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Avocado

Consumption and Health



María Guiomar Melgar-Lalanne
Alan Javier Hernández-Álvarez
Editors

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AVOCADO

CONSUMPTION AND HEALTH

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MARÍA GUIOMAR MELGAR LALANNE

AND

ALAN JAVIER HERNÁNDEZ ÁLVAREZ

EDITORS



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Chapter 1

**THERAPEUTIC AND NUTRACEUTICAL
POTENTIAL OF PERSEA AMERICANA FRUITS
AND THEIR BY-PRODUCTS: A REVIEW**

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ABSTRACT

Avocado (*Persea americana* Mill.), originated from Mexico and Central America, is the only commercially crucial edible fruit that belongs to the Lauraceae family. This fruit shows a growing value on the international market, not only because of its nutritional quality but also due to its medicinal uses and application in the cosmetic industry. Fruit constituents reveal that it abounds in various fatty acids, protein, vitamins, and minerals. Besides this, a lot of secondary metabolites have also been isolated from different parts of the avocado plant. The

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predominant carotenoid is lutein, but other carotenoids are also described, including α -carotene, β -carotene, zeaxanthin, neoxanthin, and violaxanthin. It has been reported that these lipophilic carotenoids may have, among others, potential anti-carcinogenic effects. This fruit has been recognized for its health benefits, mainly due to the compounds present in the lipidic fraction, such as omega fatty acids, phytosterols, tocopherols, and squalene. Several studies have shown the benefits of avocado associated with a balanced diet, especially in reducing cholesterol and preventing cardiovascular diseases. The processed avocado pulp is an alternative to utilize fruits, which can be used in various value-added food products.

Tocopherols have also been identified not only in avocado pulp fruits but in their seeds. For these reasons, the recovery of health benefit bioactive compounds from fruit and its wastes is a research trend not only to help minimize the waste burden but also to meet the intensive demand from the public for bioactive compounds which are believed to have protective effects against chronic diseases.

Avocado pulp and seed contain variable oil content and is widely used in the pharmaceutical and cosmetic industries, and the production of commercial oils similar to olive oil. It contains fatty acids such as lignoceric acid, arachidic acid, margaric acid, behenic acid, gadolenic acid, docosadienoic, myristic, and eicosanoic acids, β -sitosterol, lecithin, minerals, and vitamins, showing its potential as an alternative dietary supplement.

This review is focused on the nutritional characterization, polyphenolic compounds recovery from avocado fruits, and their wastes (peel and seeds) as an excellent alternative for industry, especially for pulp processing or oil extraction, considering its composition and the benefits of its compounds. Furthermore, this crop can be used for exportation and oil extraction, application in processed products, or as a raw material in the pharmaceutical and cosmetic industries, generating high value-added products.

Keywords: *Persea americana* Mill, nutraceuticals, bioactive compounds, therapeutic properties, by-products, sustainability

1. INTRODUCTION

Avocado (*Persea americana* Mill) is a flowering plant belonging to Lauraceae family, genus *Persea*, native from Mexico and Central

America, and which has recently been winning worldwide acceptance due to its benefits for human health (Araújo et al., 2018). Avocado is highly regarded today as an essential fruit for food and nutrition, and the remarkable development of this fruit has been recorded in every continent.

Avocados have been known for many years, dating back at least to 1519 when a Spanish soldier of fortune (Hernando Cortés) saw and reported the fruit tree in Colombia (Bill et al., 2014).

As already mentioned, Mexico, Central America, and northern South America are considered to be the centers of origin of avocados; however, avocados have been cultivated in a varying range of habitats, including Chile, Israel, Spain, South Africa, Peru, Kenya, USA, and the Dominican Republic, among others (Whiley et al., 2002). Archaeological and other evidence indicates that avocados were cultivated wherein very early times, possibly some 6000 years ago (Chen et al., 2009). They were not commercially exploited until the first years of the twentieth century when their potential for commercialization was developed by Californians. It was in this state that avocado growing became a recognizable industry. The crop has wide adaptability, and avocados are now grown in the whole world.

According to the Food and Agriculture Organization (FAO) (2010) reports, 13% of the avocados produced in Mexico are traded internationally. In Chile, South Africa, Israel, and Spain, the avocado production is mainly aimed at exporting the fruit to the overseas markets. The world avocado trade is focused on two major markets, more specifically, the European Union (EU), which imports 150,000–160,000 t per year, including imports from Spain, and the United States, which imports 140,000 t per year. According to De Bon (2010), Canada and Japan imported about 30,000 and 15,000 t, respectively, and the Asian, Middle East, and Eastern European markets imported less than 20,000 t per year. Peru, South Africa, and Israel are the major avocado exporters to the European markets (De Bon, 2010).

Commonly, this fruit is called avocado, characterized by its pear-shaped, egg-shaped, or spherical (Figure 1). Morphologically, avocado fruit is formed by pericarp that consists in three layers: the exocarp (1),

which comprises the skin or rind, the fleshy mesocarp (2), that is the edible portion, and the endocarp (3), which is the thin inner layer next to the outer seed coat (Cummings and Schroeder, 1942; Cowan and Wolstenholme, 2003).

Concerning the cultivars most produced worldwide, Hass and Fuerte dominate the international market (Rodríguez-Carpena et al., 2011), but Shepard, Sharwil, Pinkerton, Reed, and Wurtz are also recognized (Rodríguez-Carpena et al., 2011). According to Dembitsky et al., (2011), there are about 500 varieties of avocado varieties, which differ mostly in the fruit shape and color. Although the Fuerte cultivar displays a green skin color after-ripening and is well known in the European markets, the Hass cultivar currently dominates the international trade market due to its longer shelf life and fruit size, and higher consumer acceptance due to its rich, nut-like flavor (FAO, 2010). Hass variety is the dominant and most popular type grown in the USA for export. The avocado export markets are segmented, according to cultivars. Hass cultivar differs significantly from other cultivars, including Fuerte, Reed, and Pinkerton, which have green skin (De Bon, 2010).

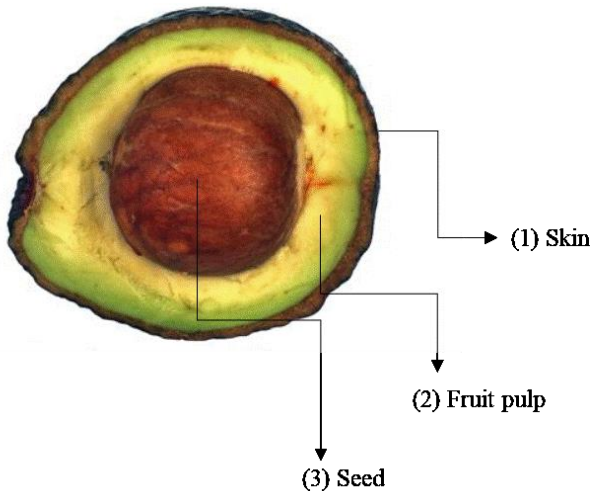


Figure 1. Morphological characteristics of avocado (*Persea americana* Mill.).

Despite their organoleptic differences, avocado varieties also present differences in their size and chemical composition. For example, Fuerte variety is larger and displays more weight than the Hass variety. Despite this, Hass variety presents a better ratio of an edible portion (pulp) than Fuerte variety. The proportion of fruit by-products (peel and seed) is higher in Fuerte variety than in the Hass variety. The pulp of Fuerte has lower fat content than the Hass variety (Rodríguez-Carpena et al., 2011).

Avocado is a well-known source of nutrients (fatty acids and proteins), bioactive compounds (carotenoids and phenolics), vitamins (E, B1, B2, and D) and minerals (calcium, iron) (Dembitsky et al., 2011; Tabeshpour et al., 2017). According to some researchers, avocado is the most nutritive among fruits and is regarded as the most significant contribution of the New World to the human diet (Rodríguez-Carpena et al., 2011; Melgar et al., 2018). The edible part (pulp) is rich in proteins (up to 4%) and fat (up to 30%), but low in carbohydrates (Tabeshpour et al., 2017). The fat is similar to olive oil in composition and is widely used in the preparation of pharmaceutical and cosmetics products (Tango et al., 2004; Ballmann and Müller, 2008; Melgar et al., 2018). Therefore, the development of avocado production will help local people to improve their nutritional standards. Furthermore, avocado has the highest energy value (245 cal/100 g) of any fruit (Bill et al., 2014).

Currently, there are many patents with avocado uses in food, health, and cosmetic field, as a nutritional fruit juice, avocado wine, an herbal cream, or avocado-derived lipids for use in treating leukemia, among others (Araújo et al., 2018). Avocados are traditionally used for various purposes, from medicinal to culinary, dermo-cosmetic applications, and others (Nayak et al., 2008; Anaka et al., 2009; Kosińska et al., 2012). In folk medicine, avocados are also used as hypotensives, hypoglycemics, and antivirals and are applied for the treatment of ulcers, cardiac and dermatological diseases (Almeida et al., 1998; Adeboye et al., 1999; Ukwe and Nwafor, 2004; Antia et al., 2005; Owolabi et al., 2005; Raharjo et al., 2008). Analgesic and anti-inflammatory effects have also been reported (Adeyemi et al., 2002). Besides the antihypertensive and cardioprotective action, avocado also contributes to lipid-lowering, antidiabetic,

anti-obesity, antithrombotic, and antiatherosclerotic effects (Tabeshpour et al., 2017). Avocados, and others such as dark chocolate, red wine, nuts, beans, are being promoted as anti-aging foods, due to their anti-oxidative and anti-inflammatory properties (Chrysohoou and Stefanadis, 2013).

Thus, in this chapter, it will refer to the nutritional, chemical, and biological properties of avocado, also highlighting its by-products (peel and seed) as industrial waste with high economic value for pharmaceutical and food industries.

2. AVOCADO NUTRITIONAL COMPOSITION

In the last decades, the evidence of the benefits of avocado for health has increased, and so, its consumption has increased, stimulating the investigation of its potential (Lu et al., 2009). Thus, in some countries, information on avocado and its importance to health has been highlighted. The independent Australian organization, “The Heart Foundation,” certified the fruit as healthy food for the heart, while the Californian Avocado Commission encouraged efforts to promote avocado in the health area (Knight, 2002).

Moreover, in recent years, there has been a growing interest in functional food that can provide not only the basic nutritional and energetic requirements but also additional physiological benefits (Zhou et al., 2016; Duresa, 2017). Avocado is classified as a functional food due to its high nutritional value and proven beneficial effects for human health (Zhou et al., 2016; Duresa, 2017). Avocado is a nutrient-rich fruit, with the composition depending on edaphic and climatic conditions (e.g., ecotype, cultivar, degree of maturity, and growing conditions). Despite everything, avocado has been recognized for its high content of bioactive compounds present in the lipid fraction, such as fatty acids, phytosterols, tocopherols and squalene (Santos et al., 2014; Duarte et al., 2016). Avocados contain an oil rich in monounsaturated fatty acids (MUFA) in a water-based matrix, which enhances nutrient and phytochemical bioavailability and masks the taste and texture of the dietetic fiber (Dreher and Davenport,

2013). The avocado oil consists of 71% MUFA, 13% polyunsaturated fatty acids (PUFA), and 16% saturated fatty acids (SFA), which helps to promote healthy blood lipid profiles (Dreher and Davenport, 2013). According to Lu et al., (2009), pulp fruit is rich in lipids, which vary from 3% to 30% of its fresh weight, taking into account that oleic, palmitic, linoleic, and palmitoleic acids are the predominant fatty acids, as well as stearic acid in trace amounts. Santos et al. (2014) reported that oleic fatty acid represented more than half of the total fatty acids of this raw material, together with substantial amounts of unsaturated linoleic and palmitoleic acids. Lately, it has been discovered a new lipid derived from the avocado fruit, avocatin B, with cytotoxic activity in acute myeloid leukemia and to inhibit fatty acid oxidation and decrease NADPH levels, resulting in ROS-dependent leukemia cell death (Araújo et al., 2018). In contrast to other vegetable oils, avocado oil is characterized by having high levels of oleic and palmitoleic acids, low linoleic acid, and relatively high levels of palmitic and stearic acids. This fatty acid composition is influenced by the cultivars, maturity stage, the anatomical region of the fruit, and geographic location for plant growth (Contreras-Gutiérrez et al., 2013; Duarte et al., 2016; Corzzini et al., 2016; Forero-Doria et al., 2017). Forero-Doria et al., (2017) studied the oxidative stability of Chilean avocado oil and assessed the relationship between the antioxidant capacity of the oil and its protection against the induced thermal oxidation, considering their different fatty acid composition. The results showed a high content of monounsaturated fatty acid, with a percentage of 69.4%, and the amount of polyunsaturated and saturated fatty acids was 16.6 and 14%, respectively. The composition of MUFA included the presence of oleic (65.3%) and palmitoleic (3.9%) fatty acids, whereas the PUFA content comprised the following fatty acids: linoleic (15.2%) > linolenic (1.3%) > araquidonic (0.1%). Additionally, the SFA content corresponded to the presence of stearic and palmitic acids in 0.6 and 13.4%, respectively. According to Bill et al., (2014), the fatty acid composition in the avocado mesocarp of different avocado cultivars is as follows: oleic acid (86 mg g⁻¹ oil), palmitic acid (32 mg g⁻¹ oil), linolenic acid (19 mg g⁻¹ oil), and palmitoleic acid (14 mg g⁻¹ oil). Dávila et al., (2017) reported that the

major fatty acids of the Hass avocado oil were oleic acid (C18:1, 50.96%), palmitic acid (C16:0, 24.74%), linoleic acid (C18:2, 15.07%), palmitoleic acid (C16:1, 5.97%) and linolenic acid (C16:3, 1.66%). Other fatty acids such as myristic (C14:0, 0.05%), margaric (C17:0, 0.03%), margaroleic (C17:1, 0.08%), stearic (C18:0, 0.84%), arachidic (C20:0, 0.14%), gadoleic (C20:1, 0.27%), behenic (C22:0, 0.27%), lignoceric (C24:0, 0.06%) and other isomers trans of C18 were present only at low concentration. However, the content of fatty acids also depends on the drying and extraction methods of oil. According to Krumreich et al., (2018), fatty acids of avocado oil were better preserved when the pulp was dried at 60°C and using mechanical pressing. Palmitic (~21.0%), palmitoleic (~7.0%), linoleic (~11.0%), and tricosanoic (~2.5%) acids and lower relative proportions of linolenic acids (~0.6%) and behenic acids (~0.76%) were identified in avocado oil in addition to oleic acid (~58.0%).

Considering other constituents, avocado fruit carbohydrates are composed of about 80% dietary fiber (70% insoluble and 30% soluble fiber) (Marlett and Cheung, 1997). Avocados contain levels between 2.0 g and 4.6 g of dietary fiber per 30 g and one-half fruit, respectively (USDA, 2011). Thus, moderate avocado consumption can help to achieve an adequate intake of 14 g dietary fiber per 1000 kcal as about one-third this fiber level can be met by consuming one-half an avocado (Dreher and Davenport, 2013). Avocados contain a low content of sugar. One-half of an avocado contains 0.2 g sugar (e.g., sucrose, glucose, and fructose). The primary sugar found in avocados is a unique seven-carbon sugar (D-mannoheptulose) Moreover, its reduced form, perseitol, that does not behave nutritionally as regular sugar and is more of a unique phytochemical to avocados (Meyer and Terry, 2008). Roth (2009) suggested that D-mannoheptulose may support blood glucose control and weight management.

Salgado et al. (2008) reported that 70% of total fruit weight corresponds to the pulp fruit with an average of 6.94 g of carbohydrates, 17.34 g of fat, 2.08 g of proteins, 2.72 g of fibers (in 100 g of fresh pulp). It

is stated here that the fat content is, undoubtedly, the nutritional fraction with the highest expression in avocados. Moreover, according to USDA databases (2011) and Bes-Rastrollo et al., (2008), avocados are a medium energy-dense fruit, just because nearly 80% of avocado fruit pulp consists of water (“72%) and dietary fiber (“6.8%) and has been shown to have similar effects on weight control as low-fat fruits and vegetables.

Avocado industrial processing generates large quantities of agro-industrial by-products (peel and seeds), ranging from 18% to 30% of dry fruit weight (Wang et al., 2010; López-Cobo et al., 2016). Thus, it is interesting to reuse these by-products both to reduce their negative impact on the environment and to add value to them, since they are sources of critical phytochemical compounds. A by-product of avocado is its peels. Forty percent of the livestock herders’ budgets, especially in zero-grazing, go to food supplements. With avocado peel, rich in oil (7%), minerals, and other acids, it is possible to cut much of the feed costs. Research has shown that the peels have become part and parcel of commercially available feed (Gómez et al., 2014; Araújo et al., 2018). According to some authors, the composition of avocado by-products varies between cultivars, climatic conditions, genetics, and others (Gómez et al., 2014; Araújo et al., 2018). The predominant constituents of avocado by-products (peel and seeds) are carbohydrates, such as fibres, hemicellulose, and starch (seed), which can be a potential source of energy (bioethanol) and produce other added-value compounds (Ruiz et al., 2013). Thus, avocado consumption, increase colonic mucin 3 and 4 gene expression as well as the number of goblet cells (mucin-producing cells) (Paturi et al., 2017). Avocado fruit seeds are a potential alternative fiber source. This makes them a candidate for study as part of the current boom in identifying applications for vegetable by-products, such as dietary fiber. Moreover, avocado by-products represent a prospective source of phytochemical compounds with biological properties, may containing more polyphenols than other fruits recognized for their antioxidant activity (Ruiz et al., 2013).

2.1. Avocado Phytochemical Profile

Natural antioxidants, notable polyphenols, have the potential to be used in therapeutic fields because of their numerous benefits, like reducing the risk of inflammatory diseases and preventing lipid oxidation (Haque and Mahadeva, 2012; Segovia et al., 2016). They are also known to have effects against some human neurodegenerative diseases (Ghasemzadeh and Ghasemzadeh, 2011; Kaur et al., 2016; Wang et al., 2016). Flavonoids and phenolics acids are the most prestigious groups of secondary metabolites and bioactive compounds in plants (Ghasemzadeh and Ghasemzadeh, 2011). According to its origin, phenolic acids can be classified as derived from benzoic acid or cinnamic acid (Hurtado-Fernández et al., 2013; Hurtado-Fernández et al., 2014; Hurtado-Fernández et al., 2015).

Due to their structural similarities with several key biological effectors and signal molecules, phenols can participate in the induction/repression of gene expression or activation/deactivation of proteins, enzymes, and transcription factors of critical metabolic pathways (Tsfay et al., 2011). Phenols can also play a role in modulating cellular homeostasis because of their physicochemical properties (Tsfay et al., 2011). Varied biological activities of phenolic acids were reported: increases bile secretion, exhibits hepatoprotective effect, reduces blood lipid levels and shows antiviral, fungicidal and antimicrobial activities and larvicidal effects (Ghasemzadeh and Ghasemzadeh, 2011; Dabas et al., 2013; Barbosa-Martin et al., 2016; Kaur et al., 2016; Yamassaki et al., 2017). Epidemiologic findings revealed that polyphenols have cardioprotective effects, which include inhibition of platelet aggregation and vascular relaxation through the production of nitric oxide (NO), which decreases low-density lipoprotein (LDL) oxidation and prevent atherosclerosis (Haque and Mahadeva, 2012). Phenolic compounds participate in the prevention of DNA adduct formation and enhanced carcinogen elimination. Additionally, phenolic plant compounds are capable of inhibiting inflammation and tumor promotion by deactivating a range of pro-oxidative enzymes (Calderón-Oliver et al., 2016; Rani et al., 2016; Wang et al., 2016).

Avocados contain a moderate level of phenolic compounds contributing 60 mg and 140 mg gallic acid equivalents (GAE) per 30 g and one-half fruit, respectively (Dreher and Davenport, 2013). It has been reported that the antioxidant capacity of fruits and vegetables has been correlated to their total phenolic content and composition (Nour et al., 2013; Calderón-Oliver et al., 2016). The avocado also has a total antioxidant capacity of 600 μmol Trolox Equivalent (TE) per 30 g or 1350 μmol TE per one-half fruit. Also, avocados have the highest fruit lipophilic antioxidant capacity, which may be one factor in helping to reduce serum lipid peroxidation and promoting vascular health (Dreher and Davenport, 2013).

A research performed by Golukcu and Ozdemir (2010) on Bacon, Zutano, Fuerte, and Hass avocado mesocarp part indicated that protocatechuic acid, caffeic acid, (-)-epicatechin, and rutin were the main phenolic compounds. A few other examples of phenolics found were p-hydroxybenzoic, protocatechuic, β -resorcylic, γ -resorcylic, α -resorcylic, gallic, isovanillic, vanillic, syringic, o-coumaric, m-coumaric, p-coumaric, ferulic, and sinapic acids.

The phenolic profiles of six varieties of avocado (Hass, Bacon, Fuerte, Pinkerton, Rincon, and Orotawa) grown in Sicily (Italy) at two different ripening stage (unripe: just harvested; ripe: ready for consumption), were investigated by ultra-high-performance liquid chromatography-heated electrospray-mass spectrometry (Stefano et al., 2017). Nineteen individual phenolic compounds were established in the studied extracts, including gallic acid, sinapinic acid, vanillin, p-coumaric acid, and gentisic acid were presented only in ripe fruits. In contrast, epicatechin decreased with fruit ripening, whereas protocatechuic acid, 4-hydroxybenzoic acid, chlorogenic acid, and benzoic acid were moderately stable with fruit ripening. Caffeic acid, ferulic acid, taxifolin, rutin, trans-cinnamic acid, isorhamnetin were also presented in ripe fruit from the six avocado cultivars, mainly in Hass variety. Poncirin and narirutin were only founded in Pinkerton cultivar. It has also been shown that the different avocado cultivars presented different phenolic total quantities, and it was found that Orotawa may provide the highest nutritional and health contribution to the human diet (Stefano et al.,

2017). Rodríguez-Carpena et al. (2011) determined the total phenolics content, phenolics profile, and antioxidant potential of different extracts (ethyl acetate, acetone, or methanol) from the peel, pulp, and seed of the two most typical avocado varieties (Hass and Fuerte). The authors observed that peels and seeds were rich in catechins, procyanidins, and hydroxycinnamic acids, whereas the pulp was particularly rich in hydroxybenzoic and hydroxycinnamic acids and procyanidins. The total phenolic content and antioxidant potential of avocado phenolics were affected by the extracting solvent and avocado variety.

The avocado processing industry generates significant amounts of waste (peel and seed) that can thus potentially be processed to yield value-added products with promising and significant applications in pharmaceutical industries (Segovia et al., 2016; Dávila et al., 2017).

Avocado seeds and leaves, as aqueous and hydroalcoholic extracts, are utilized in folk medicine because of their anti-viral, anti-inflammatory, anti-diabetic, hypoglycemic, and antioxidant properties - these beneficial biological properties may be related to the presence of polyphenolic compounds (Brai et al., 2014; Calderón-Oliver et al., 2016). Several studies of avocado seed and peel have described the presence of phenolic compounds belonging to five different groups: catechins, hydroxybenzoic acids, hydroxycinnamic acids, flavonols, and procyanidins, with the latter group being the most abundant one (Kosińska et al., 2012).

Some authors have reported the presence of phenolic acids, flavonoids, and procyanidins in avocado leaves (Kumar et al., 2017; Yamassaki et al., 2017; Tremocoldi et al., 2018). From the chemical point of view, avocado seeds contain high levels of phenolic compounds (more than 50%), such as hydroxybenzoic acids, hydroxycinnamic acids, flavanols (such as catechin, epicatechin), flavonols (such as rutin), and procyanidins (Pahua-Ramos et al., 2012; Soldera-Silva et al., 2018). According to Tremocoldi et al., (2018), the main compounds with significant contribution to the antioxidant activity were procyanidin B2 and epicatechin in the peel and trans-5-O-caffeoyl-D-quinic acid, procyanidin B1, catechin, and epicatechin in the seed of avocado varieties Hass and Fuerte.

Hepatoprotective activity of aqueous leaf extract of *P. americana* was demonstrated against carbon tetrachloride induced rat liver damage, and this effect was attributed to its phytochemicals constituent (Brai et al., 2014). Antidiabetic activity of hydroalcoholic extract of the leaves was confirmed (Lima et al., 2012), and antidiarrhoeal activeness was recognized in chloroform-methanol leaf extract of *P. americana* (Christian et al., 2014). Avocado seeds maybe use as a source of polyphenols with promising anthelmintic applications (Soldera-Silva et al., 2018).

Avocado by-products also presented a very distinct phenolic profile, presenting higher concentration in peels (227.9 mg/g of extract for total phenolic content), mainly in (epi)catechin derivatives (175 mg/g of extract), followed by chlorogenic derivatives (42.9 mg/g of extract) (Melgar et al., 2018). The main family of phenolic compounds found in avocado peels and seeds was (epi)catechin derivatives. The second major family of compounds found in avocado peels samples was flavonoids, mainly quercetin derivatives (Barbosa-Martin et al., 2016; Dávila et al., 2017; Saavedra et al., 2017). Moreover, Shehata and Soltan (2013) likewise evaluated the effect of avocado (fruit and seed) on diet-induced hypercholesterolemia in rats. The results showed that avocado seed content was the highest in phenolic compounds (285.43 mg/100 g GAE). The lowering effect of avocado seed on lipid profiles in serum and liver were investigated in high-fat diet rats for six weeks. The results showed that both the fruit and the seed, particularly the later, significantly decreased the serum levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-c).

Vinha et al. (2013) have demonstrated that the pulp of the Algarvian avocado is rich in phenolic compounds (410.2±69.0 mg/100g) and flavonoids (21.9±1.0 mg/100 g). It was concluded in the same studies that the levels of the peel were superior to the pulp with 679.0±117.0 mg/100 g of total phenolics and 44.3±3.1 mg/100 g of flavonoids. The seed, in turn, was the part of the fruit with the highest total phenolic content (704.0±130.0 mg/100 g) and flavonoids (47.97±2.69 mg/100 g). These phenolics and flavonoids are known to prevent the risk of developing

certain diseases related to age, such as premature aging, cancer, and heart disease.

Kumar et al., (2017) evaluated the anti-inflammatory activity and antigenotoxic effect of hydroalcoholic leaf extract of *Persea americana* in albino Wistar rats against the whole body X-ray irradiation. *P. americana* at the optimum dose of 100 mg/kg body weight protected animals from clastogenic effects caused by X-rays and displayed anti-inflammatory properties. This protection was attributed to free radical scavenging activity of *P. americana* by maintaining cytoplasm antioxidant levels in cells, subsequently decreasing oxidative stress and inhibiting DNA damage, where flavonoids and polyphenolic compounds played a lead role in neutralizing the free radicals formed during irradiation.

Figuroa et al., (2018) determined the phenolic profile and other polar compounds of avocado seed and seed coat using accelerated solvent extraction (ASE) and liquid chromatography coupled to Ultra-High-Definition Accurate-Mass Q-TOF. In this work, 84 compounds were classified within eight subclass groups; among these, 45 phenolic compounds were identified for first time in the avocado seed. Condensed tannins, phenolic acids, and flavonoids were the most representative groups in both samples. Respect to phenolic acids, different sub-classes of these compounds has been characterized in both sample matrix, mainly hydroxybenzoic acids, hydroxyphenyl acetic acids, and hydroxycinnamic acids. The same authors (2018b) identified the phenolic compounds present in an extract of avocado peel obtained by a green extraction technique. Accelerated solvent extraction was performed using water and ethanol as extraction solvents. Liquid chromatography, coupled to ultra-high-definition accurate-mass spectrometry, was used in order to identify the bioactive compounds. A total of sixty-one compounds belonging to eleven families were identified. Procyanidins, flavonols, hydroxybenzoic and hydroxycinnamic acids were the most common compounds.

Besides polar phytochemicals, avocado also contains other bioactive compounds, nonpolar ones. The principal carotenoids of avocado belong to a subclass identified as xanthophylls, which are oxygen-containing fat-soluble antioxidants. Xanthophylls, such as lutein, β -cryptoxanthin,

antheraxanthin, neoxanthin, violaxanthin, and zeaxanthin, are more hydrophilic than carotenes (which includes β -carotene and α -carotene), so they have a much lower tendency for pro-oxidant activity (Ortiz-Avila et al., 2013; Duarte et al., 2016).

Because carotenoids are hydrophobic, their absorption depends upon efficient release from the food matrix and subsequent solubilization by bile acids and digestive enzymes, culminating in their incorporation into micelles (Kopeck and Failla, 2018). Avocado fruit has a unique unsaturated oil and water matrix naturally designed to enhance carotenoid absorption. Some studies have demonstrated that adding avocado fruit can significantly enhance (by 2-5 times) carotenoid absorption from salad and salsa, which is attributed mostly to the lipids present in avocado. In this manner, adding avocado fruit to carotenoid-containing foods can facilitate carotenoid absorption, and consequently aids to its lipid-decreasing function (Fulgoni et al., 2013). Lutein and zeaxanthin are selectively taken up into the macula of the eye, decreasing age-related eye dysfunction. Avocado fruits comprise 185 μg of lutein/zeaxanthin per one-half fruit, which is expected to be more highly bioavailable than most other fruit and vegetable sources (Dreher and Davenport, 2013). An *in vitro* study performed by Lu et al. (2009) showed that the avocado pulp, specifically lutein, and other carotenoids (as active compounds), possess growth inhibitory effects against cancer. The authors observed that the color of avocado pulp varies from dark green just under the skin to pale green in the middle section of the flesh to yellow near the seed. The total carotenoid concentrations were found to be greatest in the dark green pulp close to peel. It was also possible to conclude that in Hass avocados, xanthophylls prevail over the carotenes, contributing about 90% of the total carotenoids. Carotenoids, including lutein (2.93 $\mu\text{g g}^{-1}$), zeaxanthin (0.11 $\mu\text{g g}^{-1}$), β -cryptoxanthin (0.25 $\mu\text{g g}^{-1}$), β -carotene (0.60 $\mu\text{g g}^{-1}$), and α -carotene (0.25 $\mu\text{g g}^{-1}$), were reported in the pulp of ripened Hass - the actual level of carotenoids in avocado was higher than the reported data because an average recovery from extraction, saponification and HPLC was 77%. Subsequently, the following carotenoids were identified: all-trans neoxanthin, all-trans violaxanthin, all-trans neochrome, 9'-cis-neoxanthin, lutein-5, six epoxide,

and chrysanthemaxanthin. Vinha et al., (2013) also reported a total content of carotenoids in avocado pulp significantly inferior to in fruit peel (0.815 ± 0.201 mg/100 g and 2.585 ± 0.117 mg/100 g, respectively). Condelli et al. (2015) reported the carotenoid content of 10.3-14.4 mg kg⁻¹, while Krumreich et al., (2018) obtained a carotenoid content of 4.63 mg kg⁻¹ using avocados of Breda variety.

Avocados are the richest known fruit source of phytosterols with about 26 mg and 57 mg per 30 g and one-half fruit, respectively (Dreher and Davenport, 2013). Some authors suggest that increased consumption of foods containing plant sterols has the potential to reduce the incidence of coronary heart disease and thus reduce costs associated with treating that disease in a significant way (Gyles et al., 2010; Kumar et al., 2017). Avocado contains substantial amounts of bioactive compounds such as phytosterols, especially in the lipid fraction, and the main representative is β -sitosterol (Ulbricht, 2016). Santos et al. (2014) investigated the influence of different procedures of pulp drying and oil extraction methods on the concentrations of several phytosterols in avocado oil. Pulp portions of Fortune variety avocados were dried either by lyophilization or under circulating air at 40 or 70°C, and the oil was obtained either by cold pressing or with Soxhlet extraction using petroleum ether. The concentration range found in this study was: β -sitosterol (86.6 - 91.2%), higher than campesterol (9.7 - 13.3%), higher than stigmaterol (0.04 - 0.06%). The highest yield (57%) was found for Soxhlet extraction after lyophilization.

The health effects of sterols and stanols have been the subject of several studies. The meta-analysis performed by Ras et al. (2013) reported that intake of 0.3-3.2 g of plant sterols reduces by 8.5% LDL-cholesterol, which is a well-known cardiovascular risk factor. The β -sitosterol in avocados has a unique effect on immunity, contributing to the treatment of diseases such as cancer, human immunodeficiency virus (HIV), and infections (Haque and Mahadeva, 2012; Dreher and Davenport, 2013). Studies have also shown that β -sitosterol activity is an aid in weight loss by reducing compulsive eating binge and fat accumulation in the abdominal region (Uchenna et al., 2017).

Furthermore, the daily consumption of phytosterols and phytostanols decreases the plasmatic levels of cholesterol, leading to the prevention of cardiovascular diseases and cancer progress (Tabeshpour et al., 2017).

An *in vitro* study showed that the avocado pulp, rich in tocopherols, lutein, and other carotenoids (as active constituents), possess growth inhibitory effects against cancer (Lu et al., 2009).

3. BIOLOGICAL PROPERTIES

There is already evidence that the ingestion of fruits confers protection against human chronic diseases, neurological disorders, and some types of cancer (Larijani et al., 2014; Reczek and Chandel, 2018). These properties are assigned to the presence of bioactive compounds in fruits (edible and not edible portion) (Krumreich et al., 2018). During the last decades, ample evidence of the benefits of avocado on health has been gathered. This promoted their consumption, also stimulating the research about their pharmacological potential. Moreover, avocado waste has gained more interest, not only because it is a cheap raw material, as well as its richness in biological compounds (Krumreich et al., 2018). Table 1 describes some of the biological properties described in the pulp and by-products of avocado fruit.

3.1. Cardiovascular Benefits

One of the essential mechanisms for the development of atherosclerosis is the oxidation of cholesterol-rich plasma lipoproteins. Oxidation of lipids increases their atherogenicity, facilitating their penetration into the arterial wall (Tiwari, 2004). The oxidation of lipoproteins is mainly due to the lipid peroxidation reaction initiated by free radicals (Tiwari, 2004). The main risks for the appearance of atherosclerosis are high levels of total cholesterol, low-density lipoproteins (LDL), triglycerides, and apolipoproteins B and C-III, as well as low levels

of high-density lipoproteins (HDL) cholesterol and apolipoproteins A-I (Tiwari, 2004). According to a study performed by Pérez-Méndez and Hernández (2007), after four weeks of a diet rich in avocado, there was a significant reduction in triglycerides, with the maintenance of low blood lipid levels and glycemic index control. Since avocado is characterized by its high content of unsaturated fatty acids, the ingestion of this fruit brings benefits in maintaining the health of the heart and the circulatory system, since the replacement of saturated fats with unsaturated fats promotes the reduction of triglyceride levels, cholesterol, and LDL-cholesterol, and may even increase the HDL-cholesterol fraction, it is therefore recommended to introduce the fruit into the diet of people with cardiovascular disorders or diabetes (Tango et al., 2004). Pahua-Ramos et al., (2012) established that avocado seed flour reduced cholesterol in a model of hypercholesterolemic mice, being this effect attributed to the phenolic content, antioxidant activity, and the dietary and crude fiber contents of the seeds. A study performed by Márquez-Ramírez et al., (2018) in hypertensive rats have proved that avocado oil mimics the effects of losartan, an angiotensin-II antagonist, decreasing blood pressure, enhancing renal vasodilation, and counteracting mitochondrial dysfunction and excessive reactive oxygen species production.

Since avocado is a nutrient-dense source of monounsaturated fatty acids, it can be used to replace saturated fatty acids in a diet to lower low-density lipoprotein cholesterol. There are several studies about the effect of avocado consumption on cardiovascular disease risk factors. As avocado is associated with cardiovascular benefits, Mahmassani et al., (2018) studied the effect of the consumption of this fruit on cardiovascular disease risk with the use of a systematic review and meta-analysis. These authors conclude that although avocado intake resulted in no difference in serum total cholesterol, LDL-cholesterol, and triglycerides concentrations, it increased serum HDL-cholesterol concentrations.

Table 1. The most important bioactive compounds of avocado

Categories	Bioactive constituents	Biological activities	Avocado layer	References
Fatty Acids	oleic, palmitic, linoleic, stearic and palmitoleic acids; *aceto-genins, (persenone-C and persediene)	decrease blood pressure, enhance renal vasodilation, and counteract mitochondrial dysfunction and excessive ROS production; prevent factor of metabolic syndrome; decrease high sensitivity C-reactive protein levels; *reduce inflammatory processes	pulp/ oil	Mquez-Ramirez et al. (2018) Dvila et al. (2017) Forero-Doria et al. (2017) Tabeshpouret al. (2017) Corzzini et al. (2016) Duarte et al. (2016) Rodrguez-Snchez et al., (2015) Bill et al. (2014) Carvajal-Zarabale et al., (2014) Santos et al. (2014) Contreras-Gutirrez et al., (2013) Rodrguez-Snchez et al., (2013) Lu et al. (2009) Tango et al. (2004)
Phytosterols	β -sitosterol	contribute to the treatment of diseases such as cancer, HIV and infections; reduce compulsive eating binge and fat accumulation in the abdominal region; decrease plasmatic levels of cholesterol, prevent cardiovascular diseases and reduce the incidence of coronary heart disease; prevent cancer progress; potential neuroprotective effect	pulp/seed	Kumar et al. (2017) Tabeshpouret al. (2017) Uchemma et al. (2017) Ulbricht (2016) Padmanabhan and Arumugam (2015) Dreher and Davenport (2013) Haque and Mahadeva (2012) Gyleset al. (2010)
Other lipids	avocatin B (avocadene and avocadyne)	cytotoxic activity in acute myeloid leukemia; inhibit fatty acid oxidation; decrease NADPH levels	pulp/seed	Ahmed et al. (2018) Araujo et al. (2018) Lee et al. (2015)
Vitamins	tocopherols	growth inhibitory effects against cancer	pulp	Thongchai (2014) Lu et al. (2009)
Carbohydrates	D-mannoheptulose and its reduced form (perseitol)	blood glucose control and weight management	pulp	Roth (2009) Meyer and Terry (2008)

Table 1. (Continued)

Categories	Bioactive constituents	Biological activities	Avocado layer	References
Carotenoids	Xanthophylls (lutein, zeaxanthin, β -cryptoxanthin), carotenes (β -carotene and α -carotene)	inhibitory effects against cancer	pulp	Dreher and Davenport (2013) Lu et al. (2009)
Polyphenolic compounds	protocatechuic, caffeic, <i>p</i> -hydroxybenzoic, hydroxycinnamic, protocatechuic, β -resorcylic, γ -resorcylic, α -resorcylic, gallic, isovanillic, vanillic, syringic, o-coumaric, m-coumaric, <i>p</i> -coumaric, ferulic, and sinapic acids, epicatechin and rutin procyanidins, hydroxybenzoic and hydroxycinnamic acids, flavonoids: flavonols (rutin), flavanols (catechin, epicatechin), (epi)catechin derivatives, chlorogenic derivatives, and quercetin derivatives	decrease serum levels of total cholesterol, triglycerides, and LDL; prevent the risk of developing certain diseases related to age, such as premature aging, cancer, and heart disease; potential neuroprotective effect anti-viral, anti-inflammatory, anti-diabetic, hypoglycemic, and antioxidant activities; decrease serum levels of total cholesterol, triglycerides, and LDL; anthelmintic applications; antigenotoxic effect against X-ray irradiation	pulp Avocado by-products (peel/seed/leaves)	Padmanabhan and Arumugam (2015) Shehata and Soltau (2013) Vinha et al. (2013) Rodríguez-Carpena et al.,(2011) Golukcu and Ozdemir (2010) Melgar et al. (2018) Soldera-Silva et al. (2018) Tremocoldiet al. (2018) Dávila et al. (2017) Kumar et al. (2017) Saavedra et al. (2017) Yamassaki et al. (2017) Barbosa-Martin et al. (2016) Calderón-Oliver et al., (2016) Brai et al. (2014) Shehata and Soltau (2013) Kosińska et al. (2012) Pahua-Ramos et al. (2012) Rodríguez-Carpena et al.,(2011) Castillo-Juarez et al., (2009) Flagg et al. (1994)
Peptides	glutathione	Reduction of the risk of the development of larynx, pharynx and oral cavity cancers		

The objective of the study of Carvajal-Zarrabal et al. (2014) was to evaluate the effects of avocado oil administration on biochemical markers of cardiovascular risk profile in rats with metabolic changes induced by sucrose ingestion. This study proved that avocado oil is a potential preventive factor of metabolic syndrome since it reduces triglycerides (TG), very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) levels, without affecting high-density lipoproteins (HDL) values. Avocado oil, extracted by centrifugation or solvent, decreased high sensitivity C-reactive protein levels, indicating that inflammatory processes were partially reversed, suggesting that the supplementation with this oil has a positive health outcome since it reduces inflammatory processes and produces positive changes in the biochemical indicators related to the development of the metabolic syndrome. Metabolic syndrome is an aggregation of risk factors like dyslipidemia, hypertension, high blood glucose, and obesity that result in an increased risk of type 2 diabetes mellitus and cardiovascular diseases, which are among leading causes of death in the world (Tabeshpour et al., 2017). Another meta-analysis with healthy adults with an average body mass index performed by Peou et al., (2016) obtained similar results: avocado consumption significantly reduced total cholesterol, LDL, and TG, decreasing HDL nonsignificantly. The aim of the work developed by Furlan et al., (2017) was to evaluate the impact of exchanging butter by Hass avocado-oil on postprandial metabolic parameters in healthy overweight volunteers consuming a hypercaloric-hyperlipidemic breakfast. This study proves that the replacement of butter by Hass avocado-oil reduced postprandial inflammation and postprandial glycemia. The results of these authors also contributed to consider Hass avocado-oil a potential atherosclerosis-protective fat.

Inclusion of one avocado per day as part of a moderate-fat and cholesterol-lowering diet of a healthy overweight adult with LDL cholesterol 105 - 194 mg/dL for males and 98 - 190 mg/dL for females and normal or well-controlled blood pressure has additional LDL and non-HDL lowering effects (Wang et al., 2015), in agreement with the results obtained by Carvajal-Zarrabal et al., (2014). As the results of other studies, this demonstrates that avocados have beneficial effects on

cardio-metabolic risk factors that extend beyond their heart-healthy fatty acid profile. So, substitute dietary fats, especially saturated ones, by avocados should be one of the health recommendations. Previous studies suggest that the daily consumption of phytosterols and phytosteranols, important bioactive phytochemicals of avocado, decreases the serum levels of cholesterol, leading to the prevention of cardiovascular disease and also possible protection in the number of cancer development (Awad and Fink, 2000; Pironen et al., 2000; Kritchevsky and Chen, 2005).

Avocado fruit is a rich source of health-related lipophilic phytochemicals such as monounsaturated fatty acids, tocopherols, carotenes, acetogenins, and sterols. Lipophilic antioxidant capacity of avocado pulp is higher than hydrophilic capacity (Rodríguez-Sánchez et al., 2013). Acetogenins, namely Persenone-C and Persediene, were identified as a novel lipophilic antioxidant present in the avocado pulp. In the presence of emulsifiers, acetogenins may serve as lipophilic food antioxidants (Rodríguez-Sánchez et al., 2013). In effect, the avocado pulp is a good source of fatty acids related to platelet aggregability reduction, preventing thrombus formation responsibly for ischaemic diseases. Rodríguez-Sánchez et al. (2015) identified Persenone-C as the most potent antiplatelet acetogenin *in vitro*. *In vivo*, Persenone A demonstrated potential protection against arterial thrombosis, as coagulation times increased, and thrombus formation was attenuated. Besides the fruit and avocado oil, its by-products also have important cardiovascular properties. Although the seed represents a considerable percentage of the total fruit, currently, it still represents an under-utilized resource and a waste issue. Avocado seeds may improve hypercholesterolemia and be useful in the treatment of hypertension, inflammatory conditions, and diabetes (Dabas et al., 2013).

3.2. Anticancer Activity

Extensive research over the last decades indicates that excessive accumulation of reactive oxygen species (ROS) can promote cancer.

Cancer cells produce increased numbers of ROS and depend on an antioxidant defense system. Besides, ROS promotes cancer cell survival. Reactive oxygen species are produced as an intracellular byproduct by mitochondria and other cellular elements and exogenously by pollutants, tobacco, smoke, drugs, xenobiotics, and radiation (Prasad et al., 2017; Reczek and Chandel, 2018). It is believed that ROS are related to the genesis of tumors at different levels, and can promote the development of cancer through different mechanisms: alterations in cellular proliferation; the decreased affinity of the polymerase enzyme; inactivation of enzymes responsible for the degradation of carcinogens; binding of end products of lipid peroxidation to the DNA molecule, creating mutagenic lesions; direct DNA attack (Min and Ebeler, 2008).

Several studies showed that phytochemicals extracted from the avocado fruit selectively induce cell cycle arrest, inhibit growth, and induce apoptosis in precancerous and cancer cell lines. Rajkumar et al. (2011) reported that some phytochemicals extracted with 50% methanol from avocado fruits help in the proliferation of human lymphocyte cells and decrease chromosomal aberrations induced by cyclophosphamide. The authors suggested that phytochemicals from the avocado fruit can be utilized for making active chemoprotective ingredients for lowering the side effect of chemotherapy in cancer therapy. The phytochemicals present in the avocado extract also inhibits the growth of oral cancer and pre-cancer cells and induces apoptosis, without affecting the healthy cells (D'Ambrosio et al., 2011).

A diet rich in antioxidants, such as carotenoids (Nagarajan et al., 2017; Eggersdorfer and Wyss, 2018) and phenolic compounds (Zhang et al., 2018; Jimenez-Garcia et al., 2018), may prevent carcinogenesis and studies are describing the beneficial effect of consumption of fruits source of these compounds in reducing the risk of various types of cancer. Studies conducted *in vitro* and *in vivo* indicate that avocado should be included in the diet for its cancer-preventive benefits. This fruit contains a large number of phytochemical compounds, among which, carotenoids, terpenoids, D-mannoheptulose, phenols, and glutathione, described as compounds with anticancer properties (Ding et al., 2009). Another *in vitro*

study showed that tocopherols, lutein, and other carotenoids, existing in the avocado pulp, possess growth inhibitory effects against cancer (Lu et al., 2009). Regular consumption of phytosterols and phytostanols, bioactive compounds of avocado, has a potential protective effect in cancer development (Awad and Fink, 2000; Piironen et al., 2000; Kritchevsky and Chen, 2005).

The effectiveness of avocado phytochemicals in cancer treatment has been investigated only on prostate, breast, oral, esophageal, and colon cancers (Larijani et al., 2014). Avocado contains soluble lipid components such as tocopherols and carotenoids with anti-cancer activities, and it can significantly reduce the risk of androgen-dependent and -independent prostate cancer.

Bonilla-Porras and coworkers (2014) demonstrated that endocarp, seed, whole seed, and leaf (0.1mg/mL) extracts from avocado *P. americana* var. Hass induces apoptosis in Jurkat lymphoblastic leukemia cells, which are eliminated through an oxidative stress mechanism.

The levels of glutathione, potent antioxidant tripeptide, are found in higher concentrations in avocado when compared to matrices of other fruits (Flagg et al., 1994), and there is scientific evidence that an increase in the consumption of glutathione promotes the reduction of the risk of the development of larynx, pharynx and oral cavity cancers (Castillo-Juarez et al., 2009). A study performed by D'Ambrosio et al. (2011) identified and isolated from avocado mesocarp two aliphatic acetogenins. The chloroform extract of these two bioactive soluble compounds inhibited the growth of human oral cancer.

One novel alkene lactone was isolated from *Persea americana* Mill root bark and characterized (Falodun et al., 2013). The compound was subjected to anticancer activity using breast cancer cell line MCF-7 and the non-tumorigenic mammary epithelial cell line MCF-12 as a control for healthy tissue. At a concentration of 10 µg/mL, a significant reduction of proliferation of MCF-7 was induced while MCF-12 A cell was significantly stimulated by ten µg/mL. This opposite effect on both cell lines offers new possibilities in anticancer treatment because it would be excellent to have a drug that causes a reduction in the growth of cancer

cells as well as stimulates the proliferation of healthy cells at the same time (Falodun et al., 2013). Mbaveng et al. (2018) also demonstrated the cytotoxic potential of *Persea americana* bark, which can be purified in order to isolate potential cytotoxic phytochemicals. *P. americana* has acceptable anti-proliferative activities in a panel of human cancer cell lines, and methanolic extracts could also be used to combat multi-drug-resistant cancer cell lines.

Antimicrobial peptides, responsible for the plants' defensins, show selective cytotoxicity toward cancer cells. Nevertheless, their mechanisms of action are not entirely understood. Guzmán-Rodríguez (2016) assessed the cytotoxicity of the antimicrobial peptides from avocado (*Persea americana* var. *drymifolia*) on the MCF-7 cancer cell line (a breast cancer cell line). This study was the first that suggested that avocado defensins are cytotoxic to cancer cells, namely to MCF-7 cells via the induction of mitochondrial apoptosis, which suggests that this defensin could be a potential molecule in the treatment of cancer. Flores-Alvarez et al., (2018) also studied the cytotoxicity defensin from avocado (PaDef) on cancer cells, in this case, K562 chronic myeloid leukemia cells. They have concluded that PaDef induces apoptosis on K562 cells, without affecting the mitochondrial membrane potential, neither the transmembranal potential nor the release of intracellular calcium. This process is related to the activation of caspase eight and involves the participation of TNF- α , which is a novel property for a plant defensin. These studies sustain that these avocado antimicrobial peptides are an attractive alternative to combat cancer cells.

A mixture of avocadene and avocadyne, two 17-carbon polyhydroxylated fatty alcohols present in seed and pulp of the avocado, designated by avocatin B, demonstrated to possess potent anticancer activity by selectively targeting and eliminating leukemia stem cells (Lee et al., 2015). Avocatin B has cytotoxic activity in human primary acute myeloid leukemia without affecting normal peripheral blood stem cells. Mechanistic investigations indicated that cytotoxicity relied on mitochondrial localization, as cells lacking functional mitochondria or carnitine palmitoyltransferase I, the enzyme that facilitates mitochondria

lipid transport, were insensitive to avocatin B (Ahmed et al., 2018). Besides, avocatin B inhibited fatty acid oxidation and decreased NADPH levels, resulting in ROS-dependent leukemia cell death characterized by the release of mitochondrial proteins, apoptosis-inducing factor, and cytochrome c (Lee et al., 2015; Ahmed et al., 2018).

Beta-sitosterol (β -SITO), a phytosterol present in avocado, has been considered a potent anti-cancer agent that interferes with microtubule assembly dynamics by binding to a novel site on tubulin (Mahaddalkar et al., 2015). β -SITO is orally bioavailable and is considered to have no undesired side effects (Mahaddalkar et al., 2015). Extracts of avocado seeds also showed anticancer activity: methanol extracts have evidenced induction of apoptosis of MDA-MB-231 cells (Abubakar et al., 2017) and triterpenoid compounds isolated from ethanol extract have significant cytotoxic activity against breast and liver cells MCF-7 and HepG2, respectively (Ambrosio et al., 2011).

3.3. Antimicrobial Activity

The scientific community already knows the antifungal properties of avocado for about some decades. Avocado toxicity is due to compounds like diene (*Z, Z*)-2-hydroxy-4-oxohenicosa-12,15-dien-1-yl acetate (persin), that exist both in young and mature leaves (Carman and Handley, 1999) or 1,2,4-trihydroxyheptadec-16-yne, 1,2,4-trihydroxyheptadec-16-ene and 1-acetoxy-2,4-dihydroxyheptadec-16-yne isolated from the peel of immature fruit (Adikaram et al., 1992). Leite et al. (2009) tested the toxicity of extracts of avocado seeds against *Artemia salina*, evaluating their larvicidal activity related to their higher larvicidal activity towards *Aedes aegypti*, in the hexane extract, with the higher concentration of β -sitosterol and 1,2,4-trihydroxy-nonadecane. This group also showed antifungal activity of avocado seed extracts against *Candida* spp, *Cryptococcus neoformans*, and *Malassezia pachydermatis*, yeasts of great importance for human and veterinary medicine. On the other hand, flavonoids are known to be synthesized by plants in response to microbial

infections exhibiting these compounds' antimicrobial activities (Melgar et al., 2017; Sansano et al., 2017). Melgar et al., (2018) studied the antibacterial and antifungal activity of *P. americana* by-products (peel and seed) against the following strains: *Staphylococcus aureus*, *Bacillus cereus*, *Micrococcus flavus* and *Listeria mono-cytogenes* (Gram-positive bacteria); *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium* and *Enterobacter cloacae* (Gram-negative bacteria); *Aspergillus fumigatus*, *Aspergillus ochraceus*, *Aspergillus versicolor*, *Aspergillus niger*, *Penicillium funiculosum*, *Penicillium ochrochloron*, *Penicillium verrucosum* var. *cyclopium* and *Trichoderma viride* (microfungi used for antifungal assays). *P. americana* by-products have revealed high anti-bacterial activity against all the gram-positive and gram-negative bacteria studied, displaying the extracts from seeds worst activity only against *E. cloacae* strain. Relativity to antifungal activity, these by-products extracts show moderate activity against the strains studied. The better fungicidal effect was against *Trichoderma viride*. Boadi et al. (2015) also studied the antimicrobial activities of methanol, ethyl acetate, chloroform, and petroleum ether leave extracts of *P. americana*. All the extracts were potent against the test microorganisms (*Bacillus subtilis*, *Escherichia coli*, *Salmonella typhi*, *Streptococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*), displaying the methanolic extract the most potent antimicrobial activities with the lowest minimum inhibitory concentration. This difference may be related to different degrees of solubility of the solvents for different phytoconstituents.

Avocado has also shown antibacterial activity against *Helicobacter pylori*, which potentiates gastric ulcers associated with the risk of gastric cancer (Liu et al., 2018). Methanol extract from avocado showed anti-*H. Pylori* activity at the lowest minimum inhibitory concentration among 53 Mexican traditional medicinal plants tested *in vitro* (Castillo-Juárez et al., 2009).

Rodríguez-Carpena et al. (2011) have studied antimicrobial properties of Hass and Fuerte varieties of avocado. The antimicrobial study with avocado pulp and by-products extracts from the two studied varieties show that Gram-positive bacteria were generally more sensitive than Gram-

negative, being Gram-positive *B. cereus* and *L. monocytogenes* the most sensitive. Among tested Gram-negative, bacteria *E. coli* was the most sensitive. This antimicrobial potential of agricultural by-products could be a preliminary response for the substitution of antibiotics in animal-production farms. In past years there is an increasing trend in the use of antibiotics and other growth promoters in farm animals in tropical areas. Fortunately, as a substitute to antibiotics, these countries have considerable antimicrobial potential in plants by-products, source of a diverse pool of bioactive compounds with antimicrobial properties, which could be employed as feed supplements to improve animal health. Among others, high activity has been detected for avocado seeds (Guil-Guerrero et al., 2016).

3.4. Bodyweight Reduction

Avocado has various health benefits, including bodyweight reduction. Padmanabhan and Ar-umugam (2015) developed a study that proved that a hydro-alcoholic extract of avocado reduced mass index, adiposity index, total fat-pad mass, blood cholesterol, triglycerides, and LDL in rats fed with a high-fat diet. Their results also show that avocado extract has a profound influence on leptin activity, which controls satiety and hunger to regulate food intake. The same authors, in a previous study, investigated the effect of a hydro-alcoholic fruit extract of *P. americana* on the level of blood lipids, glutathione, lipid peroxidation products, adiponectin and peroxisome proliferator-activated receptor (PPAR)- γ expressions in rats fed a high-fat diet. Their results showed that body mass index, total fat pad mass, and adiposity index were significantly decreased in rats that have received the extract. This suggests that hydro-alcoholic avocado extract exhibits hypolipidemic activity probably by increasing the mRNA expression of adiponectin and PPAR- γ , which reduces the risk of hyperlipidemia and obesity (Padmanabhan and Arumugam, 2014).

Othman et al. (2018) replaced butter by avocado purée and studied the influence of this change on nutritional, fatty acid, and organoleptic properties of low-fat muffins. They have prepared muffins with 25%, 50%, 75%, and 100% avocado purée and a control muffin, which was made with 100% butter. Muffins incorporated with avocado purée revealed a significant increase with respect carbohydrates; however, no significant changes were detected in all muffin formulations for protein and dietary fiber content, in comparison with the control sample. Fat content and caloric value of muffins incorporated with avocado purée were significantly decreased, showing an increment in the monounsaturated fatty acids content. Muffins were acceptable when up to 50% butter substitution, but a higher percentage led to undesirable flavor and aftertaste.

The potential use of avocado pulp as a fiber source has also been investigated in rats (Naveh et al., 2002). The total dietary fiber content of fresh avocado fruit of the Ettinger variety was 5.2 g/100 g. Food consumption and body weight gain were lower in rats fed avocado pulp compared with that fed cellulose. These data suggest that avocado pulp interferes with hepatic metabolism and causes an appetite depressant (Naveh et al., 2002).

In addition to dietary fiber, avocados contain monounsaturated fatty acids, essential nutrients, and phytochemicals. Based on this, a study was conducted with US adults of both genders, between 2001 and 2008, to investigate the relationships between avocado consumption and overall diet quality, energy and nutrient intakes, physiological indicators of health, and risk of metabolic syndrome. The results of this study proved that avocado consumers improved overall diet quality with significantly higher intakes of vegetables, fruit, total fat, monounsaturated and polyunsaturated fats, dietary fiber, vitamins E and K, magnesium, potassium; and lower intakes of added sugars. Bodyweight decreased significantly, and HDL increased, being the odds ratio for metabolic syndrome 50% lower in avocado consumers vs. non-consumers (Fulgoni et al., 2013).

3.5. Potential Neuroprotective Effect

Avocado fruit hydro-alcoholic extract contains flavonoids (rutin, quercetin, luteolin), phenolic compounds (gallic acid, ellagic acid, vanillic acid), and phytosterols (beta-sitosterol, stigmasterol) (Padmanabhan and Arumugam, 2015). This high content of phytochemicals, especially antioxidants, has a potential neuroprotective effect. Antioxidant compounds present in avocado are unique in the suppressing of radical generation, and thus may be promising as effective neuropreventive agents, preventing and curing various neurodegenerative diseases related with oxidative stress, such as Alzheimer's, Parkinson's and Huntington's diseases and amyotrophic lateral sclerosis (Ameer, 2016).

Avocado leaves and seeds are used in traditional medicine for the treatment and management of Alzheimer's disease, but information about the mechanism of actions is limited. Oboh et al., (2016) investigated the effect of these leaves and seeds aqueous extracts on the activity of the enzymes linked with Alzheimer's disease (acetylcholinesterase and butyrylcholinesterase) and their antioxidant potential *in vitro*. The extracts inhibited both enzymes activity, having the seed extract the highest inhibitory effect. Leaf extract has exhibited higher phenolic content and radical scavenging abilities, but lower Fe chelation ability compared with that of the seed. The phytochemical analysis revealed the presence of saponins and terpenoids in both extracts, and total alkaloid profile higher in the seed than in the leaf extract. These results propose that anticholinesterase and antioxidant activities of avocado leaf and seed could be related to their phytoconstituents.

Eser et al. (2011) studied the protective effects of avocado-soybean unsaponifiable (ASU) on the prefrontal cortex after global brain ischemia/reperfusion injury in rats. In the ischemia, rats that have received ASU malondialdehyde and tumor necrosis factor-alpha (TNF α) levels, as well as the number of apoptotic neurons, have decreased, and superoxide dismutase activities have increased significantly. These results suggest that ASU might have antioxidant and neuroprotective effects.

3.6. Osteoarthritis

Osteoarthritis is a disease characterized by progressive deterioration of cartilage and joint function associated with premature aging, especially in overweight or obese people (body mass index ≥ 30). This deterioration can be triggered by oxidative and inflammatory stress, which, in turn, can cause an imbalance between biosynthesis and degradation of the extracellular matrix of the joints, leading to loss of function (Dinubile, 2010).

The standard pharmacologic treatment includes agents for control of pain and inflammation (non-steroidal anti-inflammatory drugs, analgesics including opioids, intraarticular corticosteroids) and the group of the symptomatic slow-acting drugs for osteoarthritis such as glucosamine sulfate, chondroitin sulfate, diacerein, an unsaponifiable extract of soybean and avocado administered orally and intraarticular hyaluronic acid (Hermann et al., 2017).

One study reported that fruits rich in lutein and zeaxanthin are associated with decreased risk of cartilage defects (Wang et al., 2007). Also, the presence of unsaponifiable compounds in avocado and soybeans exert synergistic effects, promoting antioxidant activity against inflammatory processes (Dinubile, 2010).

Catunda et al. (2016) investigated the effectiveness of an avocado-soybean unsaponifiable extract in patients with arthralgia and osteoarthritis of the temporomandibular joint. A randomized, double-blind, placebo-controlled trial was carried out with fourteen women diagnosed with the referred diseases. The women were divided into two groups: ASU group and the placebo group. The group who received the ASU extract had a decrease in pain symptoms and an improvement in the quality of life. Furthermore, a significant decrease in the use of rescue medication was found in the ASU group compared to the placebo group. Another study in real-life situations was performed in Poland. Głuszko and Stasiak (2016) assessed the effects of oral ASU capsules on pain relief and functional ability in patients while they were receiving a routine treatment for knee osteoarthritis. The majority of patients adherent to the ASU treatment

showed gradual alleviation of joint pain, improvement in functional ability, and a significant reduction in non-steroidal anti-inflammatory drug intake.

A study performed by Al-Afify et al., (2018) proved that oral administration of avocado-soybean unsaponifiables ameliorated the histopathological changes of the knee caused by induced osteoarthritis. Avocado-soybean unsaponifiables improved the ultrastructural changes and reduced oxidative stress and inflammation in the articular cartilage and subchondral bone of articular cartilages of rats with induced osteoarthritis.

Another study determined whether the addition of avocado-soybean unsaponifiable (Arthrocen) to the drinking water of osteoarthritis rats reduced direct joint pain. Osteoarthritis was induced in rats by intra-articular injection of sodium monoiodoacetate. The joint damage induced by injection was severe and consistent with end-stage osteoarthritis. Arthrocen consumption attenuated joint edema, inflammation, and pain (Goudarzi et al., 2018).

A previous study investigated *in vivo* the effects of the treatment with avocado-soybean unsaponifiables on the development of osteoarthritic on dogs. In animals treated with the ASU, the size of macroscopic lesions on the tibial plateaus decreased, as well as the severity of cartilage lesions on both tibial plateaus and femoral condyles and the cellular infiltration in the synovium. Treatment with avocado-soybean unsaponifiables also reduced loss of subchondral bone volume and calcified cartilage thickness compared with placebo. Immunohistochemical analysis of cartilage revealed that ASU significantly reduced the level of inducible nitric oxide synthase and matrix metalloproteinase 13 in cartilage (Boileau et al., 2009).

4. AVOCADO IN DERMOCOSMETIC

Plant extracts and oils have been utilized for a variety of purposes throughout history and are commonly used in cosmetics and topical pharmaceuticals products. In the last decades, there has been a growing trend towards the use of these extracts by the cosmetic industry. Among

the reasons mentioned for this phenomenon are the decline of credibility in synthetic products and the preference for vegetal derivatives. Plant oils are nowadays recognized for their effects on both skin diseases and the restoration of cutaneous homeostasis. These oils also act as a protective barrier, allowing the skin to preserve moisture, with a decrease of transepidermal water loss. Furthermore, topical products have the benefit of higher bioavailability in the skin and having a localized effect rather than systemic effects (Kole et al., 2005; Lin et al., 2018).

Lipids are widely used by dermo-cosmetic, taking various roles, namely, bioactive agents, vehicles for the preparation of different formulations, nutritional supplements, and cosmetics, among others. Avocado oil has excellent applicability due to its emollient power and easy penetration into the skin, being absorbed more quickly than soy, corn, or almond (Athar and Nasir, 2005). Also, fatty acids increase the permeability of active substances in the skin and induce the diffusion properties of liposoluble preparations. Thus, the lipophilic extract of avocado may be a carrier of active substances in the formulation of creams, ointments, and other products for dermatological use (Stücker et al., 2001). The effect of *Persea americana* natural extracts on the subsequent dermal absorption and penetration of other cosmetics was evaluated by Muhammad et al., (2017). ¹⁴C-caffeine and ¹⁴C-salicylic acid were topically dosed with either 10% solutions of natural extracts or ethanol (control). The transdermal penetration of ¹⁴C-caffeine (hydrophilic) was significantly higher with avocado extract as compared to the control. Avocado extracts did not produce statistically significant effects on dermal penetration parameters for salicylic acid.

The avocado extract is also recommended as a basis for the preparation of various formulations that treat disorders and skin diseases, such as dermatitis or psoriasis. Stücker et al. (2001) performed a clinical trial to compare the effects of the vitamin D3 analog calcipotriol and vitamin B12 cream containing avocado oil, for use in the treatment of chronic plaque psoriasis. There was a more rapid development of beneficial effects with the use of calcipotriol in the initial eight weeks, but after twelve weeks, there were no significant differences between the two treatments. Although

the efficacy of the calcipotriol preparation reached a maximum in the first four weeks and then began to subside, the benefits of the vitamin B12 cream with avocado oil remained at a constant level over the whole observation period, suggesting that this formulation is well-tolerated and may be suitable for use in long-term therapy.

Avocado oil is an excellent source of enrichment for dry, damaged, or chapped skin (Nayak, 2008). Another attractive property is its ability to absorb perfumes, great added value for cosmetic use. All these properties make it useful for cosmetics, being used in the preparation of moisturizing creams, lipsticks, sunscreens, exfoliants, and, due to the ease with which it forms emulsions, it becomes ideal for producing soaps (Tango et al., 2004). In addition to these properties, avocado has several bioactive compounds, namely, monounsaturated fatty acids, unsaponifiable fatty acids (phytosterols, tocopherols, squalene and furans lipids), vitamins A, C and E, carotenoids, phenolic agents, which enhances their use by dermo-cosmetics as cosmeticaceuticals (Nayak et al., 2008).

Avocado can be beneficial in combating aging of the skin based on the moisturizing and emollient properties of its oil and the considerable amount of unsaponifiable compounds, which act in the fight against senescence agents, favoring the skin's trophicity (Goetz, 2005).

Oliveira et al. (2013) studied the composition of avocado oil extracted from the pulp of the fruit and the effect of a semisolid formulation of that oil on wound healing in rats. Their results proved that avocado oil contains essential fatty acids (oleic (47.20%), palmitic (23.66%), linoleic (13.46%) docosadienoic (8.88%), palmitoleic (3.58%), linolenic (1.60%), eicosenoic (1.29%), and myristic acids (0.33%)). It also contains β -sitosterol, β -carotene, lecithin, minerals, and vitamins A, C, D, and E. A significant increase was observed in percentage wound contraction and reepithelialization in the groups treated with semisolid formulation or avocado oil compared to control. The topical application of avocado oil in rats also increased anti-inflammatory activity and collagen synthesis when compared to control groups.

Identical results were obtained by Nayak et al. (2008). Their study also aimed to evaluate the effect of topical and oral administration of avocado

extract on excision and dead space wound models. The rats used in the excision wound model were divided into four groups of five each and received either topical or oral treatment. The animals used in the dead space wound model were divided into two groups of five each and were treated orally. Healing was assessed by the rate of wound contraction, period of epithelialization, granulation tissue weight, and hydroxyproline content. In the excision wound model, full epithelialization was observed on average on day 14 in the rats who receive oral or topical treatment.

In contrast, the controls took approximately 17 days to heal completely. The extract-treated wounds were found to epithelialize faster than the controls. Wet and dry granulation tissue weight and the hydroxyproline content of the tissue obtained from extract-treated animals used in the dead space wound model were significantly higher compared with the controls.

Oryan et al. (2015) investigated the effects of avocado-soybean unsaponifiables on the healing response of cutaneous wound defects in rats. Treatment increased tissue glycosaminoglycans and collagen contents at various stages of wound healing modulated inflammation, improved fibroplasia, and produced high amounts of scar tissue in the short term. In the long term, treatment reduced the scar tissue size, improved the quality, the rate of wound contraction, and the reepithelisation, being the treated lesions cosmetically more agreeable.

Skin exposure to ultraviolet radiation contributes to photoaging and the development of skin cancer by DNA mutations. *Persea americana* demonstrates a photoprotective effect against UVB radiation. Deuschle et al., (2018) investigated the antinociceptive and anti-inflammatory effects from a topical formulation containing the *P. americana* leaf extract in a UVB irradiation-induced burn model in mice and performed a gel-formulation stability study. The stability of the gel was studied, analyzing organoleptic characteristics, pH, and viscosity. The results proved that gel-formulation guaranteed stability, quality, and therapeutic effect, being able to prevent the UVB irradiation. This effect could be attributed to gel biological constituents, especially catechin, chlorogenic acid, and rutin. Polyhydroxylated fatty alcohols extracted from seed and pulp of avocados

also have photo-protective activity against UV-induced damage in skin cells (Rosenblat et al., 2011). These compounds extracted from avocado suppress inflammatory response and provide non-sunscreen protection against UV-induced damage in skin cells. Introducing polyhydroxylated fatty alcohols to keratinocytes previous to exposure to UVB radiation exercised a protective effect, rising cell viability, decreasing the secretion of interleukin six and prostaglandin E2, and increasing DNA repair.

The peptides present in avocado also have some importance for the dermatology and dermo-cosmetic area, due to its antipruritic properties. Itching is known as an unpleasant sensation that causes the urge to itch. The origin of this phenomenon is in the dermal mast cells, and mediators of these cells, such as histamine or tryptase, stimulate the terminals of the C neurons, thus inducing the sensation of pruritus. Also, pruritus is known to be related to dry skin. Thus, avocado peptides can attenuate this sensation by several processes: because of their ability to inhibit the release of histamine and tryptase by the mast cells; decrease the genetic expression at the epidermal level of the receptor involved in the release of these mediators from pruritus; positively affect the ceramides in the epidermis and the synthesis of fatty acids, essential for epidermal balance; and, ultimately, significantly increase the production of hyaluronic acid and glycosaminoglycans by the keratinocytes, which are essential for the various layers of the skin and its hydrolipidic film (Bredif et al., 2010).

CONCLUSION

In the context of a healthy diet, consumption of avocados can fit into a full range of healthy eating plans. The primary purpose of this review is to promote the production and processing of this fruit and its by-products (peel and seed), highlighting the possibility of extracting bioactive compounds and the possibility to use them as natural additives for the food industry as well as pharmaceutical and cosmetics industries. These benefits will open up as a scope for future utilization of fruit and vegetable waste for therapeutic and nutraceuticals purposes.

The edible part of avocado (pulp) has an essential quantity of hydroxybenzoic and hydroxycinnamic acids and procyanidins. However, the peel and the seed of avocado varieties present higher amounts of phenolic compounds, namely catechins, procyanidins, and hydroxycinnamic acids, displaying more antioxidant potential. In this work, it is also suggested that the reuse of avocado seed and peel can be powerful sources of natural ingredients and additives to provide new technological solutions through the application of green technology. The pulp of the avocado fruits, as well as their by-products, are rich sources of lipids, starch and fibers, and polyphenolics proving to be a potential natural source of bioactive ingredients for use in the food, cosmetic and pharmaceutical industries.

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