

The phytochemical and pharmacological profile of *Persea americana* Mill

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Submitted: 02-03-10

Revised: 20-03-10

Published: 10-07-10

ABSTRACT

Over the past decades, herbal medicine has become a thing of global significance with medicinal and economic implications. Wide spread use of herbs throughout the globe has raised serious concerns over its quality, safety, and efficacy. Thus, exact scientific assessment has become a precondition for acceptance of herbal health claims. *Persea americana* Mill. (avocado) is a tree, native to central America, cultivated in tropical and subtropical climates around the world, belonging to the family Lauraceae, is widely used in Ayurveda and evidence-based phototherapy. There are 3 principal races or groups of avocado: Mexican, Guatemalan, and West Indian named for the areas where they were originally cultivated. The plant is used in traditional medicine for the treatment of various ailments, such as monorrhagia, hypertension, stomach ache, bronchitis, diarrhea, and diabetes. Peptone, β -galactoside, glycosylated abscisic acid, alkaloids, cellulose, polygalactose, polyuronoids, cytochrome *P-450*, and volatile oils are reported to be present in this plant. Biotechnologic approaches show that modified MS medium supplemented with 1.0 mg benzyladenine/L, 0.1 mg Indole Butyric Acid/L, 0.1 mg Gibberalic Acid 3/L was optimum for adventitious shoot development. In the present review, an effort has been made to study the different aspects of *P. americana* Mill.

Key words: Antihypertension, glycosylated abscisic acid, lauraceae, *persea americana*

INTRODUCTION

During the past decade, the traditional systems have gained importance in the field of medicine. The World Health Organization estimates that 4 billion people, 80% of the world population, presently use herbal medicine for some aspect of primary health care. Herbal medicine is a major component in all indigenous people's traditional medicine and a common element in Ayurvedic, homeopathic, naturopathic, traditional, oriental, and Native American, and Indian medicine. Many drugs commonly used today are of herbal origin because of their safety, quality, and efficacy. Indeed, about 25% of the prescription drugs dispensed in the USA contain at least one active ingredient derived from plant material. The present attempt is to review and compile updated information on various aspects of *P. americana*, a plant used in the Indian system of medicine for a variety of purposes. *P. americana* Mill. is commonly known as avocado. The avocado tree has shiny evergreen, elliptic leaves 4-8 in number and 10-20 cm long. It is a much more branched, medium-sized tree and is cultivated for its delicious and highly nutritious fruit.

There are at least 500 named cultivars. One of the most popular cultivars is Fuerte and Mexican-Guatemalan hybrid with smooth-skinned, shiny green, pear-shaped fruits.

BOTANICAL DESCRIPTION

Taxonomy

Current name: *Persea Americana*

Authority: Miller

Family: Lauraceae.

Synonym(s)

Laurus persea L., *Persea drymifolia* Schlecht. and Cham, *Persea gratissima* Gaertn.f., *Persea nubigena*

Common names

Amharic: avocado

Burmese: htaw bat, kyese

Creole: zaboka

English: alligator pear, avocado, avocado-pear, butter fruit

Filipino: avocado

French: avocat, avocatier, zabelbok, zaboka

German: Alligatorbirne, Avocadobirne

Indonesian: adpukat, avokad

Khmer: avôkaa

Malay: apukado, avokado

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DOI: 10.4103/0973-7847.65332

Mandinka: avacado
 Pidgin English: bata
 Spanish: aguacate, pagua
 Swahili: mparachichi, mpea, mwembe mafuta
 Thai: awokado
 Trade name: medang
 Vietnamese: bo, lê dàu.

P. americana is a medium to large tree, 9-20 m in height. Avocado tree is distributed geographically [Figure 1]. The avocado is classified as an evergreen, although some varieties lose their leaves for a short time before flowering. The tree canopy ranges from low, dense, and symmetrical to upright and asymmetrical. Leaves are 7-41 cm in length and variable in shape (elliptic, oval, and lanceolate) [Figure 2]. They are often pubescent and reddish when young, becoming smooth, leathery, and dark green when mature. Flowers are yellowish green and 1-1.3 cm in diameter. The many-flowered inflorescences are borne in a pseudoterminal position [Figure 3]. The central axis of the inflorescence terminates in a shoot. The fruit is a berry, consisting of a single large seed, surrounded by a buttery pulp. It contains 3-30% oil (Florida varieties range from 3% to 15%). The skin is variable in thickness and texture. Fruit color at maturity is green, black, purple, or reddish, depending on the variety. Fruit shape ranges from spherical to pyriform [Figure 4], and weighs up to 2.3 kg.^[1-5]

PHYTOCHEMISTRY

Examples of the major chemical constituents^[6] of the various plant parts of avocado (*P. americana* Mill.) reported to date are summarized. These compound classes may be divided into alkanols (also sometimes termed “aliphatic acetogenins”) (1-17), terpenoid glycosides (18, 19), various furan ring-containing derivatives (20-30), flavonoids (31-41), and a coumarin (42). The highly functionalized alkanols (1-17)^[7-10] of avocado have exhibited quite diverse biological properties thus far. For example, Oberlies *et al* isolated 1,2,4-trihydroxyheptadec-16-ene (1), 1,2,4-trihydroxyheptadec-16-yne (4), and 1,2,4-trihydroxynonadecane (8) from the unripe fruits of *P. americana*, and found these substances to be moderately cytotoxic when evaluated against a small panel

of cancer cell lines.^[8] Kawagishi *et al* isolated 5 alkanols from avocado fruits with “liver suppressing activity” (as determined by the changes in plasma levels of alanine aminotransferase and aspartate aminotransferase), including compounds 9-11.^[10] An ethanol-soluble extract of the dried leaves of avocado showed antiinflammatory activity in a carrageenan-induced edema protocol, with 1,2,4-trihydroxyheptadec-16-ene



Figure 2: Leaves of *P. americana*



Figure 3: Flowers of *P. americana*



Figure 1: Geographical distribution of Avocado Tree



Figure 4 : Fruits of *P. americana*

(1) being obtained from the active fraction.^[11] In addition, 1,2,4-trihydroxyheptadec-16-ene (1) and related compounds 2-8, purified from the seeds of *P. americana*, showed moderate activity against epimastigotes and trypomastigotes.^[12] Persin [15; (2R,12Z,15Z)-2-hydroxy-4-oxoheneicosa-12,15-dienyl acetate], a constituent of avocado leaves, is regarded as a toxin for lactating livestock.^[13] In addition, persin has been found to reduce the larval growth of the beet armyworm, *Spodoptera exigua*,^[9] and is a known antifungal agent against *Colletotrichum gloeosporioides*.^[14] Two analogs, persenones A (14) and B (17), along with persin (15), were found to inhibit superoxide (O_2^-) and nitric oxide (NO) generation in cell culture, and may thus serve as cancer chemopreventive agents in inflammation-related organs.^[14] Persin (15) and 3 other analogs, compounds 3, 5, and 14, showed inhibition of acetyl CoA carboxylase activity, in the IC50 value range 4.0-9.4 M.^[15] Persin (15) has been noted to be labile under acid conditions, where it produces a furan ring-containing analog.^[9] The leaves of 17 avocado cultivars were investigated for their content of persin (15), and all but 2 of these contained discernible amounts of this compound (range 0.4-4.5 mg/g)^[16] [Figure 1]. The glycosylated abscisic acid derivatives (1S,6R)-8-hydroxy abscisic acid-D-glucoside (18) and (1R,3R,5R,8S)-*pi*-dihydrophaseic acid-D-glucoside (19) were isolated from the seeds of *P. americana*, although no biological activities were attributed to these compounds.^[17] Compounds 20-30 are furanoid constituents of avocados, [Figure 2] and have been isolated and structurally characterized or chemically synthesized by several different groups.^[7,18-21] These compounds have been termed “avocodofurans” and [Figure 3] subjected to literature review, primarily from the point of view of the effects of structural modification on their resultant antibacterial, antifungal, and insecticidal activities.^[22] Several flavonoids (31-41) have also been isolated from the leaves and seeds of avocados, with most of these being common flavones of wide distribution in the plant kingdom^[23-26] [Figure 4]. Some of these are biologically active, such as quercetin (36), which showed virustatic effects by inhibiting HIV syncytium formation and viral p24 antigen formation.^[24] An extract of avocado leaves inhibited herpes simplex virus type 1 (HSV-1) and Aujeszky's disease virus (ADV), and adenovirus type 3 (AD3). Bioactivity-guided fractionation led to the isolation of afzelin (38) and quercetin 3-O-D-arabinopyranoside (39), as inhibitors of acyclovir-resistant HSV-1.^[20] The methanolic extract of avocado seeds showed antioxidant activity in an 2,2'-azobis(2,4-dimethylvaleronitrile) (AMVN)-induced methyl linoleate peroxidation assay, and catechin (40) and epicatechin (41) were isolated as major active components.^[26] Also obtained as a constituent of avocado leaves is the commonly occurring plant coumarin, scopoletin (42).^[23] There have been several reports of biological activity showed by the extracts prepared from plant parts of avocados (*P. americana*) for which the active principles have not been characterized structurally, including anticonvulsant (in mice using standard convulsant drugs to cause seizures),^[27] antioxidant (inhibition of NADPH oxidase activity in HL-60 cells and of epithelial xanthine oxidase in AS52 cells),^[28] “chondroprotective” (ie, reducing degenerative changes in granulomatous tissue),^[29] rat

skin lysyl oxidase inhibitory,^[30] and periodontal disease related [including inhibition of the matrix metalloproteinase (TIMP-1 and TIMP-2) secretion in human fibroblasts^[31] activities.

PHARMACOLOGICAL ACTIVITIES

Vasorelaxant activity

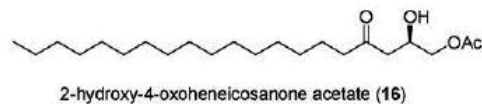
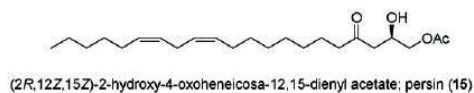
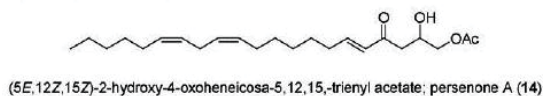
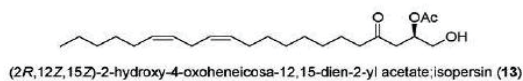
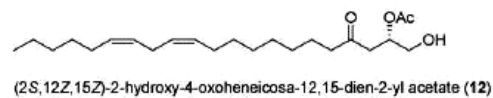
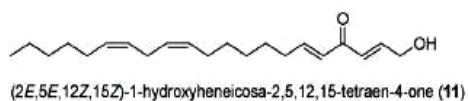
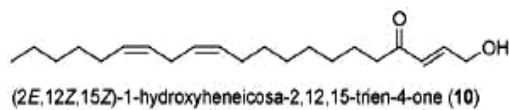
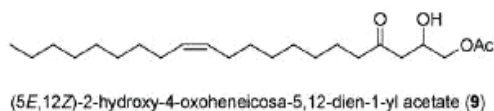
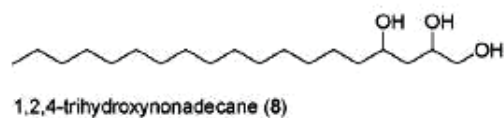
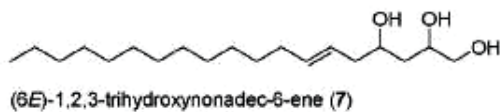
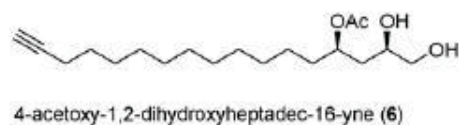
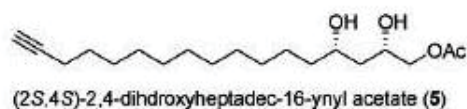
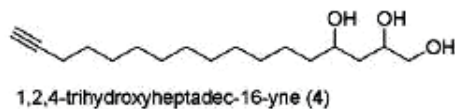
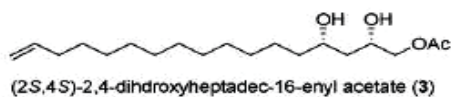
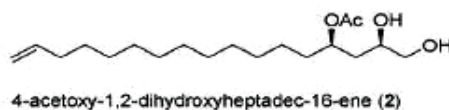
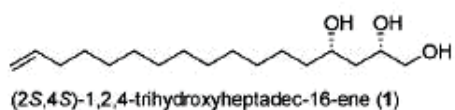
The aqueous extract of *P. americana* (0.01-12.8 mg/mL) produced a concentration-related vasorelaxation response in the rings of rat aorta with intact endothelium precontracted with noradrenaline (1×10^{-7} M), with an EC50 of 0.88 ± 0.03 mg/mL. In the endothelium-denuded rings, the vasorelaxant action of the aqueous extract of *P. americana* was significantly attenuated (EC50 .14F252.18 mg/mL). Cumulative addition of acetylcholine (1.1×10^{-8} to 1.4×10^{-5} M) produced relaxation of endothelium-intact rat aortic rings precontracted with noradrenaline (1×10^{-7} M). The vasorelaxant effect was significantly reduced by L-NAME (10^{-4} M) and methylene blue (10^{-6}), but not affected by indomethacin (10^{-5} M). The aqueous extract of *P. americana* (1 or 5 mg/mL) produced a rightward shift of the concentration-response curves to noradrenaline (1×10^{-9} to 1×10^{-9} M) and potassium chloride (10-80 mM). In fact, this activity was blocked by L-NAME or methylene blue, suggesting that the vasorelaxation is dependent on the synthesis and release of endothelium-derived relaxing factors (EDRFs). The blockade by indomethacin suggests that *P. americana* may also act by activating PGI2 and PGE2 receptors. The vasorelaxant effect may also be produced by the inhibition of Ca^{2+} mobilization through voltage-dependent channels and, to a lesser extent, through receptor-operated channels.^[32]

Analgesic and antiinflammatory activity

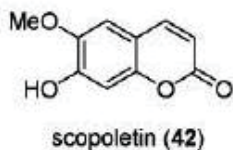
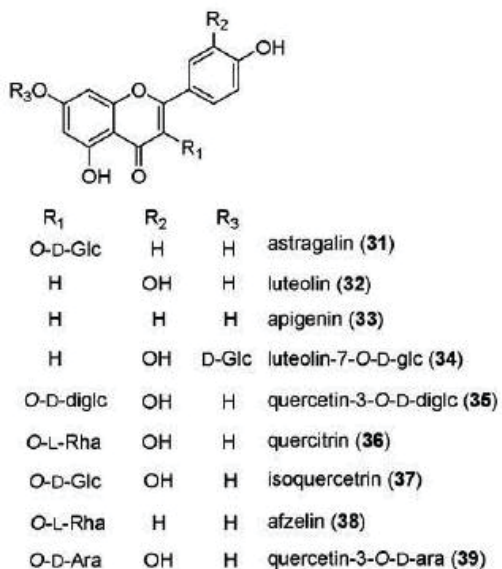
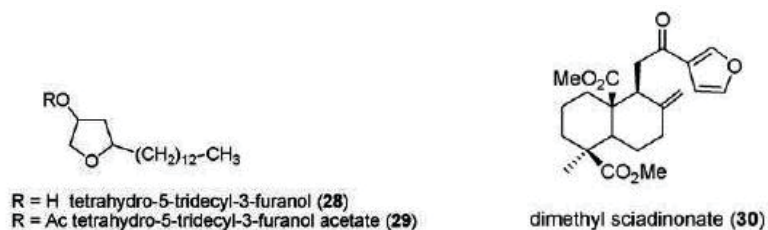
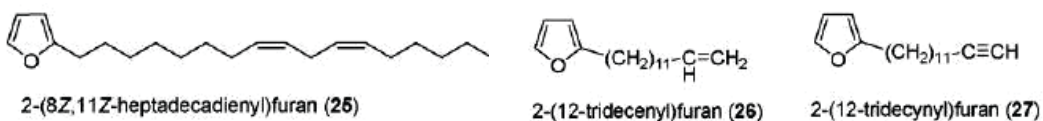
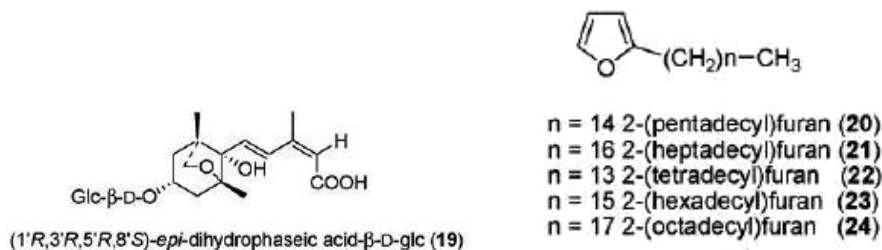
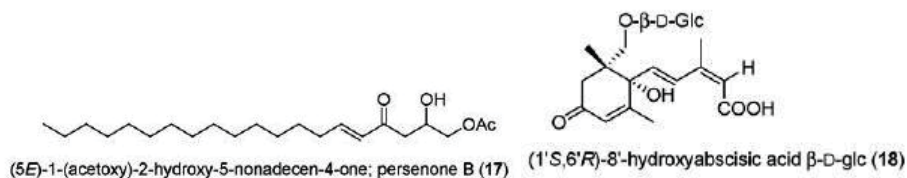
The aqueous extract of *P. americana* leaves caused a significant and dose-dependent inhibition of the control writhes. The inhibition by 1600 mg/kg extract was similar to that produced by 100 mg/kg of acetylsalicylic acid (57.2% and 58.0%, respectively). The inhibition (87.2%) shown by 800 mg/kg of the extract was same as morphine (2 mg/kg, 87.0%). There was a significant and dose-dependent inhibition of both phases, by the extract. 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 *P. americana* (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.^[33]

Hypotensive activity

The intravenous administration of doses of *P. americana* leaf aqueous and methanol extract ranging from 6.25 to 50 mg/kg (pilot study indicated that doses above 50 mg/kg caused death of rats within 10 min of administration; therefore, the highest screening dose for i.p. injections was 50 mg/kg) to normotensive anesthetized rats produced dose-related hypotensive effects. Doses above 12.5 mg/kg showed hypotensive effects, which were significantly different from those on the control. Also, the



Chemical constituents of *persea americana*



Chemical constituents of *persea americana*

duration of action appeared to be dose dependent.^[34]

Anticonvulsant effect

Aqueous leaf extract of *P. americana* possesses anticonvulsant activity in mice. The effectiveness of the plant extract in the experimental convulsion paradigm used probably suggests that the plant could be used in both *petit* and *grand mal* types of epilepsy. The plant's leaf extract was relatively more effective in Pentylenetetrazole (PTZ)- and picrotoxin (PCT)-induced convulsions than in bicuculline (BCL)-induced seizures. In general, the average onset and duration of convulsion was markedly delayed and reduced, respectively. These findings tend to suggest that *P. americana* leaf aqueous extract might have inhibited and/or attenuated PTZ-, PCT- and BCL-induced seizures of the mice used by enhancing, or in some ways interfering with, GABAergic action and/or neurotransmission.^[35]

Antiviral activity

The infusion and ethanol extract of dried leaves of *P. americana* were compared with respect to their inhibitory activities of viral replication *in vitro*. 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.^[36]

Wound healing activity

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 *P. americana* fruit extract (300 mg/kg/day). 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.^[37]

Antiulcer effect

The study was carried out to investigate the antiulcer activity of aqueous leaf extract of *P. americana*. Groups of albino rats were pretreated orally with aqueous leaf extract of the plant before the administration of the ulcerogenic drugs—indomethacin and ethanol. The extract produced significant and dose-dependent antiulcer activity against indomethacin- and ethanol-induced ulcers in rat.^[38]

Antihepatotoxic activity

Another group of scientists demonstrated action of avocado on liver. Martins Ekor *et al* carried out a study on antihepatotoxic activity in rats. The methanolic extract of *P. americana* could be protective against toxicity and oxidative stress arising from acute paracetamol intoxication. The mechanism of this protection is probably due to an antioxidant action of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase, which are the primary intracellular defense mechanisms to cope with

increased oxidant stress. The activities of the antioxidant enzymes measured (SOD and CAT) did not change significantly in normal rats treated with the methanolic leaf extract of *P. americana*; the extract, however, significantly induced the activity of these enzymes during hepatic damage produced by acute paracetamol toxicity. The methanolic leaf extract of *P. americana* and its hepatoprotective action against acute paracetamol toxicity make it a potential agent against liver diseases and other pathologies associated with oxidative stress.

Antioxidant activity

Kim *et al* isolated and demonstrated the presence of compounds persenone A and B with unique antioxidant properties in avocado fruit. 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 *P. americana* and its hepatoprotective action against acute paracetamol toxicity make it a potential agent against liver diseases and other pathologies associated with oxidative stress.

Hypoglycemic activity

Aqueous leaf extract of *P. Americana* possesses hypoglycemic effects in the normal rats. The maximum antidiabetic activity was reached at 6 h after a single dose of the extract was administered, producing $60.02 \pm 6.83\%$ reduction in blood glucose level.^[39]

Effect on body weight

It is evident from Brail *et al's* study that the administration of aqueous and methanolic leaf extracts of *P. Americana* caused a reduction in body weight compared with the hyperlipidemic controls. It could be that *P. americana* leaf extracts increase the catabolism of lipids accumulated in the adipose tissue, resulting in a decrease in the mean body weight.^[42,43]

Avocado improvement via biotechnologic

Disease resistance

Avocado has been transformed with an antifungal defensin gene *pdf1.2*^[40] and the *pac1* ribonuclease gene (Perea and Litz, unpublished data), respectively. The defensin gene was driven by the CaMV 35S promoter in binary vector pGPTV; the construct also contained the *uidA* reporter gene (GUS) and the *bar* gene for resistance to phosphinothricin, the active ingredient of the herbicide Finale®.

Extending shelf life

Avocado embryogenic cultures have been transformed with a modified bacteriophage gene S-adenosyl-L-methionine hydrolase (SAMase). SAMase is in a binary vector, pAG4092; the pPZP200 binary vector was utilized as a backbone.

Genetic improvement

Genetic transformation is viewed as having great potential for protecting avocado from infection by avocado sunblotch viroid (ASBVd), *C. gloeosporioides* and *P. cinnamomi*, and for addressing certain horticultural problems, for example, controlling fruit ripening, particularly in the Antillean (West Indian) cultivars.^[41]

CONCLUSION

Avocados are a rich source of nutrients and phytochemicals. Although some of the individual phytochemicals found in avocado have been well characterized, many new uncharacterized phytochemicals are being discovered with potential activity. Important progress has been made in recent years toward the recovery of avocado material from tissue culture. The use of biotechnology

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Source of Support: Nil, **Conflict of Interest:** None declared