

ETHNOBOTANICAL USES, PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILES, AND TOXICITY OF *PERSEA AMERICANA* MILL. : AN OVERVIEW

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Abstract

Since medieval ages, plants have been used by human being as food or as source of remedies. Various parts of *Persea americana* have been reported in many studies to be used by people from tropical countries to manage some health problems such as diarrhea, dysentery caused by helminths and amoebas, toothache, intestinal worms, diabetes, skin rashes, infectious processes caused by fungi and bacteria, asthma, high blood pressure and rheumatism, malaria and typhoid fever; to lower high blood cholesterol, to stimulate uterine contractions and to ease painful menstruations. This tree planted around the house also serves as air purifier. It is demonstrated that this plant extract can be safely taken until a dose of 500 mg/kg body weight. This review study is an endeavour to give a detailed survey of the literature on the ethnobotanical uses, phytoconstituents, pharmacological properties, as well as the toxicity of *Persea americana*.

Keywords: *Persea americana*, Ethnobotanic uses, Phytochemical, Pharmacological, Toxicity.

Introduction

Plants and herbs have been a tremendous source of food and folk remedies for mankind and have served as starting material for the development of new synthetic drugs. They have the ability to synthesize a wide variety of chemical compounds which are used to perform biological functions and to defend against attack from predators such as insects, fungi, yeasts, bacteria, virus and other pathogens [1]. Chemical compounds in plants mediate their effect on the human body through processes identical to those already well understood for the chemical compounds in conventional drugs [2]. Thus, herbal medicines do not differ greatly from conventional drugs in terms of how they work. *Persea americana* is one of those plants currently used by indigenous persons for its nutritional value and to manage health problems. This plant belongs to Lauraceae family. It is an evergreen small tree with a grey trunk, native to Central and South America [3]. It has different names depending on the country where it grows: Alligator in Florida, Xiene in Mexico, Palta in Colombia and Ecuador, Abacoteiro in Brazil, Avocado pear or (Ube Beke) in Nigeria [4] and pear in Cameroon. The avocado is a leafy tree up to 60 feet high with a trunk diameter which can reach 100 cm. It possesses alternate and elliptical leaves. The flowers are small and unisexual [5, 6]. The fruit is a drupe (fleshy fruit with seed inside) greenish and thin skin whose taste reminiscent of walnut, and has a very oily pulp, commonly used as food. Avocados are a good source of B vitamins, which help our organism to fight against diseases and infections [4].

Traditional uses

This plant has been for long time, used traditionally to treat various ailments of the human body in many parts of the globe. The root, bark, fruit, seed and leaf are used extensively in traditional medicine in many tropical and subtropical countries for the treatment of various ailments [7]. Its seed is used in the treatment of diarrhea, dysentery, toothache, intestinal parasites and for beautification [8]. In Cuba, this plant is used as antitussive, carminative, anti-diarrheal, abortifacient, diuretic, cholagogue, depurative, spasmogenic and stomachic; also indicated in cases of amenorrhea, liver obstructions, influenza and excess of uric acid [9]. The leaves of *Persea americana* have been popularly used in the treatment of diabetes in countries of Latin America and Africa [10]. The seed (crude or toasted) is employed in Mexican

traditional medicine to treat skin rashes, diarrhea, and dysentery caused by helminths and amoebas, for the cure of infectious processes caused by fungi and bacteria, as well as for the treatment of asthma, high blood pressure, and rheumatism [11 - 15]. The bark, fruit, and leaf are used in traditional medicine in South America, West Indies, and Africa to provide remedies for various ailments [16]. The fruit is employed as a vermifuge and remedy for dysentery. The leaves decoction is also taken as a remedy for diarrhea, sore throat and hemorrhage, and to stimulate and regulate menstruations [16]. Odugbemi has also documented the efficacy of the cotyledons of avocado pear seed for the treatment of hypertension. The cotyledons are then cut into pieces, dried and grinded into powder. A dessert spoonful in 200 ml of hot water taken after meals, gives relieve for the ailment [17]. In Cameroon, the leaves decoction is taken to treat toothache, high blood pressure, diabetes, malaria; to stimulate uterine contractions and to relieve painful menstruations. The leaves and stem bark are also boiled together in water and the resulting liquid is taken to cure toothache, malaria and typhoid fever. The fruit pulp is eaten to lower bad blood cholesterol, and to prevent mental strain and cardiovascular diseases; while the aqueous extract of its seed is drunk against intestinal worms. This tree planted around the house serves as air purifier.

Reported phytoconstituents and nutrients

Phytochemicals are present in all the plant parts, at different concentration. The result for the phytochemical constituents in *Persea americana* seed showed the presence of the following compounds with their respective concentration: Alkaloids (2.92 ± 0.028), Flavonoids (4.76 ± 0.053), Saponins (3.22 ± 0.055), Steroids (1.58 ± 0.05), Tanins (0.18 ± 0.00), Phenol (2.47 ± 0.03) [4]. Idris *et al* also found the same phytoconstituents in this tree extracts [18]. Some of the general characteristics of flavonoid include potent water soluble super antioxidants and free radical scavenger; they prevent oxidative cell damage, have strong anticancer activity and protect against all stages of carcinogens [19]. Flavonoids in intestinal tract lower the risk of heart disease and inflammation [4]. Isolated pure form of alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic and bacterial effects [20], antihypertensive, antiarrhythmic, antimalarial and anti-cancer activities [21]. Tannin rich medicinal plants are used to heal a lot of illnesses; such as leucorrhoea, rhinorrhoea and diarrhea. More recently, tannins have gained medical

interest, because of the high prevalence of deadly ailments such as AIDS and numerous cancers [22]. In the dyestuff industry, tannins are useful as caustics for dye and ink production. Also, in the food industry, tannins have proved usefulness in the purification of wine, beer and fruit juices and also as coagulants in rubber production [23]. Saponins are responsible for antimicrobial, antifungal, anti-inflammatory, anti-yeast and antidote activities. The function of saponins in plants generally serves as anti-feedant and to protect the plant against microbes and fungi [24]. Phenols have been extensively researched as disease preventives [25]. Steroids are antioxidants *in vitro*, and have a link with reproduction in humans [26]. The nutrients present in one-half of this tree fruit (68g), according to the NHANES analysis are given in Table 1 [27, 28]. The Avocado contains a significant amount of oil in comparison to other fruits. Its fruit oil composition in fatty acid is depicted in table 2 [29]. This oil is a rich source of monounsaturated fatty acids with oleic acid content being the highest. This phytochemicals and nutrients present in *Persea americana* gives credence to the medicinal benefits that this tree parts have been used for, in the past years as well as its nutritional value.

Pharmacological activities

The research data on *Persea americana* indicate that it possesses tremendous pharmacological value which supports its multiple traditional uses for the management of health problems. The most important are:

Anti-malarial activity

The antimalarial activities of *Persea americana* have been studied by Falodun *et al* [30]. They found that this plant extracts contain fatty alcohols metabolites, which possess potent activity against chloroquine-sensitive (D6) and chloroquine-resistant (W2) strains of *Plasmodium falciparum*. In another study on Ghanaian antimalarial plants, Gustav Komlag *et al* proved that aqueous extract of this tree's leaf possesses antimalarial effect [31]. It was active against both chloroquine sensitive 3D7 and chloroquine-resistant W2 *P falciparum* without any toxicity. More recently, Tene Tcheghebe *et al*, in an ethnobotanic survey, also mentioned the antimalarial activity of this tree [32].

Anti-helicobacter pylori, antiulcer and gastro-protective activity

Castillo-Juàrez *et al* carried out a research work to evaluate the *in vitro* anti-helicobacter pylori activity

of 53 plants used in Mexican traditional medicine for gastrointestinal disorders [33]. The results proved that methanol extracts of *Persea americana*, *Annona cherimola*, *Guaiaacum coulteri*, and *Moussonia deppeana* (MIC <7.5 to 15.6 µg/ml) showed the highest inhibitory effect. The same study showed that *Persea americana* seed is effective for gastrointestinal tract problem and dysentery. The plant extract has a lot of phenolic compounds that help to prevent gastric ulcers [4]. Also, the aqueous leaf extract of avocado consisting of alkaloids, flavonoids, saponins and tannins produced significant dose-dependent anti-ulcer activity when administered orally to sick rats (rats pre-treated with ulcerogenic drugs- indomethacin and ethanol) [34].

Anti-platelet and anti-thrombic activity

Persea americana extracts have acetogenin compounds which are responsible for anti-platelet and anti-thrombic activity [35]. Platelet aggregation and thrombus formation occur during ischemic diseases. Its fruit pulp contains bioactive compounds which inhibit platelet aggregation and prevents thrombus formation. Thus a diet supplemented with its fruit pulp can be beneficial for patients suffering with ischemic diseases.

Anti-convulsant effect

The aqueous leaf extract of Avocado was found to possess anti-convulsant activity as it antagonized seizures induced in mice by administration of the drugs, viz., pentylenetetrazole (PTZ) and picrotoxin (PCT). The anti-convulsant property of the extract was attributed to its ability to enhance the neurotransmission and/or action of GABA in the brain [36].

Anti-viral activity

Avocado seeds have a lot of phenolic compounds that help to prevent and treat viral diseases. The leaf extracts from *Persea americana* have been shown to have antiviral activity against herpes simplex type 1 virus, human immunodeficiency virus 1 and adenovirus [37, 38]. The infusion and ethanol extract of dried leaves of *Persea americana* were compared with respect to their inhibitory activities of viral replication *in vitro* [37]. The chosen viruses for the initial screening were adenovirus type 3 (AD3), HSV-1, and ADV. The ethanol extract was only tested against HSV-1 and ADV. The infusate was active against the 3 viruses, whereas the ethanol extract did not show any activity under the experimental conditions employed.

Anti-bacterial and antimicrobial activity

Too many studies have been carried out on the antibacterial and antimicrobial activity of this plant [18, 30, 39-43]. In a study on Antiprotozoal and antimycobacterial activities of *Persea americana* seeds, the chloroformic and ethanolic extracts of *Persea americana* seeds showed significant activity against *E. histolytica*, *G. lamblia* and *T. vaginalis* ($IC_{50} < 0.634 \mu\text{g/ml}$) while The chloroformic extract inhibited the growth of *M. tuberculosis* H37Rv, *M. tuberculosis* MDR SIN 4 isolate, three *M. tuberculosis* H37Rv mono-resistant reference strains and four non tuberculosis mycobacteria (*M. fortuitum*, *M. avium*, *M. smegmatis* and *M. abscessus*) showing MIC values $\leq 50 \mu\text{g/ml}$ [42]. Antimicrobial activity of seed extracts of *Persea americana* against *Escherichia coli*, *Klebsiella americana*, *Bacillus subtilis*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Corynebacterium ulcerans*, *Salmonella typhi*, *Neisseria americana* and *Candida albicans* was carried out using the disc diffusion technique [18]. The methanol, ethyl acetate and chloroform extracts demonstrated promising activity against the test organisms. Methanol and ethyl acetate extracts showed the minimum inhibitory concentration (MIC) value (10mg/ml) against *C. albicans*, indicating their higher potency. In another study, the fatty alcohols: 1,2,4-tetrahydroxyheptadecane-6,16-diene(2); 1,2,4-Trihydroxyheptadec-16-yne(3) and 1,2,4-Trihydroxyheptadecane(4), purified compounds isolated from it seed exhibited promising *in vitro* antibacterial activity against a panel of pathogenic bacteria: *Staphylococcus aureus*, methicillin resistant *Staphylococcus Aureus* and *Escherichia coli* at IC_{50} values of (21.1, 8 and $200 \mu\text{g/mL}$), (3.259 and $86.32 \mu\text{g/mL}$) and (17.18, 8.26 and $200 \mu\text{g/mL}$), respectively [30]. Phenolic compounds present in appreciate amount in Avocado seeds also help to prevent bacterial diseases [4]. This therefore, supports the traditional medicine use of *Persea americana* and suggests that further studies should be conducted to isolate and identify the active components of the extract which account for its antibacterial and antimicrobial activity.

Antioxidant activity

Owusu Boadi *et al* made a research work to determine the antioxidant properties of the leaves of *Persea americana* and they concluded that the leaves of this plant contain antioxidant which can help prevent stress related diseases [44]. Also, Ikpeme *et al* [45] evaluated the antioxidant efficacy

of fresh and dried fruits of this tree and reported that the fresh fruit is more efficient than the dried fruit. Kim *et al* isolated two compounds with unique antioxidant properties in avocado extractst [46]. It is important to clearly identify the compounds with antioxidant properties in the leaf extract of this plant. The antioxidant activity exhibited by the methanolic leaf extract of *Persea americana* and its hepatoprotective action against acute paracetamol toxicity make it a potential agent against liver diseases and other pathologies associated with oxidative stress.

Analgesic and anti-inflammatory activity

Adeyemi *et al* evaluated the anti-inflammatory activity of this plant extract on mice with Carrageenan-induced edema [47]. The aqueous extract of this tree's leaves caused a significant and dose-dependent inhibition of the control writhes. The inhibition by 1600 mg/kg extract was similar to that produced by 100 mg/kg of acetylsalicylic acid (57.2% and 58.0%, respectively). The inhibition (87.2%) shown by 800 mg/kg of the extract was same as morphine (2 mg/kg, 87.0%). A greater inhibition (77.1%) was produced by the extract (800 mg/kg) compared with acetylsalicylic acid (68%) in phase II of the test. The aqueous leaf extract of this plant (800 mg/kg) produced a significant inhibition of the swelling caused by carrageenan at 3 h. This effect was similar to that produced by indomethacin in the same duration. This supports the traditional use of this tree extract to relief pains.

Anti-hypercholesterolemic activity

It has been found that administration of aqueous leaf extracts to rats with hypercholesterolemia caused a decrease in the levels of plasma glucose, total and LDL cholesterol and a significant increase in the HDL levels [48]. Avocado oil also reduces the very-low density lipids (VLDL), low density lipids (LDL) levels without affecting the high density lipids (HDL) levels in sick mice [48]. This is probably due to the antioxidants found in the whole avocado. Another study conducted by Bartholomew *et al* also showed that aqueous and methanol leaf extracts of *Persea americana* influence lipid metabolism in hypercholesterolemic rats with consequent lowering of T-CHOL and LDL-CHOL and a restoration of HDL-CHOL levels [49]. This could represent a protective mechanism against the development of atherosclerosis.

Anti-diarrheal activity:

The anti-diarrheal property of bioactive compounds

present in avocado seeds has been reported. Administration of chloroform-methanol extracts of these seeds to castor oil induced diarrheal rats caused a significant reduction in wetness of feces in a dose-dependent manner. Also, the LD50 values of the extracts were found to be lower than 5000mg/kg body weight of the rats. This attested the safety of the extracts with only a remote chance of acute toxicity [50]

Anti-arthritic and joint diseases

Avocado seeds extract with its unique anti-inflammatory ability, can help to cure arthritics and other joint diseases [51]

Anticancer activity

Avocado seeds contain a flavonoid that prevents tumor growth [4]. It has been also reported that the lipophilic carotenoids present in this plant extract may have potential anti-carcinogenic effects [52]. In another study, a compound known as persin, isolated from avocado leaves has been used to carry out the induction of apoptosis in human breast cancer cells [53].

Cardiovascular activity

Avocado seeds help to prevent cardiovascular disease, lower cholesterol and prevent strokes [54].

Effect on body weight

It is evident from Brail *et al*'s study that the administration of aqueous and methanol leaf extracts of *Persea americana* caused a reduction in body weight compared with the hyperlipidemic controls [55]. It could be that *Persea americana* leaf extracts increase the catabolism of lipids accumulated in the adipose tissue, resulting in a decrease in the mean body weight.

Haemopoietic Activity

Omodamiro *et al* conducted a research work designed to determine the effects of oral administration of the ethanol extracts of *Persea americana* seed at different concentrations on some haematological parameters in Wistar rats [4]. The results showed an appreciable increase in the values of those parameters investigated and they explained that this is associated with the inherent-haematopoietic-stimulating properties possessed by the extract of *Persea americana* which make it capable to produce more red blood cells.

Hepatoprotective activity

A study designed to evaluate the Hepatoprotective

and haemopoietic activity of *Persea americana* ethanolic extracts on Wistar albino rats, was conducted by Omodamiro *et al* [4]. The results showed protecting effect from damage on the liver and being able to increase the haematological parameters in the test group, indicated that this tree ethanol extract has hepatoprotective and haematological properties. They suggested that this effect may be due to the reduction of oxidative stress and its ability to reduce elevated level of serum marker enzymes because of some vital phytochemicals and antioxidants it possesses [4]. Another study made by Mahmoed and Rezaq also showed the hepatoprotective capacity of Avocado fruit extract and they added that this capacity is due to its flavonoid and phenolic content [56]. Moreover, Brai *et al* found that aqueous leaf extract of *Persea americana* shows significant ($p < 0.05$) hepatoprotective activity by decreasing the activities of ALT, AST, ALP and reducing the levels of TBL, against CCL4-induced damage in rats [57]. These findings on *Persea americana* extracts make it a potential agent against liver diseases and other pathologies associated with oxidative stress.

Hypoglycemic and antidiabetic activity

A study was carried out by Thenmozhi *et al* to evaluate the most effective fraction and subfraction having hypoglycemic activity from the hydro-methanolic (2:3) extract of the fruit of *Persea americana* on streptozotocin-induced diabetic rats [58]. The results proved that sub-fraction B which was obtained from n-hexane fraction had the best antidiabetic activities. Anita *et al* also demonstrated that aqueous leaf extract of *Persea americana* possesses hypoglycemic effects in the normal rats with the maximum antidiabetic activity reached at 6 h after a single dose of the extract was administered, producing $60.02 \pm 6.83\%$ reduction in blood glucose level [59]. Many other studies have shown the same result [10, 60, 61].

Hypotensive activity

Djomeni Dzeufi *et al* demonstrated that the aqueous extract of a mixture of fresh leaf of *Persea americana*, stems and fresh leaf of *Cymbopogon citritus*, fruits of *Citrus medica* and honey possesses antihypertensive activity against ethanol and sucrose induced hypertension in rats by the improvement of biochemical and oxidative status, and by protecting liver, kidney and vascular endothelium against damages induced by chronic consumption of ethanol and sucrose [62]. Other authors have also documented the efficacy of the avocado pear extract

for the treatment of hypertension [17, 63].

Vasorelaxant activity

The vasorelaxant properties of aqueous leaf extract of *Persea americana* on isolated rat aorta has been investigated [7]. A significant vasorelaxation in aorta has been observed due to the synthesis of endothelium derived relaxing factors (EDRF's) and the release of prostanoid. The treatment of the aorta with the extract also reduces vasoconstriction, the probable reason for it being the inhibition of Ca^{2+} influx through calcium channels [7].

Wound healing activity

The wound healing properties of the *Persea americana* fruit extract has been confirmed. The topical or oral administration of the fruit extract in wounded rats resulted in the complete epithelialization of the wound [64]. Other parameters like rate of wound contraction and hydroxyproline content of tissues along healing with histological observations also indicated the wound healing property of this plant. In the excision wound model, complete healing (full epithelialization) was observed on average on day 14 in the rats, which received oral or topical treatment of *Persea americana* fruit extract (300 mg/kg/day) [54]. 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 those of the controls.

Reported toxicity

The *Persea americana* seed toxicity is dosage dependent. During a study on the toxicity of this tree seed extract, the signs of toxicity were noticed 15 hours after the administration: there was decreased locomotive activity, decreased feed intake, prostration and weakness [4]. However, it has been demonstrated in the same study that its extracts can be safely taken until a dose of 500mg/Kg (since a LD50 value of 707.1mg/kg was recorded). Given the wide ethno pharmacological applications of *Persea americana*, the present toxicity results constitute safety information that can be used in obtaining regulatory approval for its commercialization.

Conclusion

Persea americana is a tree cultivated in most tropical countries, particularly for its edible fruits. But all parts of the plant, including leaves, bark, root, seed and fruit pulp are used for medicinal purposes. Its oil has applications in cosmetics, in the form of topical creams, to manage some skin problems.

Biological tests carried out on this plant for its antioxidant, anti-helicobacter pylori, anti-ulcer and gastro-protective, antibacterial and antimicrobial, anti-platelet and anti-thrombic, wound healing, hepatoprotective, vasorelaxant, analgesic and anti-inflammatory, hypoglycemic and antidiabetic, anti-hypercholesterolemic, anti-diarrheal, anti-arthritic, antimalarial, haemopoietic and cardiovascular activities revealed positive results. More interesting yet, it has been reported that its extracts can be safely taken to cure diseases till doses as greater as 500mg/kg.

Bioactive constituents such as alkaloids, flavonoids, phenolic compounds, saponins, steroids and tannins significantly present in the *Persea americana* extracts, account for its various activities and uses in medicine, while the great amount of nutrients like high-monounsaturated fatty acid, sugar, phytosterols, dietary fiber, minerals and vitamins, present in the plant extracts validate its high nutritional value. Although some of the individual phytochemicals found in avocado have been well characterized, many new uncharacterized bioactive constituents are to be discovered, with potential activities.

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Kingdom: Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order: Laurales
Genus: persea
Family: Lauraceae
Scientific name: <i>Persea americana</i> Mill.
Common name: avocado pear, alligator, palta, pear
  
Fruits and seed images

Table1. The nutrients present in one-half of *Persea americana* fruit (68g)

Analyte	Quantity (g)	Analyte	Quantity (g)	Analyte	Quantity (g)
High-monounsaturated fatty acid	6.7 g or 114 kcal	Vitamin C	6.0 mg	Pantothenic acid	1.0 mg
Total sugar	0.2 g	Vitamin E	1.3 mg	Riboflavin	0.1 mg
Potassium	345 mg	Vitamin K1	14 µg	Choline	10 mg
Magnesium	19.5 mg	Folate	60 mg	Lutein/Zeaxanthin	85 µg
Sodium	5.5 mg	Vitamin B6	0.2 mg	Phytosterols	57 mg
Vitamin A	43 µg	Niacin	1.3 mg	Dietary fiber	4.6 g

Table 2. Fatty acid composition of Avocado oil

Fatty acid	Quantity (%)	Fatty acid	Quantity (%)	Fatty acid	Quantity (%)
Palmitic acid	28.21	Stearic acid	0.69	Linoleic acid	13.87
Palmitoleic acid	5.69	Oleic acid	50.95	Linolenic acid	0.58