562 chronic myeloid leukemia cells through extrinsic apoptosis. Int. J. Biochem. Cell Biol. 2018, 99, 10–18.

158. Brooke, D.G.; Shelley, E.J.; Roberts, C.G.; Denny, W.A.; Sutherland, R.L.; Butt, A.J. Synthesis and in vitro evaluation of analogues of avocado-produced toxin (+)-(R)-persin in human breast cancer cells. Bioorg. Med. Chem. 2011, 19, 7033–7043.

159. Jackson, M.D.; Walker, S.P.; Simpson-Smith, C.M.; Lindsay, C.M.; Smith, G.; McFarlane-Anderson, N.; Bennett, F.I.; Coard, K.C.M.; Aiken, W.D.; Tulloch, T.; et al. Associations of whole-blood fatty acids and dietary intakes with prostate cancer in Jamaica. Cancer Causes Control 2012, 23, 23–33.

160. Aubrey, B.J.; Kelly, G.L.; Janic, A.; Herold, M.J.; Strasser, A. How does p53 induce apoptosis and how does this relate to p53-mediated tumour suppression? Cell Death Differ. 2017, 25, 104.

161. Gondi, C.S.; Dinh, D.H.; Klopfenstein, J.D.; Gujrati, M.; Rao, J.S. MMP-2 downregulation mediates differential regulation of cell death via ErbB-2 in glioma xenografts. Int. J. Oncol. 2009, 35, 257–263.

162. Valacca, C.; Tassone, E.; Mignatti, P. TIMP-2 Interaction with MT1-MMP Activates the AKT Pathway and Protects Tumor Cells from Apoptosis. PLoS ONE 2015, 10, e0136797.

163. Hata, A.N.; Engelman, J.A.; Faber, A.C. The BCL2 Family: Key Mediators of the Apoptotic Response to Targeted Anticancer Therapeutics. Cancer Discov. 2015, 5, 475–487.

164. O'Connor, L.; Strasser, A.; O'Reilly, L.A.; Hausmann, G.; Adams, J.M.; Cory, S.; Huang, D.C. Bim: A novel member of the Bcl-2 family that promotes apoptosis. Embo J. 1998, 17, 384–395.

165. Li, R.; Moudgil, T.; Ross, H.J.; Hu, H.-M. The BH3-only proapoptotic protein Bim directly links the microtubule poison Paclitaxel to mitochondrial damage and apoptosis. Cancer Res. 2004, 64, 1296.

166. Guzmán-Rodríguez, J.J.; López-Gómez, R.; Suárez-Rodríguez, L.M.; Salgado-Garciglia, R.; Rodríguez-Zapata, L.C.; Ochoa-Zarzosa, A.; López-Meza, J.E. Antibacterial activity of defensin PaDef from avocado fruit (Persea americana var. drymifolia) expressed in endothelial cells against Escherichia coli and Staphylococcus aureus. Biomed Res. Int. 2013, 2013, 986273.

167. Meneguetti, B.T.; Machado, L.d.S.; Oshiro, K.G.N.; Nogueira, M.L.; Carvalho, C.M.E.; Franco, O.L. Antimicrobial Peptides from Fruits and Their Potential Use as Biotechnological Tools—A Review and Outlook. Front. Microbiol. 2017, 7.

168. Kulkarni, P.; Paul, R.; Ganesh, N. In Vitro evaluation of genotoxicity of avocado (Persea americana) fruit and leaf extracts in human peripheral lymphocytes. J. Environ. Sci. Health C 2010, 28, 172–187.

169. Engel, N.; Oppermann, C.; Falodun, A.; Kragl, U. Proliferative effects of five traditional Nigerian medicinal plant extracts on human breast and bone cancer cell lines. J. Ethnopharmacol. 2011, 137, 1003–1010.

170. Hughes, K.J.; Mayne, S.T.; Blumberg, J.B.; Ribaya-Mercado, J.D.; Johnson, E.J.; Cartmel, B. Plasma Carotenoids and Biomarkers of Oxidative Stress in Patients with prior Head and Neck Cancer. Biomark. Insights 2009, 4, 17–26.

171. Tamimi, R.M.; Colditz, G.A.; Hankinson, S.E. Circulating carotenoids, mammographic density, and subsequent risk of breast cancer. Cancer Res. 2009, 69, 9323–9329.

172. Thomson, C.A.; Stendell-Hollis, N.R.; Rock, C.L.; Cussler, E.C.; Flatt, S.W.; Pierce, J.P. Plasma and dietary carotenoids are associated with reduced oxidative stress in women previously treated for breast cancer.

Cancer Epidemiol. Biomark. Prev. 2007, 16, 2008–2015.

173. Jones, D.P.; Coates, R.J.; Flagg, E.W.; Eley, J.W.; Block, G.; Greenberg, R.S.; Gunter, E.W.; Jackson, B. Glutathione in foods listed in the National Cancer Institute's Health Habits and History Food Frequency Questionnaire. Nutr. Cancer 1992, 17, 57–75.
174. Papoutsis, K.; Mathioudakis, M.M.; Hasperué, J.H.; Ziogas, V. Non-chemical treatments for preventing the postharvest fungal rotting of citrus caused by Penicillium digitatum (green mold) and Penicillium italicum (blue mold). Trends Food Sci. Technol. 2019, 86, 479–491.
175. Athaydes, B.R.; Alves, G.M.; Assis, A.L.E.M.D.; Gomes, J.V.D.; Rodrigues, R.P.; Campagnaro, B.P.; Nogueira, B.V.; Silveira, D.; Kuster, R.M.; Pereira, T.M.C.; et al. Avocado seeds (Persea americana Mill.) prevents indomethacin-induced gastric ulcer in mice. Food Res. Int. 2019, 119, 751–760.
176. Raymond Chia, T.W.; Dykes, G.A. Antimicrobial activity of crude epicarp and seed extracts from mature avocado fruit (Persea americana) of three cultivars. Pharm. Biol. 2010, 48, 753–756.
177. Salinas-Salazar, C.; Hernández-Brenes, C.; Rodríguez-Sánchez, D.G.; Castillo, E.C.; Navarro-Silva, J.M.; Pacheco, A. Inhibitory Activity of Avocado Seed Fatty Acid Derivatives (Acetogenins) Against Listeria Monocytogenes. J. Food Sci. 2017, 82, 134–144.
178. Cardoso, P.F.; Scarpassa, J.A.; Pretto-Giordano, L.G.; Otaguiri, E.S.; Yamada-Ogatta, S.F.; Nakazato, G.; Perugini, M.R.E.; Moreira, I.C.; Vilas-Boâs, G.T. Antibacterial activity of avocado extracts (Persea americana Mill.) against streptococcus agalactiae. Phyton 2016, 85, 218–224.
179. Hennessey-Ramos, L.; Murillo-Arango, W.; Guayabo, G.T. Evaluation of a colorant and oil extracted from avocado waste as functional components of a liquid soap formulation. Rev. Fac. Nac. Agron. Medellin 2019, 72, 8855–8862.
180. Bamoniri, A.; Ebrahimabadi, A.H.; Mazoochi, A.; Behpour, M.; Kashi, F.J.; Batooli, H. Antioxidant and antimicrobial activity evaluation and essential oil analysis of Semenovia tragioides Boiss. from Iran. Food Chem. 2010, 122, 553–558.
181. Bouic, P.J.; Etsebeth, S.; Liebenberg, R.W.; Albrecht, C.F.; Pegel, K.; Van Jaarsveld, P.P. beta-Sitosterol and beta-sitosterol glucoside stimulate human peripheral blood lymphocyte proliferation: Implications for their use as an immunomodulatory vitamin combination. Int. Immunopharmacol. 1996, 18, 693–700.
182. Simpson, D.; Amos, S. Chapter 12—Other Plant Metabolites. In Pharmacognosy; Badal, S., Delgoda, R., Eds.; Academic Press: Boston, MA, USA, 2017; pp. 267–280.
183. Pacheco, A.; Rodríguez-Sánchez, D.G.; Villarreal-Lara, R.; Navarro-Silva, J.M.; Senés-Guerrero, C.; Hernández-Brenes, C. Stability of the antimicrobial activity of acetogenins from avocado seed, under common food processing conditions, against Clostridium sporogenes vegetative cell growth and endospore germination. Int. J. Food Sci. Technol. 2017, 52, 2311–2323.
184. Singh, B.; Singh, J.P.; Kaur, A.; Singh, N. Antimicrobial potential of pomegranate peel: A review. Int. J. Food Sci. Technol. 2019, 54, 959–965.
185. Adeyemi, O.; Okpo, S.; O Ogunti, O. Analgesic and anti-inflammatory effects of Persea americana Mill (Lauraceae). Fitoterapia 2002, 73, 375–380.
186. de Oliveira, A.P.; Franco, E.d.S.; Rodrigues Barreto, R.; Cordeiro, D.P.; de Melo, R.G.; de Aquino, C.M.F.; e Silva, A.A.R.; de Medeiros, P.L.; et al. Effect of Semisolid Formulation of Persea Americana Mill (Avocado) Oil on Wound Healing in Rats. Evid. Based Complement. Alternat. Med. 2013, 2013, 8.

187. Henrotin, Y.E.; Labasse, A.H.; Jaspar, J.M.; De Groote, D.D.; Zheng, S.X.; Guillou, G.B.; Reginster, J.Y. Effects of three avocado/soybean unsaponifiable mixtures on metalloproteinases, cytokines and prostaglandin E2 production by human articular chondrocytes. Clin. Rheumatol. 1998, 17, 31–39.
188. Khayyal, M.T.; el-Ghazaly, M.A. The possible “chondroprotective” effect of the unsaponifiable constituents of avocado and soya in vivo. Drugs Exp. Clin. Res. 1998, 24, 41–50.
189. Goudarzi, R.; Taylor, J.F.; Yazdi, P.G.; Pedersen, B.A. Effects of Arthrocen, an avocado/soy unsaponifiables agent, on inflammatory mediators and gene expression in human chondrocytes. FEBS Open Bio 2017, 7, 187–194.
190. Gabay, O.; Gosset, M.; Levy, A.; Salvat, C.; Sanchez, C.; Pigenet, A.; Sautet, A.; Jacques, C.; Berenbaum, F. Stress-induced signaling pathways in hyalin chondrocytes: Inhibition by Avocado–Soybean Unsaponifiables (ASU). Osteoarthr. Cartil. 2008, 16, 373–384.
191. Au, R.Y.; Al-Talib, T.K.; Au, A.Y.; Phan, P.V.; Frondoza, C.G. Avocado soybean unsaponifiables (ASU) suppress TNF-α, IL-1β, COX-2, iNOS gene expression, and prostaglandin E2 and nitric oxide production in articular chondrocytes and monocyte/macrophages. Osteoarthr. Cartil. 2007, 15, 1249–1255.
192. Oliveira, G.J.P.L.; Paula, L.G.F.; Souza, J.A.C.; Spin-Neto, R.; Stavropoulos, A.; Marcantonio, R.A.C. Effect of avocado/soybean unsaponifiables on ligature-induced bone loss and bone repair after ligature removal in rats. J. Periodontal Res. 2016, 51, 332–341.
193. Catunda, I.S.; Vasconcelos, B.C.d.E.; Andrade, E.S.d.S.; Costa, D.F.N. Clinical effects of an avocado–soybean unsaponifiable extract on arthralgia and osteoarthritis of the temporomandibular joint: Preliminary study. Int. J. Oral Maxillofac. Surg. 2016, 45, 1015–1022.
194. Andriamanalijaona, R.; Benateau, H.; Barre, P.E.; Boumediene, K.; Labbe, D.; Compere, J.F.; Pujol, J.P. Effect of Interleukin-1β on Transforming Growth Factor-Beta and Bone Morphogenetic Protein-2 Expression in Human Periodontal Ligament and Alveolar Bone Cells in Culture: Modulation by Avocado and Soybean Unsaponifiables. J. Periodontol. 2006, 77, 1156–1166.
195. Heinecke, L.F.; Grzanna, M.W.; Au, A.Y.; Mochal, C.A.; Rashmir-Raven, A.; Frondoza, C.G. Inhibition of cyclooxygenase-2 expression and prostaglandin E2 production in chondrocytes by avocado soybean unsaponifiables and epigallocatechin gallate. Osteoarthr. Cartil. 2010, 18, 220–227.
196. Ownby, S.L.; Fortuno, L.V.; Au, A.Y.; Grzanna, M.W.; Rashmir-Raven, A.M.; Frondoza, C.G. Expression of pro-inflammatory mediators is inhibited by an avocado/soybean unsaponifiables and epigallocatechin gallate combination. J. Inflamm. 2014, 11, 8.
197. Kim, Y.; Oh, H.-C.; Park, J.W.; Kim, I.-S.; Kim, J.-Y.; Kim, K.-C.; Chae, D.-S.; Jo, W.-L.; Song, J.-H. Diagnosis and Treatment of Inflammatory Joint Disease. Hip Pelvis 2017, 29, 211–222.
198. Berenbaum, F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). Osteoarthr. Cartil. 2013, 21, 16–21.
199. Angermann, P. Avocado/soybean unsaponifiables in the treatment of knee and hip osteoarthritis. Ugeskr. Laeger 2005, 167, 3023–3025.
200. Christiansen, B.A.; Bhatti, S.; Goudarzi, R.; Emami, S. Management of Osteoarthritis with Avocado/Soybean Unsaponifiables. Cartilage 2015, 6, 30–44.
201. Lippiello, L.; Nardo, J.V.; Harlan, R.; Chiou, T. Metabolic Effects of Avocado/Soy Unsaponifiables on Articular Chondrocytes. Evid. Based Complement. Alternat. Med. 2008, 5, 191–197.

202. Kawcak, C.E.; Frisbie, D.D.; McIlwraith, C.W.; Werpy, N.M.; Park, R.D. Evaluation of avocado and soybean unsaponifiable extracts for treatment of horses with experimentally induced osteoarthritis. Am. J. Vet. Res. 2007, 68, 598–604.

203. Blotman, F.; Maheu, E.; Wulwik, A.; Caspard, H.; Lopez, A. Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial. Rev. Rhum. Engl. Ed. 1997, 64, 825–834.

204. Lequesne, M.; Maheu, E.; Cadet, C.; Dreiser, R.-L. Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip. Arthritis Care Res. 2002, 47, 50–58.

205. Maheu, E.; Cadet, C.; Marty, M.; Moyse, D.; Kerloch, I.; Coste, P.; Dougados, M.; Mazieres, B.; Spector, T.D.; Halhol, H.; et al. Randomised, controlled trial of avocado-soybean unsaponifiable (Piascledine) effect on structure modification in hip osteoarthritis: The ERADIAS study. Ann. Rheum. Dis. 2014, 73, 376–384.

206. Frondoza, C.G.; Fortuno, L.V.; Grzanna, M.W.; Ownby, S.L.; Au, A.Y.; Rashmir-Raven, A.M. α-Lipoic Acid Potentiates the Anti-Inflammatory Activity of Avocado/Soybean Unsaponifiables in Chondrocyte Cultures. Cartilage 2017, 9, 304–312.

207. Oliveira, G.J.P.L.D.; Paula, L.G.F.D.; Souza, J.A.C.D.; Spin-Neto, R.; Stavropoulos, A.; Marcantonio, R.A.C. Effects of avocado/soybean unsaponifiables (ASU) on the treatment of ligature-induced periodontitis in rats. Braz. Oral Res. 2017, 31.