

A Summary of the Pharmacological Activity, Phytochemistry and Pharmacognosy of *Parthenocissus quinquefolia* (L.): A Review

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Historically, medicinal herbs have been utilized as an important origin of chemicals with particular therapeutic potentials, and they continue to be a great place to find new medication candidates. *Parthenocissus quinquefolia* L. is a member of the grape-growing family Vitaceae. It is indigenous to Central and North America. It is widely dispersed in Iraqi gardens and plant houses from north to south. Traditionally, it has many uses, like relieving constipation, treating jaundice, expectorant, emetic, and others. At the same time, its proven activities include antioxidant activity, antimicrobial, anti-diabetic, thrombin inhibitor effect, and medicine for treating eyelid eczema. *Parthenocissus quinquefolia* contains valuable phytochemicals like alkaloids, saponins, steroids, terpenoids, polyphenolic compounds (flavonoids, phenolic acids, and tannins), anthraquinones, cardiac glycosides, coumarins, and reducing sugars that make it responsible for its critical pharmacological effects. The current review discussed the pharmacognosy, phytochemistry, and pharmacological activity of *Parthenocissus quinquefolia* (L.).

Keywords: Creeper; *Parthenocissus*; Pharmacognosy; Phytochemistry; *Quinquefolia*; Virginia.

Parthenocissus quinquefolia (L.) is a significant member of the Vitaceae family of medicinal herbs. Due to their reputation as the origin of wine, raisin, and grape cultivation, this family is highly significant economically¹. Additionally, this family is well-known for its pharmacological activity, which includes its ability to prevent cancer², relieve sore throats, treat rheumatism, arthritis, gastrointestinal tract issues, heal fractures, protect bone coming from postmenopausal bone loss, and have anti-parasitic, anti-diabetic, anti-dysentery, anti-diarrhea, diuretic, anti-inflammatory, anti-convulsant, anxiolytic, and anti-cholesterol formation activity³.

Of the approximately twelve species of the *Parthenocissus* genus, nine are in Asia, three are in North America, and just one is in Central America and the Caribbean⁴. Greek terms parthenos (meaning “virgin”) and kissos (meaning “ivy,” which was Latinized to form Cissus) are the sources of the *Parthenocissus* name. This naming is related to the ability of these creepers to form seeds without pollination⁵. Most of this genus plants are used as ornamental creepers for decorative requirements, as they appear most obviously in the spring with their new bright green leaves. At the same time, in the autumn, they shine in dramatic changes in leaf color that may vary from yellow, orange-brown,

and red to violet ⁶. It has become naturalized in southern Africa, Australia, tropical and temperate Asia, and Europe. Although *P. quinquefolia* is widely recognized to grow in household gardens from north to south and to germinate in numerous plant houses, its distribution in Iraq has yet to be formally documented ⁷.

Taxonomic classification

Plantae or plant is the Kingdom, Viridiplantae is the Subkingdom, Streptophyta is the Infrakingdom, Embryophyta is the Superphylum, Tracheophyta is the Phylum, and Spermatophytina is the Subphylum.

Magnoliopsida is the class; Rosanae is the superorder; Vitales is the order; Vitaceae is the family; *Parthenocissus Planch* is the genus; and *Parthenocissus quinquefolia* is the species ^{8,9}.

Common names of *Parthenocissus quinquefolia*

Parthenocissus quinquefolia is also called woodbine, Virginia creeper, American ivy, and five-

leaved ivy. In Iraq, it's known as MAKHALEB AL-KETT ⁷. The plant synonyms are *Ampelopsis hederacea*, *Ampelopsis quinquefolia*, and *Hedera quinquefolia* L. ^{8,9}.

Plant description

Quinquefolia is derived from the Greek word meaning "five leaves." *Quinque* signifies five, whereas *folia* refers to leaves or foliage ¹⁰.

Parthenocissus quinquefolia (Fig. 1) shows climbing characteristics that may reach up to 30 meters in height; its five leaflet leaves, which have enlarged or jointed nodes, emerge sporadically on shoots. These may produce little, forked tendrils with flower clusters; the greenish clusters develop in late spring and ripen into small, hard, purplish-black berries in early fall, opposing the leaves. The tendrils are capped with small, intensely sticky pads. The stamens develop opposing the petals, and most of the tiny flowers' components appear in groups of four or five ¹¹.

Table 1: Traditional uses of *Parthenocissus quinquefolia* in populations/Tribes

Traditional uses	Different populations/Tribes
Infusion used for jaundice.	Native American /The Cherokee and Iroquois.
Herbal remedy for diarrhea, swelling, and as a urinary aid.	Native American /The Cherokee and Iroquois.
Decoction of the root for diarrhea treatment.	Native American /Mesquakie.
Pink dye from the fruit for the skin	Northern American Indian /Kiowa.
Antihyperglycemic agent.	Indian population.

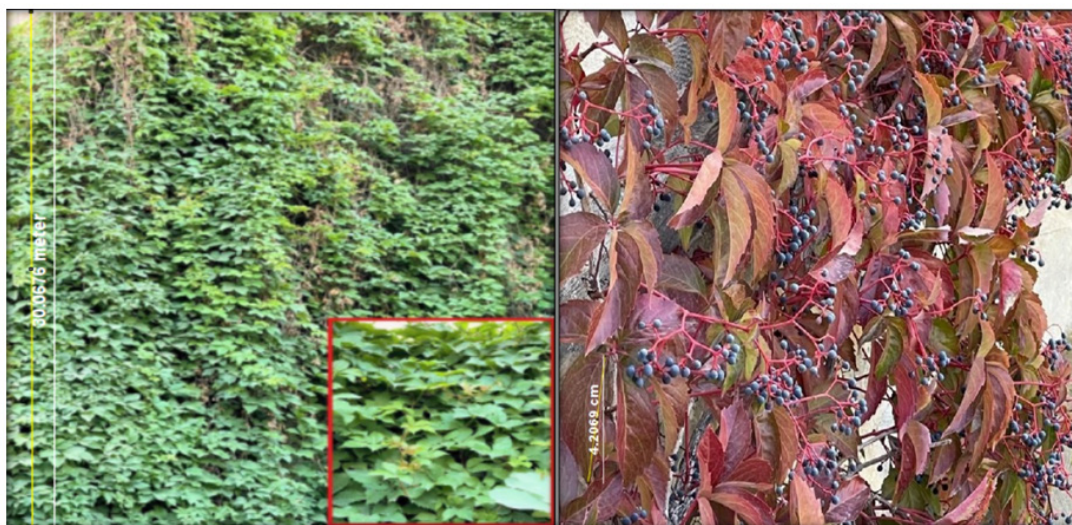


Fig. 1. *Parthenocissus quinquefolia*. A- Climbing feature at the Iraqi gardens.
B- Red-colored leaves and berry clusters.

Traditional uses of *Parthenocissus quinquefolia*

The bark and fresh young stem are traditionally used to relieve constipation, besides their usage as emetic, expectorant, and tonic ¹². A soft and moist material prepared by a hot plant decoction can be applied to the body to reduce edema ¹³. While a tea prepared from the plant is used to treat jaundice, a tea prepared from the roots is used to treat diarrhea and gonorrhea. A tea made from the leaves is an astringent, aperient, and diuretic ^{13, 14}. Fruit aids with fever treatment ¹⁵. Also, the plant was used as a natural source of pink dye obtained from the fruit ¹³. As an Ayurvedic ethno-medicinal plant, *P. quinquefolia* is used as an antihyperglycemic agent by the Indian population ¹⁶.

Native Americans (Cherokee people) have a rich ethnobotanical heritage; they prepared *P. quinquefolia* as an infusion for jaundice ¹⁷. *Parthenocissus quinquefolia* berries are rich in oxalic acid, and this gives the expectation of being poisonous upon eating ¹⁸. Since the plant was indigenous to Central and North America, most of the traditional uses were in the different tribes of the Native Americans, which are summarized in tab.1.

Phytochemical constituents of *Parthenocissus quinquefolia*

Phytochemical investigation performed on the bark, stem, leaves, and fruit extracts of *P. quinquefolia* indicated the presence of significant

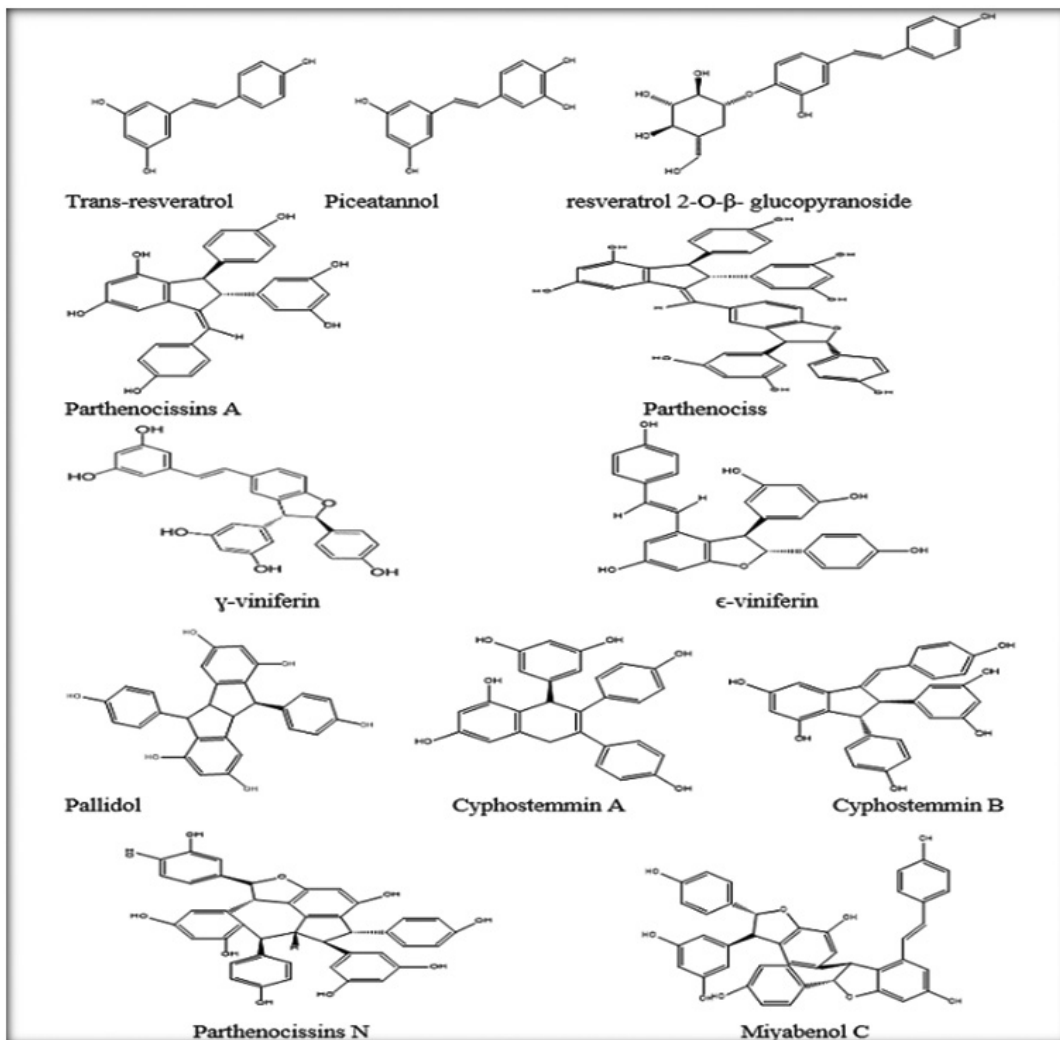


Fig. 2. Some Stilbenes compounds' chemical structures of *Parthenocissus quinquefolia* ²⁷⁻²⁹

secondary metabolites, including terpenoids, alkaloids, saponins, steroids, polyphenolic compounds (flavonoids, phenolic acids, and tannins), anthraquinones, cardiac glycosides, coumarins, and reducing sugars. The essential secondary metabolites identified and isolated from *P. quinquefolia* include stilbenes, polyphenolic compounds, terpenes⁷, fatty acids, and others¹⁹⁻²¹.

Stilbenes compounds

The name “stilbenes” comes from the Greek word “stilbos,” which means “shining”; these plants exhibit fluorescence²². Stilbenes are phytoalexins that plants create as a defense mechanism or a means of fending off illness when they are harmed, stressed, or exposed to other environmental factors. Stilbenes exist in two stereoisomer configurations: the crowded Cis (Z) isomer and the relieved Trans (E) isomer, and have a skeleton composed of C6-C2-C6 carbon atoms²³. Many types of stilbenes were detected and isolated from *P. quinquefolia*, including two monomeric stilbenes (trans-resveratrol, piceatannol), one glycoside stilbene (resveratrol 2-O- β -glucopyranoside), two resveratrol oligomer (parthenocissins A, B), three resveratrol dimers (resveratrol trans-dehydromer named c-viniferin, δ -viniferin, and pallidol), one oligostilbene (parthenocissins N), two oligostilbene resveratrol dimer (cyphostemmin A, cyphostemmin B), and one resveratrol trimer (Miyabenol C)²⁴⁻²⁶. Some Stilbenes compounds’ chemical structures of *P. quinquefolia* have been demonstrated in Fig.2.

Polyphenolic compounds

A- Flavonoids are essential secondary metabolites extracted from different medicinal plants and known for their use in nutraceutical, pharmaceutical, therapeutic, and cosmetic applications³⁰. In terms of chemistry, flavonoids are composed of a 15-carbon skeleton that is arranged in the C6-C3-C6 structure, in which both of the C6 are benzene rings named A and B, while the C3 acts as a bridge link between the A and B rings. This later bridge can again be cyclized by oxygen and produce a new ring called the C ring (oxygen-containing pyrene ring³¹).

This compound’s ability to modify important cellular enzyme activities results in several health advantages, including anti-inflammatory, anti-mutagenic, anti-carcinogenic, and antioxidant properties. Furthermore, flavonoids are valuable against many diseases, including cancer, Alzheimer’s, atherosclerosis, and others.

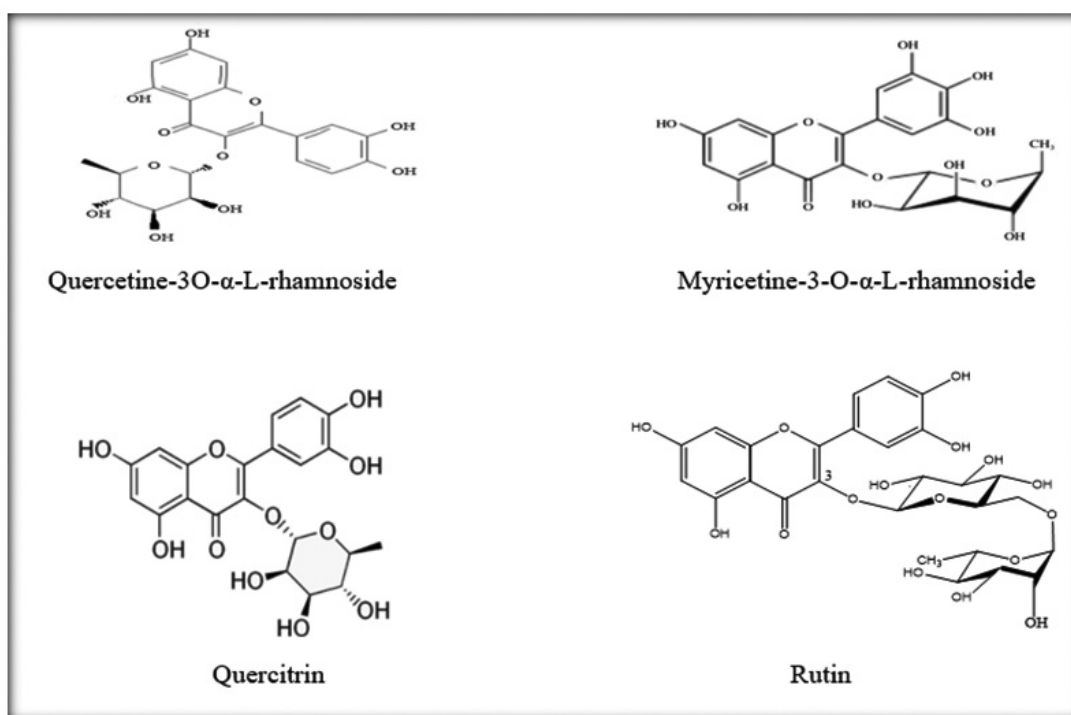


Fig. 3. Flavonoid chemical structures as glycosides of *Parthenocissus quinquefolia*^{33, 34}

This is due to their potent inhibition of numerous enzymes like phosphoinositide 3 kinase, cyclooxygenase, xanthine oxidase, and lipoxygenase^{30, 32}. Numerous flavonoids, including quercetin-3-O- α -L-rhamnoside, myricetin-3-O- α -L-rhamnoside, quercitrin (quercetin O-glycoside), and rutin (quercetin 3-O-rutinoside), have been found as glycosides (Fig. 3)²⁴. On the other hand, flavonoids can exist as free aglycones (Fig. 4), like quercetin, kaempferol, isorhamnetin, and luteolin⁷.

Also, other types of flavonoids, which are anthocyanins (Fig. 5), were isolated and identified from the fruit (berries) of *P. quinquefolia* and considered natural colorants like delphinidin (blue pigment), petunidin (dark-red or purple pigment), cyaniding (reddish-purple pigment), malvidin (reddish blue pigment), peonidin (purplish-red pigment), and pelargonidin (orange pigment)³⁶.

B- Phenolic acids are one of the simple and essential secondary metabolites with phenol

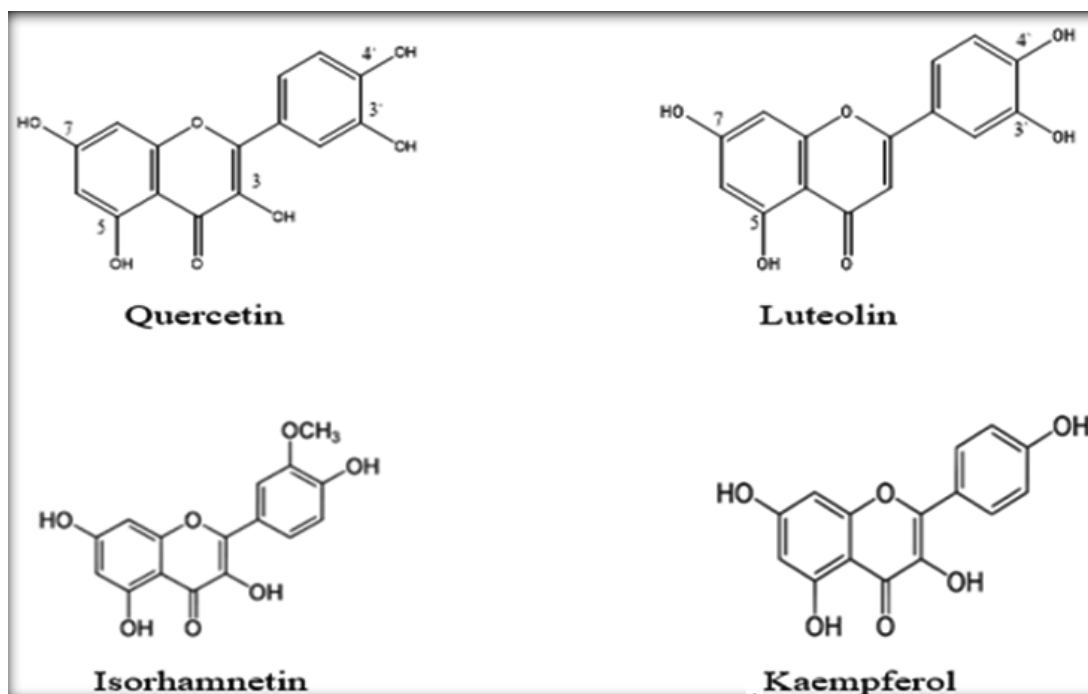


Fig. 4. Flavonoid chemical structures as an aglycone of *Parthenocissus quinquefolia*^{34, 35}

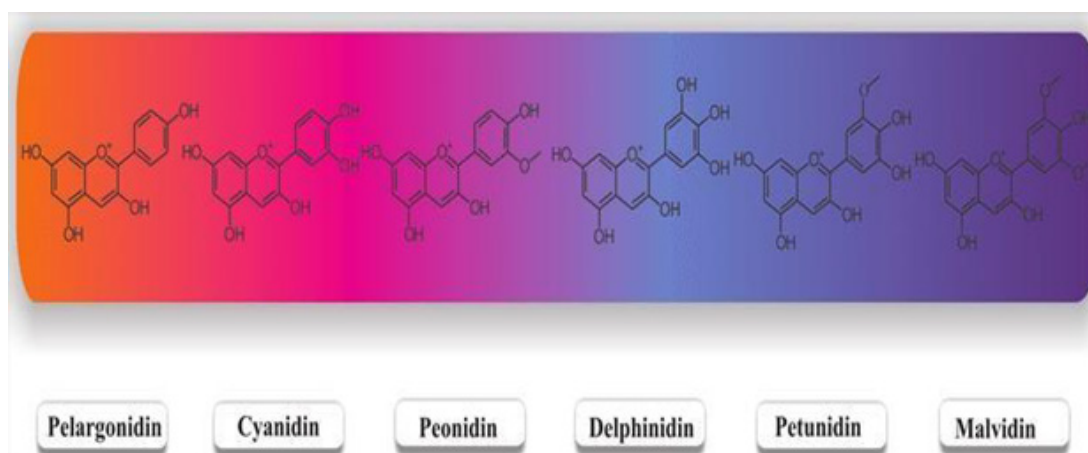


Fig. 5. Anthocyanins visible pigmentation range³⁷

units in their structure³⁸. Some essential phenolic acids (Fig. 6) have been demonstrated in the whole plant of *P. quinquefolia*, like coumaric acid, caffeic acid, and chlorogenic acid, which is derived from cinnamic acid. It also contains gallic acid, a benzoic acid derivative^{39,7}.

Terpenes and Terpenoids

Among phytochemicals, triterpenes are the most representative class, with approximately 30,000 known constituents representing a portion

of all plants' lipid substances⁴¹. Only one triterpenic compound was identified from *P. quinquefolia*, which is β -Amyrine (β -Amyrylhexadecanoate hexadecanoate), and its structure is shown in Fig. 7. This compound was extracted from dried leaves using dichloromethane for 24 h in a Soxhlet apparatus, then eluted with a mixture of solvents of increasing polarity using column chromatography and evaluated for antithrombotic effect⁴².

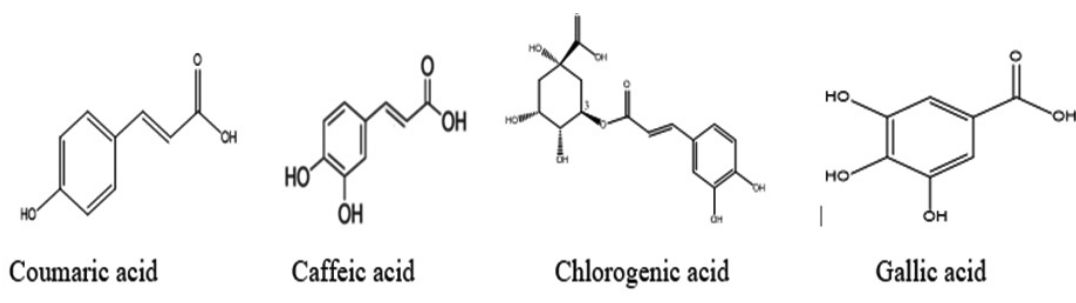


Fig. 6. Phenolic acid compounds' chemical structures of *Parthenocissus quinquefolia*^{40,34}

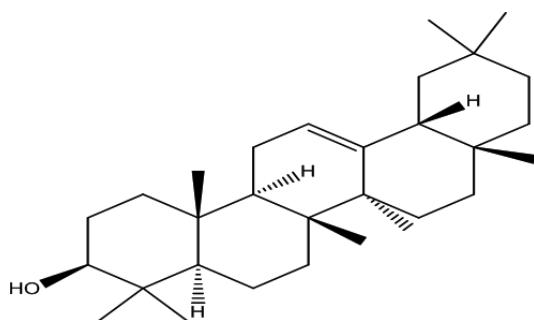


Fig. 7. β -Amyrin chemical structure isolated from *Parthenocissus quinquefolia*

B- Phytosterols are cholesterol-like molecules found in higher plants⁴³. Upon TLC and HPLC examination of the petroleum ether fraction of the whole plant demonstrated the presence of stigmasterol and beta-sitosterol, and the quantities of both compounds in the petroleum ether fraction were calculated and found to be 2.33 μ g for stigmasterol and 4.4 μ g for beta-sitosterol⁷.

Fatty acids

Aliphatic monocarboxylic acids are known as fatty acids and typically consist of a 4–28 carbon chain that is even-numbered, unbranched,

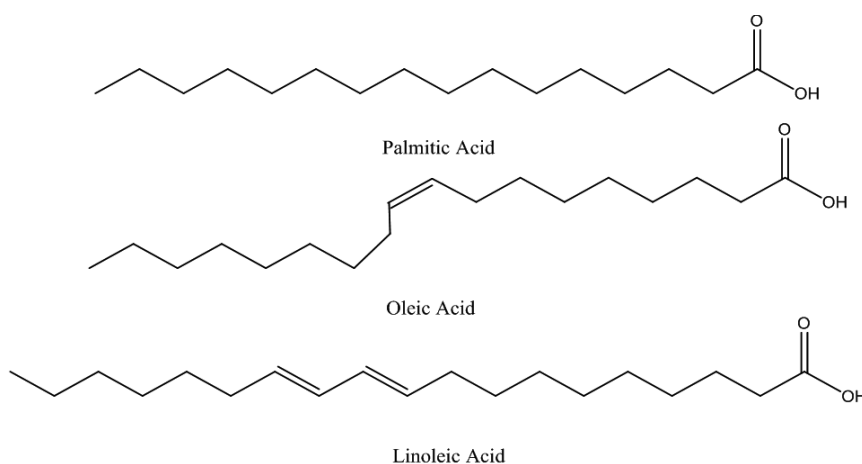


Fig. 8. Chemical structure of the most abundant and significant fatty acids of *P. quinquefolia*⁴⁸

and perhaps saturated or unsaturated^{44, 45}. Plants synthesize a wide variety of fatty acids, although only a few are major and standard constituents⁴⁶. So, the most abundant and significant fatty acids of *P. quinquefolia* seeds were palmitic, oleic, and linoleic acids, which evaluated the plant's seed extract for antioxidant capacity.^{20, 47} The most abundant and significant fatty acids of *P. quinquefolia* are demonstrated in Fig. 8.

Others

Other constituents of *P. quinquefolia* have been reported, including tropane alkaloid in glycosidic form, which was isolated from the chloroform fraction of the whole plant, and the proposed structure has been identified using liquid chromatography-mass spectrometry and Fourier transform infrared analysis. Butanol fraction of the whole plant could contain sennoside C, Asiatic acid or its analogue, Madecassic acid, and triglyceride 1, 2-dipalmitoyl-3-oleoyl-glycerol, which were identified based on the NIST library and multiple analytical tests⁷.

Pharmacological activity of *Parthenocissus quinquefolia*

Antidiabetic activity

Diabetes mellitus (DM), is a chronic metabolic illness, a significant global health issue, and one of the leading causes of morbidity in the world, with a significant burden in developing countries^{16,49}. The number of people with diabetes was 171 million in 2000; by 2030, it is predicted to reach 366 million^{50, 51}.

Exercise and diet are crucial for managing hyperglycemia, yet 90% of patients with type 2 diabetes struggle to maintain long-term glucose control and need antihyperglycemic medications to achieve this⁵².

An Indian Ayurvedic herb was tested for its antidiabetic properties in a Zucker diabetic rat model using blood insulin levels and an oral glucose tolerance test. To ascertain the plant's mode of action, 250 mg/kg body weight of lyophilized 70% ethanolic extract was used. Consequently, a potent antidiabetic impact was observed, wherein blood glucose levels decreased in direct proportion to insulin levels. This suggests that *P. quinquefolia* contributes to improving insulin release⁵³.

Anti-inflammatory activity

Inflammation is a body response and physiological defense mechanism against foreign

invaders or exposure to tissue injury, oxidative stress, or pre-existing disease^{54, 55}. Inflammation is of two types, acute and chronic, in which the accumulation of plasma proteins in tissues occurs, leading to increased fluid perfusion that results in swelling. This is followed by leukocyte release, which moves toward the affected area and subsequently releases cytokines, which are pro-inflammatory mediators and cause immune cell activation⁵⁶⁻⁵⁸. These cytokines include tumor necrosis factor-alpha and different types of interleukins (IL-1, 6, 8, and 10)^{47,59}.

Three groups of six albino rats of each gender, weighing between 150 and 170 g, were used to affirm the anti-inflammatory properties of *P. quinquefolia*. The first group received a vehicle, which is dimethyl sulfoxide, and was designed as a positive control. The second group received oral treatment with an n-hexane fraction of *P. quinquefolia* (250 mg/kg⁵³) by gastric gavage for seven consecutive days. Ten milligrams of diclofenac sodium were administered to the third group⁶⁰. This group is used as an indicator to determine the level of anti-inflammatory activity.

The plant's n-hexane fraction, which was analyzed using the GC/Mass technique, revealed that it contains unsaturated fatty acids, mainly oleic and palmitoleic acid. Through nuclear factor suppression, these fatty acids block the expression of pro-inflammatory cytokines such TNF α and IL-6, which contribute significantly to their reduction. DNA transcription, cytokine synthesis, and cell proliferation are all facilitated by the protein complex known as kappa-light-chain enhancer of activated B cell (NF)- κ B signaling. When NF- κ B translocates into the nucleus, two genes associated to inflammation, TNF- α and IL-6, are elevated^{61, 62}.

Furthermore, in the visceral adipose tissue, they inhibit NF- κ B activation and diminish messenger ribonucleic acid mRNA expression for IL6 and TNF- α . Also, Sirtin-1 (SIRT-1) is an enzyme in the cell nucleus and has a regulatory role in the cell⁶³. Similarly, polyphenols block the development of COX-2 enzymes, which convert arachidonic acid to prostaglandin, which is involved in swelling, discomfort, and redness and is released during inflammation⁶⁴. Thus, by reducing the percentage of exudate and granuloma in rat models of inflammation, *P. quinquefolia*

demonstrated its anti-inflammatory properties. Moreover, it markedly decreased serum levels of IL-6 and TNF- α ⁶⁵.

Antimicrobial activity

The ethanolic extract of *P. quinquefolia* roots functions as an antifungal agent against different fungal species like *yeast candida* and *Aspergillus niger*. Furthermore, it is used as an antibacterial agent against gram-positive bacteria like *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Bacillus subtilis*, and also against gram-negative bacteria like *Salmonella typhi*, *Pseudomonas fluorescense*, and *Klebsiella pneumonia* ²¹. *Aeromonas hydrophila* and *Aeromonas caviae* were significantly suppressed by *P. quinquefolia* aqueous extract, with 59.68% and 55.90% inhibition, respectively, in a study on antibacterial activity ⁶⁶. Therefore, *P. quinquefolia* evolves broad-spectrum activity against bacteria; again, this supports the traditional use of the plant.

Antioxidant activity

The ethanolic extract of *P. quinquefolia* bark and stem demonstrated a robust protective effect against free radicals, including reactive oxygen species produced in humans by both endogenous and external sources. The main factor stimulating many diseases is oxidative stress, such as degenerative and chronic diseases like diabetes mellitus, cardiac conditions, atherosclerosis, cancer, and immunosuppression ^{67, 68}. As a result, antioxidants are the most effective at eradicating free radicals ⁶⁹. On the other hand, the chloroformic extract of the leaves and berries revealed such high free radical-scavenging activity. These findings support the plant's traditional usage in treating dangerous human ailments ¹⁹.

Another hexane extract study demonstrated the strong antiradical activity of *P. quinquefolia* seed oil. The fatty acid content of the plant seeds, with oleic acid (21.96%), palmitic acid (20.61%), and linoleic acid (48.23%) as the main constituents, exhibits this activity ²⁰.

Medicine for treating eyelid eczema

Virginia creeper (*P. quinquefolia*) is formulated in combination with other plant materials (*Artemisia rupestris*, *saffron*, *Rubiaceae borreria stricta*, *C. sativus*, *Tea begonia*, and others) to produce a medicine for eyelid eczema.

That effect is exerted by prompting blood circulation, clearing toxins and heat, removing dampness, and moisturizing dryness ⁷⁰.

Thrombin inhibitor effect

Serious coronary disorders such as myocardial infarction and stroke are highly affected by blood coagulation control, which may represent the critical point in the treatment of these cases. The dichloromethane extract from *P. quinquefolia* applies a new effective antithrombin natural agent identified as amyrylhexadecanoate-amyrin ⁴².

CONCLUSION

Parthenocissus quinquefolia L. is a vibrant plant that produces a variety of valuable secondary metabolites such as stilbenes (trans-resveratrol, piceatannol, resveratrol 2-O- β -glucopyranoside, parthenocissins A, c-viniferin, pallidol, cyphostemmin A, and miyabenol C), polyphenolic compounds (phenolic acids like gallic acid, caffeic acid, chlorogenic acid coumaric acid, and flavonoids like quercetine-3-O- β -L-rhamnoside, myricetine-3-O- β -L-rhamnoside, quercitrin, rutin, quercetin, kaempferol, isorhamnetin, and luteolin), triterpene (β -Amyrine), fatty acids (palmitic acid, oleic acid, and linoleic acids), steroids (stigmasterol and β - sitosterol), an alkaloid (tropane alkaloidal compound in a glycosidic form), and others (sennoside C, Asiatic acid or its analogue Madecassic acid, and the triglyceride 1, 2-dipalmitoyl-3-oleoyl-glycerol). These important secondary metabolites support the pharmacological activity of *P. quinquefolia*, known for its antioxidant effect, antimicrobial, anti-diabetic, thrombin inhibitor effect, medicine for treating eyelid eczema, and anti-inflammatory effect.

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Conflicts of Interest

There are no conflicts of interest.

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