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ABSTRACT

Avocado (*Persea americana Mill)* is a native American fruit. Its industrial processing generates a large number of wastes (leaves, peels, and seeds). These wastes are a source of bioactive compounds which have been attributed biological activities. We aim to compile scientific research on bioactive compounds of avocado pulp and wastes and their potential biological properties. Main bioactive compounds identified in pulp and wastes are polyphenols, carotenoids, tocopherols, and phytosterols. Thus, wastes extracts have reported numerous biological activities, e.g., antimicrobial, anti–inflammatory, anticancer, antidiabetic, antihypertensive. Therefore, potential applications in food and pharmaceutical industries can be issued.

KEYWORDS

Avocado; peel; leaf; pulp; bioactive compounds

Introduction

Avocado (*Persea americana Mill*) also known as aguacate, is a tropical native American fruit. The genus *Persea* (Clus.) Miller belongs to the family *Lauraceae*. The avocado is a polymorphic tree species that apparently originated from a broad geographical area stretching from the eastern and central highlands of Mexico through Guatemala to the Pacific coast of Central America.[1] During the XIX century, the cultivation of *P. americana* spread across Asia, and today it is cultivated and harvested worldwide. In 2014, world avocado production reached about 5.0 million tons.[2] Mexico is the largest avocado producer, accounting for 30% of the world production (Food and Agriculture Organization [FAO], 2014). Avocado is an evergreen tree, although some varieties lose their leaves for a short time before flowering. It is a species with several taxa or subspecies, which include the botanical varieties Mexican (*P. americana* var. *drymifolia*), West Indian or Antillean (*P. americana* var. *americana*) and Guatemalan (*P. nubigena* var. *nubigena* and *P. nubigena* var. *guatemalensis)*. The Mexican varieties have the highest oil content (>20%) and higher resistant to low temperatures (−6°C), followed by Guatemalan and West Indian race, respectively.[3] The current commercial varieties are hybrids of the races. For example, the Hass variety belongs to the Guatemalan-Mexican hybrid group,

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and it is the most commercial variety. Other common varieties in commerce include Bacon, Fuerte, Gwen, Lamb Hass, Pinkerton, Reed, and Zutano.[4]

Avocado is consumed mainly as fresh pulp. However, a few years ago, its industrialization began with the processing of pulp (avocado purée or guacamole, packaged slices and chunks, dehydrated or dried avocado), and the extraction of oil. Both, direct consumption and industrial processing of avocado, generates a significant quantity of wastes, such as leaves, peel, and seeds. Avocado peel[5] and seeds[6] represent 11% and 16% of the total weight of the fruit, respectively.

Avocado, including pulp and wastes, has been widely used for centuries in ancient cultures or folk medicine, generally as infusions with therapeutic properties[7] such as antimicrobial, anti–inflammatory, antioxidative, anticarcinogenic, among others. These features are attributed to several bioactive compounds groups (phytochemicals) as polyphenols, carotenoids, tocopherols, among others.

In the present review, we will discuss the current literature regarding the bioactive compounds of avocado and its wastes (leaves, peel, and seeds) and their potential biological properties.

The composition of avocado fruit

Avocado pulp represents between 52.9 and 81.3% of the fruit mass.[8] It contains from 67 to 78% of the moisture, 13.5 to 24% of the lipids, 0.8 to 4.8% of the carbohydrates, 1.0 to 3.0% of the protein, 0.8 to 1.5% of the ash and 1.4 to 3.0% of the fiber.[2,9] The edible fruit pulp contains vitamins, bioactive compounds, and oil rich in monounsaturated fatty acids (MUFA) (33%) among others.[6] It has been reported ascorbic acid contents ranging from 1.12 to 3.03 mg/100 g in the Ettinger variety.[10] A higher value of ascorbic acid (10.5 mg/100 g) was reported by Gouegni and Abubakar (2013)[11], who also determined vitamin A (7.00 ± 0.071 IU/100 g), vitamin B_2 (47.00 ± 0.013 mg/100 g), vitamin K (0.171 ± 0.300 mg/100 g), folic acid (1.699 ± 0.071 mg/100 g) and coenzyme Q10 (0.070 ± 0.076 mg/100 g) contents. However, the variety was not specified. The proximate composition of the seeds from the Hass and Fuerte varieties are similar: 52.7 to 54.1% moisture, 1.2% ash, 2.4 to 2.5% protein, 42.5% nitrogen-free extract, 27.5% starch and 0.5% fat (lower fat content than the pulp).[4,12] The majority of the lipids (77-80%) in the seeds are neutral lipids, whereas glycolipids and phospholipids represent the 7.4 and 10.9%, respectively.[4] Also, the seed has a high content of dietary fiber (34.8%).[13]

Avocado peels are wastes that have been mainly underutilized.[5] Its proximate composition shows ranges from 65.7 to 76.9% moisture, 0.75 to 1.6% ash, 1.51 to 6.3% protein, 2.89 to 11.04% total lipids, 20.8% nitrogen-free extract, and 6.85 to 56.9% fiber.[12,14,15]

On the other hand, Rodriguez-Carpena et al reported that Hass variety presents in seeds (in g/100 g): 55.76 ± 4.34 moisture, 1.39 ± 0.54 fat, 2.19 ± 0.38 protein, and 0.70 ± 0.14 ash, and Fuerte variety presents (in g/100 g): 52.69 ± 1.49 moisture, 1.52 ± 0.83 fat, 2.22 ± 0.46 protein, and 0.83 ± 0.21 ash.[16] On the other hand, Ejiofor et al reported that its presents (in g/100 g): 15.10 ± 0.14 moisture, 17.90 ± 0.4 fat, 15.55 ± 0.36 protein, 49.03 ± 0.02 carbohydrate, and 2.26 ± 0.23 ash.[17] And recently, Bahru et al[18] reviewed the information from 5 previous reports and gather the following values (ranging in g/100 g): 5.33–34.28 ± 0.45 moisture, 0.33–16.54 ± 2.10 fat, 1.33 ± 0.01–17.94 ± 1.40 protein, 44.7–80.12 ± 0.16 carbohydrate, 2.87–26.33 ± 1.53 fiber, and 2.4–3.82 ash. As observed, the data shown a wide dispersion in the

results. This issue can be related to geographical emplacements, variety, ripening time, analysis methodology, etc. Finally, a proximal analysis developed by Arukwe 2012, revealed that leaf presented (in g/100 g): 5.33 ± 0.62 moisture, 4.01 ± 0.16 fat, 25.54 ± 2.52 protein, 7.34 ± 0.41 carbohydrate, 38.40 ± 5.12 fiber, and 19.38 ± 4.34 ash.[19] Nevertheless, the avocado leaf is a waste, which has often been used for therapeutic purposes and as teas in folk medicine.[3]

Bioactive compounds of avocado

The main bioactive compounds described in avocado pulp and its wastes (peel, seed, and leaf) have been polyphenols[20] followed by carotenoids, tocopherols, and sterols. Polyphenols are distributed in pulp, peel, seed, and leaves, whereas carotenoids and tocopherols are found mainly in the avocado pulp. Identification and quantification of bioactive components present in avocado extracts (pulp, peel, seed, and leaves) are summarized in Table 1 and Table 2, respectively.

Polyphenols

According Table 2, pulp avocado shows the lowest total polyphenol content (TPC) (61 to 1,681 mg GAE/100g) than seed, peel and leaf.[5,10,48–51] Oboh et al. (2013)[49] reported the highest TPC (1681 mg GAE/100g) using HCl-methanol as the extraction solvent; however, the avocado variety is not specified. Conversely, the lowest TPC (61 mg GAE/100g) was obtained in Ettinger cv. with hexane extract.[10] The same authors reported a higher TPC with more polar solvents such as methanol, acetone, water, ethyl acetate, among others, showing the solvent effect on the extraction process. The same behavior was observed in total flavonoid content (TFC).[50] The treatment of the raw material, as thermal processing and state of ripening of pulp influences on the bioactive compounds content. Highest TPC has been reported in dried avocado pulp than in fresh pulp (535 and 297 mg GAE/100 g, respectively)[51] and over ripped pulp.[31]

Leaf avocado has shown TPC between 1,700 to 4,382 mg GAE/100g, mainly in methanolic extracts.[32,49] As well as in the pulp, the leaf showed the highest TPC (4,382 mg GAE/100g) using HCl-methanol as extraction solvent.[49] However, a value of 370 mg caffeic acid equivalent (CAE)/100 g was reported in a hydroalcoholic extract (ethanol/water) from Hass variety.[43]

Avocado peel has shown values of TPC between 181.2 to 22,790 mg GAE/100g.-[5,15,16,24,34,35,40,41,49,53] High values of TPC were obtained using water, ethyl acetate, acetone and methanol and blends of acetone/water. However, Morais et al. (2015)[15] reported lower TPC in methanolic extract of peel freeze-dried. Therefore, this pre-treatment decreased the TPC (22 mg GAE/100g) significantly. For seed avocado, a TPC between 155 to 29,200 mg GAE/100g has been reported.[5,13,15,24,34,48,53] The highest value was obtained with seed flour in a methanol/water extract. In general, the TPC was higher in blends of organic solvent with water. On the other hand, López-Cobo et al. (2016)[31], quantified and identified polyphenolic compounds in avocado pulp, peel and seed, when the fruit was at optimal ripeness for consumption and when overripe. Phenolic compounds quantified were in higher concentration in overripe than in pulp and seed of the optimally ripe fruit, probably due to the effect

Table 1. Bioactive compounds of pulp, seed, peel and leaf of avocado.

Compounds	Source	Content (mg/100g)	References
Polyphenols			
Apigenin	Leaf, pulp, peel	12,800 (peel)	[7,10,21–23]
Catechin	Pulp, seed, peel	0.082–1,920 (peel) 24.3–2,000 (seed)	[12,16,23–30]
Caffeic acid	Leaf, peel, seed	13.7–22.5 (seed) 8,010 (peel)	[10,12,22,25,26,28,31–33]
Cinnamic acid	Pulp, seed, peel		[16,26]
Chlorogenic acid	Leaf, pulp, peel, seed	0.0516–1,953 (seed) 137.6–4,290 (peel)	[10,12,13,22,24,25,30,31,34–38]
Coumaric acid	Leaf, pulp, peel, seed	1.74–2.2 (peel)	[12,25,26,28,31,32]
Cyanidin 3-O-glucoside	Peel	3,000 (peel)	[23,39]
Dihydroxyphenylacetic acid	Peel Seed	11.7–16.6	[27,28]
(Epi)catechin	Leaf, pulp, seed peel	0.062–17,502 (peel) 1,106–2,906 (seed)	[10,16,21–25,27-30,34,35,37,40,41]
Ellagic acid	Pulp	238.22	[38]
Epicatechin gallate	Seed		[28,34,35]
(Epi)gallocatechin	Peel Seed	13.5–21.1	[27,28]
Ferulic acid	Leaf, pulp, peel, seed	5.0–6,540 (peel) 0.09–1.2 (seed)	[10,12,23,26,28,31–33]
Gallic acid	Leaf, pulp	198.57 (pulp)	[26,32,38]
Gentisic acid	Pulp, peel, seed		[25,26,28]
Homovanillic acid	Pulp		[26]
Hydroxybenzoic acid	Peel, leaf, pulp, seed	9,920 (*p*-hydroxy, peel) 47–83 (4-hydroxy, peel) 6,650 (*m*-hydroxy, peel)	[10,16,22,23,27,28,32,33]
Hydroxytyrosol glucoside	Seed, peel		[25,28,31]
Isorhamnetin	Leaf		[7]
Kaempferol	Seed, peel	10.74 (seed) 1.8–5.1 (peel)	[13,27]
Kaempferol 3-O-arabinopyranoside	Leaf		[36,42]
Kaempferol 3-O-β-glucopyranoside	Leaf		[21,42]
Kaempferol 3-O-rhamnopyranoside	Leaf, peel	2.4–12.4 (peel)	[21,25,27,36,42]
Kaempferide	seed	10.74	[13]
Luteolin	Leaf, pulp	165 (pulp)	[7,21,38]
Luteolin pentosylhexoside	peel	1.3–4.8	[27]
Luteolin 7-O- glucoside	Leaf		[21]
Naringenin	Pulp, peel, seed	1.2–1.9 (peel)	[10,25,26]
Multinoside	Peel	9.7- 85	[27,28]
Neochlorogenic acid	Seed		[28,37]
Pyrocatechuic acid	Leaf		[32]
Pyrocatechol	Peel, seed	8.8–10.1 (peel)	[27,28]
Protocatechuic acid	Leaf, pulp, peel, seed	1,281 (seed) 10.4–980 (peel)	[10,13,22,25,27,28,31–33]
Procyanidins	Leaf, pulp, peel, seed	110 (pulp) 152–5,560 (seed) 28.9 – 29,080 (peel)	[5,16,23,25,27–31,35,37,40,42,43]
O-caffeoylquinic acid	Peel, seed	21.3–131 (peel)	[27,28]
Resorcylic acid	Leaf, pulp		[26,32]
Sakuranetin	Peel, seed	1.7–2.2 (peel)	[27,28]
Sinapic acid	Leaf, pulp, peel	250 (peel)	[10,22,31,32]
Syringic acid	Leaf, seed		[13,26,32]

(*Continued*)

Table 1. (Continued).

Compounds	Source	Content (mg/100g)	References
Quercetin	Leaf, pulp, peel, seed	5.25 (pulp) 2.2–1,230 (peel)	[7,23–28,36,38,42]
Quercetrin	Leaf		[21,36,42]
Quercetin hexose	peel	1.1–3.9	[27]
Quercetin-diglucoside	peel	1.2–23.5	[27]
Quercetin 3-O-arabinose	Seed, peel	2.7–23.3 (peel)	[27,31,34,37,42]
Quercetin 3-O-arapyranoside	Leaf		[21,36]
Quercetin 3-O-β-glucopyranoside	Leaf		[36]
Quercetin 3-O-β-D-glucoside	Leaf, peel	0.3–10.6 (peel)	[21,27]
Quercetin-xylosylrhamnoside	Peel	2 – 11	[27]
Rutin	Pulp, peel, seed, leaf	141.79 (pulp) 0.22 (seeds) 1.5–1,090 (peel)	[7,13,23,25,27,38,42]
Trans-5-*O*-caffeoyl-D-quinicacid	Seed	163 – 574	[29]
Tyrosol glucoside	Pulp, peel, seed	7.4–28.2 (peel)	[25,27,28,31]
Vanillic acid	Leaf, pulp, peel, seed	4.79 (pulp) 286 (seeds) 7–3,160 (peel)	[10,13,22,23,25,27,28,32,38]
Vanillin	Pulp, peel	25.3–31.2 (peel)	[10,27,28]
Carotenoids			
Lutein	Pulp	0.015–0.842	[5,11,44,45]
Zeaxanthin	Pulp	0.011–0.060	[11,44]
α-carotene	Pulp	0.0289	[44,46]
β-carotene	Pulp	0.006-950	[10,11,44,46]
β-criptoxanthin	Pulp	2.5	[44]
Neoxantin, neochrome, lutein-5,6-epoxide, chrysanthemaxanthin	Pulp		[45]
Tocopherols			
α-tocopherol	Pulp	1.78–3.5	[44,45]
γ-tocopherol	Pulp	5.6-199	[44,46]
δ-tocopherol	Pulp	60.1	[46]
Sterols			
β-sitosterol	Pulp	70-212	[38,47]
Campesterol	Pulp	23.2	[47]
Stigmasterol	Pulp	2.40–12.5	[38,47]

of Phenylalanine ammonia-lyase (PAL), which could increase its activity as fruit ripening. On the contrary, phenolic and other polar compounds in avocado peel were lower in over ripped avocado than with optimum ripeness.

Some studies have determined the total flavonoid content (TFC), showing that pulp and leaf have higher TCF respect to the peel and seed. Furthermore, total flavanols (TFLAVC), total anthocyanins (TAC) and total tannins (TTANC)[10,15,39,49–52] have been determined in avocado pulp, indicating that the TFLAVC is significantly lower than the TAC and TTANC.[10,50]

Among the main polyphenol compounds identified by HPLC in avocado pulp, seed, peel, and leaf are procyanidins (PCs), highlighting their content in seed (2,370–5,560 mg/100 g) and peel (490–29,080 mg/100 g). PCs have type A, B, and C. Type A and B have been reported in seed and peel of avocado[31], whereas C in leaves.[42] PCs present different degrees of polymerization (up to 13), as was reported for PCs type A and B in seed and peel of avocado.[31] In addition, these same authors have reported that PCs content in avocado peel and seed increases with fruit ripening, probably due to the release of tannins linked to cell-wall structures.

Table 2. Quantification and identification of bioactive compounds in avocado extracts (pulp, leaf, peel and seed).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
PULP								
Eight varieties	Acetone/water/acetic acid (70:29,7:0,3, v/v)	60-490 mg GAE/100g FW					Procyanidins	[5]
	Ethanol/water (50:50, v/v)	130 mg GAE/100g DW						[48]
Hass.cv	Ethylacetate	76 mg GAE/100g DW						[16]
	Acetone	100 mg GAE/100g DW						
	Methanol	92 mg GAE/100g DW						
Fuerte.cv	Ethylacetate	116 mg GAE/100g DW					Catechin, hydroxybenzoic acid, hydroxycinnamic acid, procyanidins	[16]
	Acetone	175 mg GAE/100g DW						
	Methanol	145 mg GAE/100g DW						
	HCl-methanol (1:1, v/v)	1,681 mg GAE/100g	346 mg QE/100g					[49]
	Methanol	297 mg GAE/100g	49.5 mg QE/100g					[15]
Ettinger. cv	Methanol	504 mg GAE/100g DW	709 mg CE/100g DW	1.02 mg CE/100g DW	497 mg CE/100g DW		Protocatechuic acid, *p*-hydroxybenzoic acid, vanillic acid, caffeic acid, ferulic acid, sinapic acid, anisic acid, quercetin, apigenin	[10]
	Water	286 mg GAE/100g DW	19 mg CE/100g DW	3.4 mg CE/100g DW	72 mg CE/100g DW			[10]
	Acetone	335 mg GAE/100g DW	1,271 mg CE/100g DW	3.7 mg CE/100g DW	832 mg CE/100g DW			[10]
	Hexane	61 mg GAE/100g DW	16.8 mg CE/100g DW	0.8 mg CE/100g DW	625 mg CE/100g DW		anisic acid, quercetin, apigenin	[10]
	Water	286 mg GAE/100g DW	19.4 mg CE/100g DW	3.4 mg CE/100g DW	144 mg CE/100g DW	438mg CGE/100g DW		[50]
a) Dried pulp	Ethanol	535 mg GAE/100g	246 mg RE/100 g					[51]
b) Fresh pulp		297 mg GAE/100g	913 mg RE/100 g					[51]

(*Continued*)

Table 2. (Continued).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
Rugoro cv.	Methanol						protocatechic acid, gentisic acid, 4-hydroxybenzoic acid, chlorogenic acid, catechin, caffeic acid, epicatechin, vanillin, *p*-coumaric acid, ferulic acid, sinapinic acid, trans-cinnamic acid, laricitrin, naringenin, chrysin, kaempferide. All less, 4-hydroxybenzoic acid, chlorogenic acid, vanillin, sinapinic acid, laricitrin, naringenin, chrysin, kaempferide. All less, gentisic acid, 4-hydroxybenzoic acid, chlorogenic acid, caffeic acid, vanillin, laricitrin, naringenin, chrysin, kaempferide.	[22]
13 varieties	Methanolic						Quinic, abscisic acid, syringic, *p*-coumaric, caffeic and chlorogenic acids, and epicatechin	[26]
Hass cv.						23.5 mg/100g		[39]
Hass cv.	Water	410.2 mg GAE/100g FW	21.9 mg/100 g FW					[52]
	Acetone/water	< 4,000 mg GAE/g						[37]
	Ethanol/water (70:30, v/v)						Rutin, quercetin, luteolin, gallic acid, ellagic acid and vanillic acid	[38]
		297.7 mg GAE/100g FW	49.58 mg QE/100 g FW					[15]
LEAF								
	HCL/metanol 1:1, v/v)	4,382 mg GAE/100g	552 mg QE/100g					[49]
Hass cv. Gwen cv. Fuerte cv. Duke cv.	Methanolic	1,750–1,930 mg GAE/100g 1,650–1,700 mg GAE/100g 1,500–2,400 mg GAE/100g 1,850–2,200 mg GAE/100g					Pyrocatechuic acid, *p*-hydroxybenzoic acid, protocatechuic acid, caffeic acid, vanillic acid, *p*-coumaric acid, ferulic acid, sinapic acid, resorcylic acid, gallic acid, syringic acid	[32]
Hass cv.	Ethanol/water (50:50, v/v)	370 mg CAE/100g DW					caffeic acid, chlorogenic acid, procyanidins, quercetin, quercetin glucosides, kaempferol glucosides	[43]
PEEL								

(*Continued*)

Table 2. (Continued).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
Hass cv.	Ethanol/water (50:50, v/v)	5,800 mg GAE/100g					Procyanidin dimer A2, trimer B2, catechin, chlorogenic acid, epicatechin, quercetin-3-β-glucoside, rutin, protocatechuic acid, quercetin, naringenin, 4-hydroxybenzoic	[27]
Hass cv. Fuerte cv.	Ethanol/water (80:20, v/v)	6,350 mg GAE/100g DW 12,030 mg GAE/100g DW					Procyanidin B2, Epicatechin	[29]
Hass cv.	Water	679 mg GAE/100g FW	44.3 mg/100 g FW					[52]
Hass cv.	Ethanolic	535 mg GAE/100g	246 mg RE/100 g					[51]
Eight varieties	Acetone/water/acetic acid (70:29,7:0,3, v/v)	430-126 mg GAE/100g FW					Procyanidins	[5]
Hass cv. Fuerte cv.	Acetone/water (70:10, v/v)	8,997 mg GAE/100g DW 17,218mg GAE/100g DW						[53]
	Water	1,970 mg GAE/100g DW					Kaempferide, epicatechin, chlorogenic acid, epicatechingallate, procyanidins, quercetin 3-O-arabinoside, quinic acid	[34]
Hass cv. Shepard cv.	Methanolic 80%	2,532 mg CE/100g DW 1,561 mg CE/100g DW					5-*O*-caffeoylquinic acid, catechin, procyanidins and quercetin glucosides. 5-*O*-caffeoylquinic acid, quercetin glucosides.	[35]
	Water	4,570 mg GAE/100g					Catechin and epicatechin	[41]
Fuerte.cv	Ethylacetate Acetone Methanol	4,054 mg GAE/100g DW 17,218mg GAE/100g DW 13,770mg GAE/100g DW					Catechin, hydroxybenzoic acid, flavonols, hydroxycinnamic acid, procyanidins	[16]
Hass.cv	Ethylacetate Acetone Methanol	3,293 mg GAE/100g DW 8,997mg GAE/100g DW 7,841 mg GAE/100g DW					Catechin, hydroxybenzoic acid, flavonols, hydroxycinnamic acid, procyanidins	[16]
	Water	7,713 mg GAE/100g DW					Procyanidins	[40]

(*Continued*)

Table 2. (Continued).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
	HCL/metanol (1:1, v/v)	3,001 mg GAE/100g	339 mg QE/100g					[49]
	Acetone/water	>30,000 mg GAE/ 100 g					Epicatechin, procyanidins, chlorogenic acid, quercetin arabinoglucoside	[37]
Raw	Methanolic	181.2 mg GAE/100g FW	156.3 mg QE/100 g FW			3,000 mg/ 100g	Malic acid, catechin, epicatechin	[15]
Oven dried	Water	1,252 mg GAE/100g FW	140 mg QE/100 g FW 11 mg QE/100 g FW				Malic acid, tartaric acid, catechin, epicatechin gallate, epicatechin.	[23]
Lyophilized								
Hass cv.		22 mg GAE/100g FW	15,120 mg/100 gFW				Quercetin, rutin, apigenin, epicatechin, catechin, cyanidin-3-O-glucoside, vanillic acid, chlorogenic acid, caffeic acid, sinapic acid, ferulic acid, anisic acid, protocatechic acid, *p*-m-hydroxybenzoic acid	
Hass cv.	Ethanol/water (80:20 v/v)	22,700 mg/100g extract					Chlorogenic acid, epicatechin (dimer, trimer, hexamer), quercetin	[24]
SEED								
Hass cv.	Ethanol/water (50:50, v/v)	30.98 mg GAE/100g DW					Procyanidin, chlorogenic acid, Catechin, Epicatechin	[30]
Hass cv.	Methanol	25.35 mg GAE/100g DW						
Hass cv.	Ethanol/water	5,730 mg GAE/100g DW					Trans-5-*O*-caffeoyl-D-quinic acid, Procyanidin B1, Catechin, Epicatechin	[29]
Fuerte cv.	(80:20, v/v)	5,920 mg GAE/100g DW						
Hass cv.	Water	704 mg GAE/100g FW	47.9 mg/100 g FW					[52]
	Ethanol/water (50:50, v/v)	8,820 mg GAE/100g DW						[48]
Eight varieties	Acetone/water/acetic acid (70:29,7:0,3, v/v)	1,920mg GAE/100g FW					Procyanidins	[5]
Hass cv.	Acetone/water	6,082 mg GAE/100g DW						[53]
Fuerte cv.	(70:10, v/v)	6,912 mg GAE/100g DW						
Flour	Methanol/water (75:25, v/v)	29,200 mg/100g seed DW					protocatechic acid, chlorogenic acid, syring acid, vanillic acid, rutin, kaempferol and kaempferide	[13]

(*Continued*)

Table 2. (Continued).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
	Water	570 mg GAE/100g DW					Kaempferide, epicatechin, chlorogenic acid, epicatechingallate, procyanidins, quercetin 3-O-arabinoside, quinic acid	[34]
Hass cv.	Methanol 80%	951 mg CE/100g DW					Catechin	[35]
Shepard cv.		1304 mg CE/100g DW					Epicatechin gallate, procyanidins, 3-O-caffeoylquinic acid and 3-O-*p*-caffeoylquinic acid	
Fuerte.cv	Ethylacetate	2,029 mg GAE/100g DW					Catechin, hydroxybenzoic acid, flavonols, hydroxycinnamic acid, procyanidins	[16]
	Acetone							
	Methanol	6,912 mg GAE/100g DW						
		4,164 mg GAE/100g DW						
Hass.cv	Ethylacetate	1,699 mg GAE/100g DW					Catechin, hydroxybenzoic acid, flavonols, hydroxycinnamic acid, procyanidins	[16]
	Acetone							
	Methanol	6,082 mg GAE/100g DW						
		3,511 mg GAE/100g DW						
	Methanol	155 mg GAE/100g FW	30 mg QE/100 g FW					[15]
	HCL/methanol (1:1, v/v)	2,937 mg GAE/100g	232 mg QE/100g					[49]
	Acetone/water	>30,000 mg GAE/ 100 g DW					Epicatechin, procyanidins, chlorogenic acid, neo chlorogenic acid.	[37]
Dried (Hass cv.)	Acetone/water	4,132.7 mg GAE/100g FW					Catechin, chlorogenic acid, caffeic acid, ferulic acid	[12]
Hass cv.	Ethanol/water (80:20 v/v)	7,250 mg/100 g extract					Chlorogenic acid, 3-*p*-coumarouylquinic, catechin, epicatehin trimer	[24]
CAROTENOIDS		TCC	β- carotene					
PULP								
	Acetone/water/acetic acid (70:29,7:0,3, v/v)	0.15–0.71 mg/100g FW					Lutein	[5]
Ettinger.cv		2.49 mg/100g DW	1.2 mg/100g					[10]
		0.9 mg/100g	0.3 mg/100g DW					[50]
Hass cv.	Water	0.815 mg/100g						[52]

(*Continued*)

Table 2. (Continued).

SOURCE		BIOACTIVE COMPOUNDS						
POLYPHENOLS	EXTRACT	TPC	TFC	TFLAVC	TTANC	TAC	COMPOUND IDENTIFIED	REFERENCES
Hass cv.							Lutein, neoxanthin, zeaxanthin, β-carotene, antheraxanthin, violaxanthin, α-carotene	[39]
Hass cv							Lutein, zeaxanthin, β-carotene, α-carotene, β-criptoxanthin	[44]
Hass cv							Lutein, zeaxanthin, β-carotene, α-carotene, β-criptoxanthin	[44]
Hass cv							Lutein, neoxanthin, zeaxanthin, β-carotene, neochrome,violaxanthin, α-carotene, β-criptoxanthin, 9-cis-neoxanthin, lutein-5,6-epoxide, chrysanthemaxanthin	[45]
Hass cv							cis β-carotene, trans β-carotene, α-carotene, β-criptoxanthin, trans lycopene and cis lycopene.	[46]
							β-carotene, zeaxanthin and lutein	[11]
PEEL								
Hass cv.	Water	2.6 mg/100g						[52]
Eight varieties	Acetone/water/acetic acid (70:29,7:0,3, v/v)	0.89–1.77 mg/100g FW						[5]
Seed								
Hass cv.	Water	0.9 mg/100g						[52]
Eight varieties	Acetone/water/acetic acid (70:29,7:0,3, v/v)	0.07–0.63 mg/100 gFW						[5]
TOCOPHEROLS								
PULP								
Hass cv	Acetone						α-tocopherol and γ-tocopherol	[44]
Hass cv							α-tocopherol	[45]
Hass cv							γ -tocopherol and δ-tocopherol	[46]
STEROLS								
PULP								
Hass cv							β-sitosterol, campesterol, stigmasterol	[47]
	Ethanol/water (70:30, v/v)						β-sitosterol and stigmasterol	[38]

TPC: total polyphenol content; TFC: total flavonoid content; TFLAVC: total flavanol content; TTANC: total tannins content; TAC: total anthocyanin content; TCC: total carotenoids content; GAE: gallic acid equivalent; QE: quercetin equivalent; CE: catechin equivalent; CGE: cyaniding-3-glucoside equivalent; CAE: caffeic acid equivalent; RE: rutin equivalent; DW: dry weight; FW: fresh weight

Other compounds identified have been phenolic acids (hydroxybenzoic, vanillic, caffeic, ferulic, protocatechuic, gallic, sinapic, chlorogenic, resorcylic, syringic and cinnamic), and flavonoids (luteolin, quercetin, apigenin, rutin, catechin and epicatechin).[10,12,16,21–26,32,33,36,37,53]

López-Cobo et al. (2016)[31] also identified for the first time in avocado pulp one alcohol phenolic called tyrosol hexoside pentoside, whereas in pulp, seed and peel identified two iridoids known as penstemide and its isomer.

Table 1 and Table 2 show different polyphenol compounds identified in pulp and wastes.

Carotenoids

Studies about the profile and quantification of carotenoids have been made mainly in Hass variety; however, they are scarce in relation to polyphenol studies. Pulp and peel have a similar total carotenoid content (TCC), while seed has a considerably lower content.

TCC in avocado pulp has been reported between 0.15 to 2.5 mg/100 g in different varieties[5,10,50,52] where Ettinger variety reported the highest value.[10]

Avocado peel has shown a TCC from 0.89 to 2.6 mg/100 g.[5,52] Nevertheless, the highest content was found in Nabal variety (4 mg/100 g).[54]

Regarding the available literature, carotenoids have been identified mainly in the avocado pulp, being the xanthophylls (contain oxygen functions in the molecules) such as lutein, zeaxanthin, and β-cryptoxanthin the major carotenoids (Table 1). Lutein is the most common xanthophyll in avocado pulp with values from 15 to 84.2 βg lutein/100 g, where Hass variety has shown the highest content.[5,44,45] Likewise, zeaxanthin[11,44] and β-cryptoxanthin[44] also were identified and quantified in avocado varieties.

Carotenes, such as α-carotene, for Hass variety, reported content from 25 -μg/100 g DW[44] to 28.9 μg/100 g DW[46], whereas lower content of β-carotene (38 to 9870 μg/100 g DW) has been reported.[10,44,46,50] However, an ethanolic extract of pulp showed a significantly higher content of β-carotene (950 mg/100 g), but in an unspecified variety.[11] Other carotenoids that have been identified include neoxanthin, neochrome, lutein-5,6-epoxide and chrysanthemaxanthin.[45]

Finally, Gross et al reported that leaf from avocado presents (expressed in % as β-carotene from total carotenoids) major contents of lutein (51%), α-carotene (16%), β-carotene (11.3%) neoxanthin a (7.5%) and violaxanthin (5%).[54]

Tocopherols and sterols

As was mentioned above, sterols, α-, γ- and δ-tocopherol have been identified mainly in Hass pulp, being γ- tocopherol the main compound[46], followed by δ- and α-tocopherol, respectively.[44,45] Regarding sterols, approximately 89% of the total sterol content in Hass pulp is β-sitosterol (212.9 mg/100 g). Lower amounts of campesterol and stigmasterol have been observed in pulp[47] and in a hydroalcoholic avocado pulp extract (70% ethanol).[38]

Therefore, these data indicate that the profile and content of bioactive compounds vary depending upon agronomical characteristics (cultivar, climate, irrigation, and harvest, between others), pre-treatment of raw material, as thermal processing, extraction method and analytical determinations, among others. Avocado seed and peel have a higher TPC

than pulp and leaf, in according to Wang et al.(2010)[5] who conclude that the phenolic components ratio in seed, peel, and pulp were 64%, 23%, and 13% of those in whole fruit. However, pulp and leaf have a higher TFC than seed and peel. Besides, these latter have higher levels compounds than those that exist in other fruits and vegetables such as apple (*Malus pumila*) (100 mg/100g FW), red cabbage (*Brassica oleracae* var. botrytis) (139 mg/100 g FW), tomatoes (*Solanum lycopersicum*) (76.9 mg/100 g FW)[55] and banana (*Musa acuminata*) (1.5–22.9 mg/100 g FW).[56] In general, TCC is significantly lower than TPC in all fractions mentioned. Avocado pulp and peel show similar TCC, as expected. These results demonstrate the potential of the wastes of the avocado as a source of bioactive compounds suitable for food or nutraceutical applications.

Antioxidant activity

The antioxidant activity (AA) of avocado extracts (Table 3) shows a high variability of the results, which makes their comparison difficult. In this context, Wang et al. (2010)[5] indicated that the seed and peel had a higher AA (ORAC y DPPH) than pulp, in eight avocado varieties. Likewise, Soong and Barlow (2004)[48] indicated that the ethanolic/aqueous extract of seed had a higher AA (ABTS) than pulp. Conversely, Morais et al. (2015)[15] showed that the methanolic extract of pulp was higher AA (FRAP and DPPH) than peel and seed. Kosińska et al. (2012)[35] reported that the AA (TEAC and ORAC) in methanolic extracts from the peel was not significantly different than seed in two avocado varieties (Shepard and Hass). Rodriguez-Carpena et al. (2011)[53] observed a similar behavior in acetone/water avocado extract from Hass and Fuerte varieties. Since the avocado seed has a high content of the phenolic compounds (>60%), it would be expected that this one had a higher AA than peel and pulp. Nevertheless, the results reported are inconclusive. This behavior could be explained by different factors such as AA assays (CUPRAC, ABTS, DPPH, FRAP, ORAC TEAC, and Ascorbic acid); units of expression of results, extraction method from wastes and avocado variety, among others, all of which influence the outcomes.

Biological properties and therapeutic applications of avocado fruit

The extracts of all parts of the avocado fruit exhibit therapeutic properties.[57] A large number of articles concerning antimicrobial, anti–inflammatory, anticancer, antidiabetic, antihypertensive properties of avocado were reviewed (Table 4). Besides, protective effects on hepatic function on glucose metabolism are also discussed below.

Anticancer activity

Avocado shows interesting properties that suggest its potential role in cancer prevention/treatment. In this context, pulp extracts of avocado inhibited the growth of prostate cancer cell lines[44], peripheral blood mononuclear cells, oesophageal squamous cell carcinoma, and colon adenocarcinoma cell lines.[61] Ding et al. (2007)[21] showed that a chloroform extract of Hass avocado pulp (D003) induced apoptosis in premalignant and malignant human oral cell lines, inhibiting its growth. Later, these same authors showed that D003 increased the levels of reactive oxygen species (ROS) and induced apoptosis in the cancer-

Table 3. Antioxidant activity of avocado extracts (pulp, leaf, peel and seed).

SOURCE	CUPRAC	ABTS	DPPH	FRAP	ORAC	ascorbic acid	TEAC	Reference
PULP								
Ethanol/water extract of fresh pulp		4.9 µmol AEAC/g						[48]
Ethanol/water extract of freeze dried pulp		13.1 µmol AEAC/g		9.6 µmol AEAC/g				[48]
Lyophilized extract cv. Ettinger	1.2-30µM TE/g DW	0.9–15.7 µM TE/g DW	0.8–8.3 µM TE/g DW	3.1–6.2 µM TE/g DW				[10]
Eight varieties			0.4–1.3 µmolTE/g FW		2.6–11.6 µmolTE/g FW			[5]
Methanol extract			594 µg/mL	32 µmol $FeSO_4$g/DW				[15]
LEAF								
Ethanol/water extract cv. Hass			110 µg/mL (EC_{50})					[43]
Ethanol/water extract			57.8 µg/mL(EC_{50})					[42]
PEEL								
Eight varieties			39-189 µmolTE/g FW		58-631 µmolTE/g FW			[5]
Acetone/water extract cv. Hass			89 mM TE/g FW					[53]
Acetone/water extract cv. Fuerte			200 mM TE/g FW					[53]
Methanol extract cv. Shepard			0.93 mg DW (EC_{50})		290 µmolTE/g DW		110 µmolTE/g DW	[35]
Methanol extract cv. Hass			0.36 mg DW (EC_{50})		470 µmolTE/g DW		160 µmolTE/g DW	[35]
Methanol extract of raw peel			46.4 µg/mL	27.8 µmol $FeSO_4$ g/DW				[15]
Methanol extract of freeze dried peel			121 µg/mL	10.2 µmol $FeSO_4$ g/DW				[15]
Methanol extract of oven dried peel			18.2 µg/mL	442 µmol $FeSO_4$ g/DW				[15]
Aqueous extract Hass variety				23 mg TE/g extract DW	0.2 mg TE/g extract DW			[34]
Dried (Hass cv.)			1,110 µmolTE/g DW					[12]
Ethanol/water extract cv. Hass			149 µg/mL (EC_{50})					[24]
Ethanol/water extract cv. Hass		791.5 µmolTE/g DW	310 µmolTE/g DW	1,175 µmol $FeSO_4$ g/DW			28.07 µmolTE/g DW (Epicatechin)	[29]

Ethanol/water extract cv. Fuerte	1,004 µmolTE/g DW	420.5 µmolTE/g DW	1,881 µmol $FeSO_4$ g/DW		84.95 µmolTE/g DW (Trans-5-*O*-caffeoyl-D-quinicacid)	[29]
SEED						
Ethanol/water extract of fresh pulp	236 µmol AEAC/g					[48]
Ethanol/water extract of freeze dried	725 µmol AEAC/g		1.5 µmol AEAC/g			[48]
Eight varieties		128-240 µmolTE/g FW		229-464 µmolTE/g FW		[5]
Acetone/water extract cv. Hass		130 mM TE/g FW				[53]
Acetone/water extract cv. Fuerte		168 mM TE/g FW				[53]
Methanol extract cv. Shepard		0.8 mg DW(EC_{50})		350 µmolTE/g	91 µmolTE/g	[35]
Methanol extract cv. Hass		0.9 mg DW (EC_{50})		210 µmolTE/g	94 µmolTE/g	[35]
Methanol extract		370 µg/mL	23 µmol $FeSO_{4/}$ g DW			[15]
Aqueous extract cv. Hass			9.5 mgTE/g extractDW	1.6 µgTE/g extract DW		[34]
Dried (Hass cv.)		1,650 µmolTE/g DW				[12]
Ethanol/water extract cv. Hass		220 µg/mL (EC_{50})				[24]
Ethanol/water extract cv. Hass	645.8 µmolTE/g DW	410.7 µmolTE/g DW	656.9 µmol $FeSO_4$ g/DW		188.99 µmolTE/g DW (Epicatechin) 176.48 µmolTE/g DW (Procyanidin B2)	[29]
Ethanol/water extract cv. Fuerte	580.8 µmolTE/g DW	464.9 µmolTE/g DW	931.7 µmol $FeSO_4$ g/DW		131.18 µmolTE/g DW (Epicatechin) 75.32 µmolTE/g DW (Procyanidin B2)	[29]
Ethanol/water extract cv. Hass		15.0 µg/mL (EC_{50})		310 µmolTE/g DW	300 µmolTE/g DW	[28]
Ethanol/water extract cv. Hass	263.6 µmolTE/g DW		438.9 µmolTE/g DW	1,310 µmolTE/g DW		[30]
Methanol extract cv. Hass	123.7 µmolTE/g DW		316.6 µmolTE/g DW	1,240 µmolTE/g DW		[30]
SEED COAT						
Ethanol/water extract cv. Hass		10.4 µg/mL (EC_{50})		460 µmolTE/g DW	432 µmolTE/g DW	[28]

CUPRAC: cupric reducing antioxidant capacity; ABTS: 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid); DPPH: 2,2-diphenyl-1-picrylhydrazyl; FRAP: ferric reducing antioxidant power; ORAC: oxygen radical absorption capacity; TEAC: trolox equivalent antioxidant capacity; AEAC: L-ascorbic acid-equivalent antioxidant capacity; TE: trolox equivalent; DW: dry weight; FW: fresh weight

Table 4. Biological properties and therapeutic applications of avocado extracts (pulp, leaf, peel and seed).

Source	Solvent extraction	Effect	Compounds	References
Pulp	Acetone Methanol Heptane	Antiplatelet and antithrombotic activities	(2S,4S)-1-Acetoxy-2,4-di-hydroxy-nheptadeca-16-ene, persediene, persenone-A, persenone-B, persenone-C, persin, and (12Z,15Z)-1-Acetoxy-2,4-dihydroxyheneicosa-12,15-diene.	[58]
Pulp		Antibacterial activity against *E. coli* and *S. aureus*	defensin *PaDef* cDNA (antimicrobial peptides, AMPs)	[59]
Pulp (unripe)	Methanol	Antimycobacterial activity against *M. tuberculosis*	avocadenol A avocadenol B 2R,4R)-1,2,4-trihydroxynonadecane (2R,4R)- 1,2,4-trihydroxyheptadec-16-ene	[60]
Pulp	Acetone	Inhibition of prostate cancer in human prostate cell lines LNCaP and PC3	lipid-soluble bioactive substances (lutein, zeaxanthin, β-cryptoxanthin, α-carotene, β-carotene, α-tocopherol and γ-tocopherol).	[44]
Pulp	Ethanol Ethyl acetate Petroleum ether Chloroform	Inhibition of growth of esophageal squamous cell carcinoma (ESCC) and colon adenocarcinoma (CC) in cell lines > effect of extracts on ESCC		[61]
Pulp	Chloroform	Anticancer effect on premalignant and malignant human oral epithelial cell lines	Aliphatic acetogenins: (2*S,4S*)-2,4-dihydroxyheptadec-16-enyl acetate and (2*S*,4*S*)-2,4-dihydroxyheptadec-16-ynyl acetate.	[62][63]
Pulp	Hexane	Protective activity against liver injury in male Wistar rats.	(2*E*,5*E*,12*Z*,15*Z*)-1-Hydroxyheneicosa-2,5,12,15-tetraen-4-one; (5*E*,12*Z*,15*Z*)-2-Hydroxy-4-oxoheneicosa-5,12,15-trien-1-yl acetate; (2*R*,12*Z*,15*Z*)-2-Hydroxy-4-oxoheneicosa-12,15-dien-1-yl acetate; (2*E*,12*Z*,15*Z*)-1-Hydroxyheneicosa-2,12,15-trien-4-one and (5*E*,12*Z*)-2-Hydroxy-4-oxoheneicosa-5,12-dien-1-yl acetate	[64]
Pulp	Ethanol	Antihyperglycaemic and antioxidative properties in diabetic male Wistar albino rats.		[65]
Pulp	Ethanol	Normoglycemia in diabetes by modulating the activities of carbohydrate metabolic enzymes in Albino rats.		[66]
Pulp	Water	Antifungal activity against *C. gloeosporioides*	(E,Z,Z)-1-Acetoxy-2-hydroxy-4-oxo-heneicosa-5,12,15-triene	[67]
Leaf	Water	Analgesic and anti–inflammatory activities using different animal models.		[68]
Leaf		Potential novel cancer therapeutic agent in human breast cancer cell lines	Persin	[69,70]
Leaf	Methanol	Moderate trypanocidal activity in vitro against epimastigote form of *T. cruzi*		[71]
Leaf	Water	Vasorelaxation effects on rat aortic rings		[72]
Leaf	Water	Bradycardia, vasorelaxation and hypotension in guinea pigs and Wistar rats (in vitro and in vivo assays)		[73]

Leaf	Ethanol	Treatment acute in diabetic rats: anti-hyperglycemic effects (dose-dependent), decrease urine flow and electrolyte excretion rates. Treatment subchronic in diabetic rats: increase in hepatic glycogen concentrations, decrease in plasma creatinine and urea.		[74]
Leaf	Water/ methanol	Hypoglycemic and Hypocholesterolemic effects in vivo (Albino rats) Reduction in plasma glucose, LDL and total cholesterol		[75]
Leaf	Ethanol/water	Antihyperglycaemic and protective effect against the hepatotoxicity in male Wistar rats Decrease in levels of transaminases and alkaline phosphatase.	tannins, saponines, steroids/triterpenoids and flavonoids (quercetin-3-glucoside (isoquercitrin) and quercetin-3-rhamnoside (quercitrin)	[76]
Leaf	Water	Hepatoprotective effects in Wistar albino rats		[77]
Leaf	Water	Anti-ulcer effect in albino rats.		[78]
Leaf	Water	Anticonvulsant activity on male Balb C mices		[79]
Leaf	Water/ methanol	Anti–inflammatory activity and antigenotoxic effects in albino Wistar rats against X-rays irradiation.		[80]
Leaf, seed	Water	The anti-cholinesterase and antioxidant activities in vitro	Saponins, alkaloids, and terpenoids	[81]
Peel	Water	Antimicrobial activity in vitro against *H. pylori*	Procyanidins	[40]
Seeds	Water/ methanol	*In vitro* anti–inflammatory effects of a colored extract obtained from avocado seed		[82]
Seeds	Hexane Methanol	Antifungal activity in vitro: *Candida* spp, *C. neoformans* and *M.pachydermatis*. *Candida* spp, *C. neoformans* and *M. pachydermatis*.	Sterols and triterpenes 1,2,4-trihydroxy-nonadecane β-sitosterol flavonoids, anthocyanins, condensed tannins, alkaloids and triterpenes	[83]
Seeds	Methanol ethyl acetate	Antimicrobial activity in vitro against *S. aureus, S.pyogenes, C. ulcerans* and *C. albicans*.	Carbohydrates, flavonoids, steroids, terpenoids, saponins, tannins, cardiac glycoside and alkaloids.	[84]
Seeds	Methanol Chloroform Petroleum ether	Antifungal activity in vitro against *C. neoformans*		[85]
Seeds	Chloroform/ methanol	Acute toxicity investigation and anti-diarrhoeal effect of the-chloroform-methanol extract of the seeds of Persea americana in albino rats		[86]

(*Continued*)

Table 4. (Continued).

Source	Solvent extraction	Effect	Compounds	References
Seeds	Chloroform/ methanol Chloroform	Antimicrobial activity in vitro against methicillin resistant S. aureus (MRSA). Antiprotozoal activity in vitro against E. *E. histolytica and G. lamblia* Antimycobacterial activity in vitro against *M. tuberculosis* drug-resistant species: *M. fortuitum, M. avium, M. smegmatis* and *M. absessus.*		[87]
Seeds	Acetone	Antimicrobial activity in vitro against *C.sporogenes* endospore germination	Persenone-A; persenone-B, and persenone-C.	[88]
Seed	Water	Hypocholesterolemic effect in vivo (Albino rats) Reduction in total cholesterol, LDL and triacylglycerols		[89]
Seed flour		Hypocholesterolemic effect in vivo (adult mice). Reduction in total cholesterol, LDL and atherogenic index.	Protocatechuic acid, kaempferide and vanillic acid, rutin, kaempferol	[13]
Seed	Water	Anti-hyperglycemic effects in vivo in adult male rabbits		[90]
Seed	Water	Hypoglycemic effect in vivo of male Wistar albino diabetic rats. Histopathological studies of the pancreas of diabetic treated rat show evidence of signs of regeneration of B cells in groups receiving extracts		[91]
Seed	Ethanol/water Methanol	Protective Effect of extract in Sunflower Oil Fatty Acid Mixture	Procyanidin, chlorogenic acid, epicatechin, catechin	[30]
Seed	Water	Hypoglycaemic and tissue-protective effects (pancreas, kidneys, and liver) on alloxan-induced albino rats	Alkaloids, glycosides, saponins, tannins, and flavonoids	[92]
Peel and seed	Hydroalcoholic	High antibacterial and moderate antifungal activity .	Peel and seed: chlorogenic acid, epicatechin (dimer, trimer, hexamer); seed: quercetin; peel: 3-*p*-coumarouylquinic, catechin	[24]
Peel and seed	Ethanol/water	Cytotoxicity and anti–inflammatory activity in vitro	Trans-5-*O*-caffeoyl-D-quinicacid, Procyanidin B1, Catechin, Procyanidin B2, Epicatechin.	[29]
Leaf, peel, pulp and seed	Methanol	Anti-diabetic properties in vitro. Inhibition of α-amylase and α-glucosidase activities	syringic acid, eugenol, vanillic acid, kaempferol, catechin, epicatechin, ferulic acid, apigenin, naringenin, lupeol, epigallocatechin and epigallocatechin-3-*O*-gallate	[93]

derived cell lines while not affecting the normal oral cell lines. They found that D003 extract initiates apoptosis via ROS activating both the intrinsic and extrinsic pathways.[62] Added to the above, this same research group showed that an isolated compound from D003, aliphatic acetogenin, inhibited cellular proliferation in human oral cancer cells through the inhibition of the EGFR/RAS/RAF/MEK/ERK1/2 pathway by diminishing EGFR (Tyr1173), c-RAF (Ser338) and ERK1/2 (Thr202/Tyr204) phosphorylation.[63]

Breast cancer is the leading cause of cancer death amongst women in developed countries. Butt et al. (2006)[69] reported that persin, which is an oil-soluble compound synthesized in the leaves and pulp of avocado, induced G2-M cell cycle arrest and caspase-dependent apoptosis in human breast cancer cell lines (MCF-7 and T-47D cells). In addition, Roberts et al. (2007)[70] described that the persin might attenuate steroid hormone receptor signaling, showing an antiestrogen effect. The same authors showed a synergistic interaction between persin and 4-hydroxytamoxifen (4-OHT) in human breast cancer cells, inducing a potent proapoptotic impact. Also, the persin-induced apoptotic response was related to an increase in endoplasmic reticulum stress markers. By the other hand, a methanolic extract of avocado root showed anti-proliferative activity against estrogen receptor positive breast cancer cell lines (MCF-7).[94] Besides, PaDef defensin from avocado (*P. americana* var. drymifolia) triggers of apoptosis, inducing the expression of cytochrome c, Apaf-1, and the caspase 7 and 9 genes.[59] All these results suggest that the avocado could be a potential therapeutic fruit in the treatment of cancer; however, more studies are needed.

Anti-inflammatory activity

According to the literature reviewed, only one study directly associated an extract of avocado pulp with an anti–inflammatory effect. The other studies found are related to the anti–inflammatory effect of an unsaponifiable mixture of avocado and soy oils (ASU).

ASU is a mixture of fat-soluble extracts in a ratio of 1:2 (avocado/soy). ASU has shown anti–inflammatory, antioxidant and analgesic activities.[95–97] It was reported that in osteoarthritis induced by interleukin-1beta in human chondrocytes cultured in alginate beads, ASU (300 mg/day) increased the production of aggrecan, inhibited basal production of macrophage inflammatory proteins 1 beta (MIP-1beta), interleukin-6 (IL-6), interleukin-6 (IL-8), nitric oxide (NO), and prostaglandin E2 (PGE2) by chondrocytes.[96] The same authors described the inhibitory effects of the ASU on co-culture of human chondrocytes with osteoarthritic subchondral osteoblasts, increasing aggrecan and type II collagen formation.[97] Altinel et al. (2007)[98] indicated that ASU showed an antiarthritic effect increasing the levels of two isoforms of growth factor-β (TGF-β1 and TGF-β2) in knee joint fluids in canines. Additionally, Au et al. (2007)[95] found that this same extract (ASU, 25 μg/mL) inhibited pro-inflammatory marker expression or release (interleukin-1ß (IL-1ß), cyclooxygenase-2 (COX-2), inducible NO synthase (iNOS), PGE2 and NO) in auricular chondrocytes (bovine) and monocyte/macrophages (human THP-1 cells) previously activated with lipopolysaccharide *in vitro*. The same results were reported by a different group[99], who demonstrated anti–inflammatory activity of the combination of ASU and epigallocatechin gallate in cell cultures of auricular chondrocyte of horses. ASU extracts, also have been associated with the inhibition of metalloproteinase-13 (jointly with lesion remission and lower synovium cellular

infiltration)[100], as detected by immunohistochemistry, in canines (10 mg/kg/day for 8 weeks) that had knee osteoarthritis induced by anterior cruciate ligament transection.

ASU presented inhibitory effects in a stress-induced signaling pathway in cell cultures of mouse costal chondrocytes. Doses of 10 μg/mL of ASU inhibited the activation of Nuclear factor kB (NFkB) and ERK1/2 induced by either IL-1ß incubation or by mechanical stress, resulting in lower expression of metalloproteinases 3 and 13, and PGE2.[101] In addition, recently it was reported the potential inhibitory effect of ASU and α-lipoic acid (LA) on chondrocyte PGE2 production in articular cartilage of equine joints.[102] Interestingly, according to a meta-analysis in patients with knee and hip osteoarthritis (OA) symptoms (mostly pain) were reduced for an average of 6 months following treatment with ASU. This summary points towards an improved recovery in knee OA.[103]

Recently, it was described anti–inflammatory activities of hydroalcoholic leaf extract of avocado in an albino Wistar rat model that were exposed to X-ray irradiation. Rats orally administered with a dose of 100 mg/kg body weight of extract for five days. On the fifth day after last administration, the rats were exposed to X-ray irradiation (4 Gy), reducing the levels of cyclooxygenase-2 in liver homogenates.[80]

Antimicrobial activity

Avocado pulp and wastes (seeds, leaves, and peel) have demonstrated antimicrobial effects. Antimicrobial peptides (Defensin PaDef) from avocado pulp showed activity against *Escherichia coli* and *Staphylococcus aureus*.[59] Additionally, methanolic extracts from pulp showed antimycobacterial activity *in vitro* against *Mycobacterium tuberculosis* H37RV, with minimum inhibitory concentration (MIC) values of 24.0, 33.8, 24.9, and 35.7 μg/mL for avocadenol A, avocadenol B, (2R,4R)-1,2,4-trihydroxy-nonadecane and (2R,4R)-1,2,4-trihydroxyheptadec-16-ene, respectively.[60]

Organic extracts from seed avocado inhibited the growth *in vitro* of strains of *Candida* spp., *Cryptococcus neoformans* and *Malassezia pachydermatis*[83], *S. aureus, S. pyogenes, C. ulcerans, C. albicans, E. coli*, and *S. typhi*.[84] Besides, seed extracts showed antifungal activity against *Cryptococcus neoformans* (IC50 < 8 μg/mL (methanol) and 8.211 μg/mL (chloroform), and methicillin-resistant *S. aureus*, IC50 8.7 μg/mL (petroleum ether).[85] An ethanolic seed extract had activity against two intestinal parasites, *E. histolytica*, and *G. lamblia*.[87] In addition, a chloroform extract inhibited the growth of *M. tuberculosis* drug-resistant species and was active against non-tuberculosis *Mycobacterium* such as *M. fortuitum, M. avium, M. smegmatis* and *M. abscessus* (MIC < 50 μg/mL).[87]

Rodriguez-Sánchez et al. (2013)[88] identified avocado seed persenones (A, B and C), which inhibited the germination and vegetative cell growth of *C. sporogenes* endospores (MICs ranged from 7.8 to 15.6 μg/mL).

Regarding the leaves and peel of avocado, methanolic extracts of leaves showed a moderate level of activity against *T. cruzi* epimastigotes with 61.32% inhibition at 150 μg/mL.[71] An extract aqueous of Hass avocado peel showed inhibitory activity against *H. pylori* urease, with an IC50 of 1.02 μg GAE/mL.[40]

In vitro assays have shown the antimicrobial activity of the avocado suggesting that the avocado could be a potential antimicrobial agent for pathologies produced by bacteria, fungus, and others. However, i*n vivo* studies are lacking and should be performed to validate the antimicrobial activity of avocado.

Cardiovascular disease

There is extensive evidence regarding avocado effects on cardiovascular disease. In fact, avocado plants were used ancestrally for the treatment of hypertension. In this sense, a study in rats (Wistar male) demonstrated that consumption of avocado reduced triglyceride levels and increased high-density lipoprotein cholesterol (HDL-C) compared to a control group. Likewise, the group that consumed avocado had a lower mean HDL-C Stokes diameter, which was associated with a lower content of Apolipoprotein A-I (ApoA1) and a higher proportion of phospholipids.[104] Furthermore, the avocado treatment increased serum paraoxonase/arylesterase 1(PON1) levels, an anti-atherosclerotic component of HDL-C.[105] Daily supplementation with aqueous and methanolic leaf extracts of avocado, at a dose of 10 mg/kg body weight, during eight weeks in Albino rats with a hypercholesterolemic diet, showed decreased plasma glucose levels and total cholesterol, while HDL-C levels increased.[75] Aqueous seed extract reduced the blood pressure in hypertensive Albino rats, and showed a reduction in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) levels in the plasma, kidney, liver and heart (dose of 500 mg/kg body weight).[89] Additionally, avocado seed flour supplementation in CD-1 adult male mice significantly reduced the levels of total cholesterol and LDL-C and the prediction of the atherogenic index.[13] Aqueous leaf extract of avocado also increased the synthesis or release of endothelium-derived relaxing factors, as well as, the release of prostanoids, producing a significant vasorelaxation in rats aortic ring.[72] Studies of avocado aqueous leaf extract on isolated guinea pig atrial muscle strips performed indicated that this extract produced negative inotropic and chronotropic effects, concentration dependent (25–800 mg/mL). This extract reduced, the rhythmic, spontaneous, myogenic contractions of portal veins isolated from healthy normal Wistar rats.[73]

All these results highlight avocado as a potential agent for the treatment of cardiovascular diseases.

Diabetes

The first evidence of avocado use in diabetes treatments came from a screening study reported by Alarcon-Aguilar et al. (1998)[90] with adult male rabbits. It was observed that after an oral glucose overdose, aqueous seed extract (intragastric treatment) reduced the hyperglycemia.

Other studies investigated the effects of daily treatment with aqueous or methanolic extracts of the avocado leaf (10 mg/kg body weight) on glucose and lipid metabolism in diet-induced hypercholesterolemic albino rats.[75] The treatments with both extracts reduced the levels of plasma glucose, TC, and LDL-C in plasma. Furthermore, HDL-C levels were significantly higher compared to the hypercholesterolemic rats. The observed effects on glucose metabolism could be attributed to the previously studied properties of avocado in restoring pancreatic tissue function or inhibiting intestinal glucose absorption. Additionally, an acute infusion of ethanolic leaf extracts showed a dose-dependent hypoglycemic response in Streptozotocin (STZ)-induced diabetic rats. Besides, the acute infusion showed the effect on kidney function decreasing urine flow and electrolyte excretion. Treatment subchronic in diabetic rats increased hepatic glycogen concentration and reduced plasma creatinine and urea levels.[74]

Another study investigated the inhibitory effect of methanolic extracts from avocado leaves, seed, peel, and pulp on crucial enzymes linked to type 2 diabetes.[93] The results revealed that all extracts inhibited both α-amylase and α-glucosidase activities in a dose-dependent manner. However, the peel and leaf extracts have the highest α-amylase and α-glucosidase inhibitory activities, respectively, as was revealed by their IC50 values.

Alloxan-induced diabetic rats after a 21-day treatment, the administration of aqueous extracts of avocado seeds (300 or 600 mg/kg body weight) showed to reduce blood glucose up to 78-73% levels. Furthermore, the extracts inhibited drug-induced pancreatic islet cells deterioration.[91] Once again, the authors noted the presence of insulin-like substances in plants extracts, stimulation of beta cells, an increase in glucose metabolism, and a regenerative feature of pancreatic islets as possible explanations of the findings.

It was reported that the oral administration of 300 mg/Kg of ethanolic extract of avocado fruit, improved the altered levels of blood glucose, plasma insulin, glycosylated hemoglobin and modulated the activities of carbohydrate metabolizing enzymes in diabetic rats undergoing treatment for 30 days.[66]

Effects on liver

It was observed that avocado has protective activity against liver damage.[64] Wistar rats were supplemented with 22 different freeze-dried fruits for 14 days (5 wt% basis). Then, the rats were injected intraperitoneally with D-galactosamine at a dose of 350 mg/kg body weight and the levels of plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured. Avocado showed higher protective activity than the other fruits, reflecting lower plasma aminotransferase activity. Another study, an ethanolic pulp extract was orally administered at 300 mg/kg/day during 30-days to STZ-induced diabetic rats, preventing body weight loss and restored blood glucose, glycosylated hemoglobin, blood urea and serum creatinine levels to normal parameters.[65] Additionally, plasma insulin and hemoglobin levels were restored, suggesting insulin-stimulating effects. Furthermore, the authors observed lower AST, ALT and plasma alkaline phosphatase (ALP) activities in plasma from hyperglycaemic rats treated with the extract compared to the STZ alone-treated group, suggesting hepatic protection. On the other hand, the extract showed antioxidant properties by reduction of liver Thiobarbituric Acid Reactive Substances (TBARS) and hydroperoxide levels and increase of ascorbic acid, tocopherol and glutathione (GSH) liver content, as well as, liver superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione-S-transferase (GST) activities compared to the hyperglycaemic group of animals.[65]

Lima et al. (2012)[76] orally administered a hydroalcoholic leaf extract (0.15 and 0.3 g/kg/day) and metformin (0.5 g/kg/day) during one month to STZ-induced diabetic rats. The authors observed hypoglycaemic effects after an oral glucose tolerance test; maintenance of body weight gain, increase in liver and tissue mass, except for the absolute mass of soleus muscle. Also, some biochemical parameters were decreased, such as blood urea nitrogen, uric acid, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase (at the same level or lower than the metformin treatment), improving the metabolic state of the animals. Furthermore, the work described the significant prevention of STZ-induced pancreatic beta cell injury by the extract treatment. Finally, regarding molecular mechanisms, the authors observed the full restoration of Akt phosphorylation

in the soleus muscle and the liver, induced by the extract treatment compared to the diabetic group of rats. Moreover, it was observed that hydroalcoholic leaf extracts of avocado induced lower glucose intestinal absorption in control healthy rats, although this treatment did not reach the same levels of the metformin treatment.

The protective effects, antioxidants and hepatoprotective activities of aqueous leaf extract of avocado against carbon tetrachloride (CCl_4)-induced hepatotoxicity in male albino rats were evaluated.[77] Hepatoprotective effects were assessed by estimating the activities of ALT, AST, ALP and levels of total bilirubin. The effects of the extract on biomarkers of oxidative damage (lipid peroxidation) and antioxidant enzymes, namely CAT, SOD, GPx, and GST, were measured in the liver post-mitochondrial fraction. Avocado leaf extract showed significant hepatoprotective effects against CCl_4-induced toxicity attributable to its constituent phytochemicals. The mechanism of hepatoprotection seems to occur through modulation of the antioxidant enzyme system.

Another study investigated the hypoglycaemic and tissue-protective effects of aqueous seed extracts of avocado on alloxan-induced diabetic albino rats.[92] The effects of different concentrations of the extract on alloxan-induced Wistar albino rats were compared with those of a reference drug, glibenclamide. The extract showed a significant hypoglycemic effect and reversed the histopathological damage that occurred in alloxan-induced diabetic rats, comparable to the effects of glibenclamide, and also had anti-diabetic and protective effects in some rat tissues, such as the pancreas, kidneys, and liver.

Carvajal-Zarrabal et al. (2014)[106] evaluated the effect of avocado oil supplementation compared with olive oil, on the hepatic function of sucrose-fed rats. It was observed that the consumption of avocado oil could be beneficial in the control of an altered metabolic profile, as it can affect hepatic function biochemical markers in a similar way as olive oil.

Neurological effects

Ojewole and Amabeoku (2006)[79] evaluated *in vivo* the properties of an aqueous extract of avocado leaves on epileptic convulsant, which was induced in Balb C male mice by pentylenetetrazol, picrotoxin and bicuculline administration. The avocado leaf extract was intraperitoneally administered (100–800 mg/kg) and demonstrated an anti-convulsant effect related to enhanced GABAergic neurotransmission.

In Alzheimer's disease (AD) an i*n vitro* approach demonstrated the anti-cholinesterase and antioxidant activities of an aqueous extract of avocado leaves and seeds.[81] These results suggest a possible role for avocado in AD treatment; however, *in vivo* studies must be performed.

Clinical studies

Some works have been done in humans. The first evidence came from 1992, when Alvizouri-Muñoz and colleagues examine the effects of avocado consumption on plasma lipids concentration on healthy volunteers.[107] Subjects were exposed to three different diets (for 2 weeks), the first rich on MUFA with avocado as their major source (75% of total fat), the second a free diet with addition of the same amount of avocado, and the third a low-saturated fat diet without avocado. It was observed interesting positive results regarding plasma triglycerides, total cholesterol and LDL-C and HDL-C, on subjects that were on diet 1 and 2, regarding 3. That same year, Colquhoun et al compare the effects

(after 3 weeks) of a high MUFA diet (enriched with avocado), against a high-carbohydrate diet, on 15 healthy females.[108] Both diets lower total cholesterol, although the diet with avocado was more effective to lower total cholesterol levels, and also was the only one to induce a decrease on LDL-C. Four years later, Lopez-Ledesma evaluated the effect of an avocado-enriched MUFA diet on healthy and hypercholesterolemic subjects.[109] It was observed a 16% decrease on serum total cholesterol (related to controls) in healthy ones, and also a decrease in total cholesterol, LDL-C and triglycerides (17%, 22% and 22%, respectively), and an increase on HDL-C (11%), on hypercholesterolemic subjects (related to controls). Next year, Carranza-Madrigal evaluated the effects of a vegetarian diet vs a vegetarian diet + avocado (75% of total lipids) on hypercholesterolemic patients[110] for 4 weeks. The diet with avocado reduced significantly triglycerides, and more reduced HDL-C levels. Later on 2013, Fulgoni and colleagues associate avocado consumption with better nutrient intake and lower metabolic syndrome risk on the NHANES 2001–2008.[111] The same year, Li et al described how avocado hass addition to a hamburger modulates vasodilatation and inflammation on eleven healthy subjects.[112] The consumption of this hamburger prevents vasoconstriction two hours following ingestion, also prevents the IkBα degradation and blunted NFkB activation on peripheral blood mononuclear cells after 3 hours of ingestion, and finally prevents serum triglyceride increase. Also, in 2013, a randomized 3 × 3 crossover study was performed.[113] It was evaluated post-ingestive satiety, glucose and insulin levels, and energy intake in 26 overweight adults after a hass avocado intake. It was observed positive results on self-reported feelings of satisfaction (higher), desire to eat (lower), and blood insulin (lower). On the other hand, Kopec and colleagues[114], observed that avocado consumption promotes improved vitamin A absorption and metabolism on 12 healthy man and women. On 2015, Wang et al reported the effect of an intake of a moderate fat diet with avocado on lipoprotein particles in overweight and obese adults.[115] In this trial, it was included 45 overweight or obese participants with normal LDL-C serum levels, which were treated for 5 weeks. The diet, that included one avocado, induced a greater reduction of LDL-C and LDL-C/HDL-C ratio than the moderate fat diet alone. On the other hand, on a six-month randomized controlled trial[116], including 40 healthy subjects, it was tested the potential of the intake of avocado on cognition. Avocado intake increases lutein levels, macular pigment density, memory and spatial working memory, and attention. The author concluded that including avocado in diet could be an effective strategy for cognitive health. Recently, Haddad et al studied changes of post-ingestive gut hormones after the consumption of hass avocado, and their association with appetite, on a crossover trial.[117] On 26 healthy subjects, three test meals were applied (one week separated from each other): avocado-free control (C); isoenergic avocado inclusive (AI); and, energy increased avocado added (AA). Appetite hormones, plus appetite sensations variables were assayed. AA meal induced a decrease in glucagon like peptide 1 (GLP-1) levels. Negative associations were observed between YY peptide (PYY) and gastric inhibitory peptide (GIP) against hunger-like variables, and negatives against fullness-like variables. For GLP-1, the associations were backwards. Also, in 2018, Park et al evaluated markers of cardio-metabolic risk on a randomized controlled dose response trial in overweight men and women (n = 31)[118] replacing carbohydrate energy in meals with half or whole avocado. Post-glycemic, insulinemic, and flow mediated responses were reduced as compared to controls. Moreover, lower triglyceride-rich lipoproteins and higher HDL-C levels were detected. Finally, in the present year,

a study finds associations between avocado intake and weight and BMI changes in an adult cohort.[119] In the Adventist Health Study (55,407 subjects from US and Canada), avocado intake (32 g/day) was related with repeated weight measures. It was observed that subjects that consume avocado, who were normal weight at baseline, gained less weight than non-consumers. Overall, as observed in Table 5, a quite important mass of evidence had rose from studies in humans, mostly of them focusing the efforts in variables related to cardiometabolic risk. Giving the impact of these type of conditions in human life span and well-being, these gathered information rise the definitive relevance for this specie to be constantly included in our diet.

Toxicity of avocado

Although avocado has known biomedical effects, acute toxicity of the pulp and leaves has been reported. In this context, avocado leaf consumption presented myocardial and mammary gland damage in animals.[120–122] Goats that ate avocado leaf showed tachycardia, hyperpnoe, and evidence of lung edema. Histological examination revealed severe myocardial degeneration, necrosis, and fibrosis.[122] Mammary gland damage in goats was observed at doses higher than 20 g/kg of fresh leaf, showing edema and reddening; microscopic analysis revealed extensive degeneration and necrosis of the secretory epithelium and sloughing of necrotic cells into the lumen.[123]

Ostriches and hens that ingested avocado foliage and immature pulp had severe cardiomyopathy, characterized by degeneration and necrosis of myocytes.[124] Additionally, canaries and budgerigars that were fed, via feeding cannula, with mashed avocados exhibited poisoning symptoms, producing death within 24 to 47 hours. Necropsy showed subcutaneous edema in the pectoral area and hydropericardium.[125]

Due to the toxic effect of avocado leaves and pulp on animals, the toxicity of avocado extracts has also been studied. Aqueous extract of avocado did not present toxic effects by the orogastric administration at 10 g/kg in adult male rats.[121] In contrast, avocado seed ethanolic extract showed acute toxicity in male BALB/mice by oral gavage with an LD_{50} (oral median lethal dose, LD_{50}) value of 1200.75 mg/kg.[126] Furthermore, *in vitro* studies showed that avocado pulp and leaves methanolic extracts have genotoxic effects on cultured human peripheral lymphocytes. Both leaf and pulp extracts, at doses of 100 mg/kg and 300 mg/kg, respectively, have a concentration-dependent increase in chromosomal aberrations as compared to the control group. Also, acrocentric associations and premature centromeric separation were the two most common abnormalities observed in both the exposed groups.[127]

Silva-Platas et al. (2012)[128] studied the toxic effects of acetogenin-enriched extract from the avocado seed in isolated rat hearts (male Wistar). Their results showed that a dose of 77 μg/mL of this extract produced complete inhibition of contractibility in an isolated perfused heart. Additionally, 43 μg/mL of this extract induced apoptosis in isolated cardiomyocytes through activation of the intrinsic pathway. This result indicates that acetogenin-enriched extract from avocado could have cardiotoxic effects.

It has been described that the most toxic compound of avocado is the "persin", which is found in avocado leaves. This compound is a non-polar toxin that has toxic effects on of the lactating mammary gland at doses ranging from 60 to100 mg/kg. At doses above

Table 5. Clinical trials performed including avocado as treatment.

Sample	Intervention	Significant results	Reference
16 healthy subjects	2 weeks trial: 1) Diet rich in avocado (75% of total fat from avocado) 2) Free diet with same amount of avocado 3) Low-saturated fat diet without avocado	↑ serum HDL-C ↓ serum LDL-C Both diets (1) (2), related to (3)	[107]
15 healthy females, 37–58 y	3 weeks randomized trial: 1) Diet high in MUFA enriched with avocado 2) High complex carbohydrate diet	(1) more effective in ↓ blood TC ↓ LDL-C and apoB ↓ HDL-C on (2)	[108]
30 healthy adults 37 adults with hypercholesterolemia (15 of them with hypertriglyceridemia)	7 days trial: - 15 healthy and 30 hypercholesterolemic (with T2D) received avocado enriched diet (MUFA 49g; s/u 0.54; 1) - 7 hypercholesterolemic (without T2D) received isocaloric control diet (MUFA 34 g; s/u 0.7; 2)	Healthy subjects: ↓ serum TC on (1) Hypercholesterolemic subjects: ↓ TC ↓ LDL-C ↓ TG ↑ HDL-C	[109]
13 subjects with dyslipidemia	Prospective, transversal, comparative 3 × 4 weeks trial: 1) Vegetarian diet 2) Vegetarian diet with avocado as source of MUFA (75% of lipids) 3) Avocado-added free diet	↓ LDL-C on (2) ↓ TG on (2) ↓ HDL-C three diets	[110]
NHANES 2001–2008 US Cohort (17,567 subjects, over 19 y, 49% females)	Observational 8 y trial	Avocado consumers showed: ↑ vegetable intake ↑ fruit intake ↑ diet quality ↑ total fat intake ↑ MUFA and PUFA intake ↑ dietary fiber intake ↑ vitamins E and K, magnesium and potassium intake ↓ added sugar intake ↓ body weight, BMI, waist circumference ↑ HDL-C ↓ metabolic syndrome OR	[111]
11 male healthy subjects, 25.4 y	Randomized crossover 1–6 h trial: 1) 250 g burger alone 2) with 68 g avocado flesh	↑ vasoconstriction at 2 h on (1) Preservation of IkBα and ↓ NFkB on PBMC at 3 h on (2) ↑ serum IL-6 and TG on (1)	[112]
26 overweight adults (40.8 y, 28.1 BMI)	Randomized 3 × 3 crossover 3–5 h trial: 1) control diet 2) avocado inclusive 3) avocado added	↑ satisfaction and ↓ desire to eat on (3) regarding (1) ↓ blood insulin on (2) regarding (1) and (3)	[113]

(*Continued*)

Table 5. (Continued).

Sample	Intervention	Significant results	Reference
Two sets of 12 healthy men and women, 19–32 y	2 randomized, 2-way crossover 12 h trials: 1) meal with avocado (23 g lipids) 2) meal without avocado Source of provitamin A carotenoids: In first set: tomato sauce from a high-ß-carotene variety In second set: raw carrots	↑ ß-carotene absorption and ↑ efficiency to conversion to vitamin A (meal 1, on first and second sets)	[114]
45 overweight or obese subjects, with baseline LDL-C between 25th and 90th percentile, 45 y	Randomized, crossover, controlled feeding 5 weeks trial: 1) lower fat diet 2) moderate fat diet including avocado (136 g) 3) moderate fat diet including oleic acid oils matching avocado fatty acid content	Greater reduction of LDL-C and HDL-C compared to baseline on (2) ↓ LDL-C particle number, small dense LDL-C, LDL-C/HDL-C, compared to baseline on (2)	[115]
40 healthy subjects, 62–63 y	Randomized, controlled, 6 month trial: 1) one avocado (0.5 mg/day lutein) 2) one potato or one cup of chickpeas (0 mg/day lutein)	↑ serum lutein levels and macular pigment density on (1) ↑ improvement in memory and spatial work memory, on both (1) and (2) ↑ improvement in sustained attention on (1)	[116]
26 healthy overweight adults	Randomized 3 × 3 controlled trial: 1) avocado-free 2) isoenergetic avocado inclusive 3) energy increased avocado added	↓ 3 h GLP-1 AUC on (3) compared to (1) Negative associations: PYY and GIP against Hunger, Desire and How Much; GLP-1 against Hunger Positive associations: PYY and GIP against Fullness, Satisfied and VAS; GLP-1 against Satisfied and VAS	[117]
31 overweight/obese middle age adults	Single-center, randomized, controlled, 3-arm, 6 h, crossover trial: 1) 0 g fresh avocado 2) 68 g (half avocado) 3) 136 g (whole avocado) Meals (breakfasts) were energy-matched	↓ post-meal glycemic, insulinemic, and flor mediated vasodilation responses on (2) and (3) as compared to (1) ↓ TG-rich lipoproteins and ↑ HDL-C on (3) compared to (1)	[118]
55,407 adults, 56 y	Observational 11 y trial	Subjects that consume avocado, who were normal weight at baseline, gained less weight than non-consumers	[119]

MUFA, monounsaturated fatty acids, TC, total cholesterol; T2D, type 2 diabetic; s/u, saturated/unsaturated; TG, tryglycerides; PUFA, polyunsaturated fatty acids; BMI, body mass index; OR, odds ratio; PBMC, peripheral blood mononuclear cells; GLP-1, glucagon like peptide 1; AUC, area under curve; PYY, YY peptide; GIP, gastric inhibitory peptide; VAS, visual analogue scale.

100 mg/kg, necrosis of myocardial fibers may occur, and hydrothorax may be present in severely affected animals.[120]

These studies exhibit the toxic effects of supplementation with avocado pulp, leaves or seeds. Thus, it is necessary to determine the LD_{50} of this plant in future studies, as this plant is used as a treatment for the pathologies mentioned above.

Conclusions and future trends

During recent decades has been given particular attention to the agroindustrial wastes, both for the reduction of the environmental damage caused by them and for their potential use in the development of high value-added products. Avocado pulp and wastes such as peel, seed, and leaves, obtained from industrial processing of avocado, contain bioactive compounds (phytochemicals) including polyphenols, carotenoid, and tocopherols, among others. These bioactive compounds have acquired a great interest in the scientific society due to their potential to prevent and control various pathologies. Thus, pulp, seed, leaf and peel extracts have reported activities such as anticancer, antihypertensive, anticonvulsant, hypoglycemic, anti–inflammatory, antimicrobial, and also as hepato-protective. Therefore, pulp and wastes of avocado are a potential source of bioactive compounds suitable for food or nutraceutical applications. However, the studies have been carried out on cell culture and animals, showing in some case a certain degree of toxicity. In this context, more studies are needed to establish safe doses of intake and administration of avocado extracts. However, the results observed in clinical trials so far highlights the importance of this specie to be always considered in our diet.

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Declaration of interests

The authors have nothing to declare

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