



Review Article

A REVIEW ON PHARMACOGNOSTIC, PHYTOCHEMICAL AND ETHNOPHARMACOLOGICAL FINDINGS OF *PEPEROMIA PELLUCIDA* (L.) KUNTH: PEPPER ELDER

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Article Received on: 12/10/17 Approved for publication: 03/11/17

DOI: 10.7897/2230-8407.0811211

ABSTRACT

Peperomia pellucida (L.) Kunth (Family Piperaceae) has been utilizing in folk medicine for many years worldwide and much research have been devoted. This review focused to summarize updated most interesting findings on the morphological, phytochemical, ethnopharmacological and toxicological aspects obtained in the research related to the plant. Local communities around the world have been consumed this plant as a leafy vegetable and in the treatment of gastrointestinal disorders including dysentery, diarrhoea, stomachache; respiratory tract disorders including asthma, nasopharyngeal infections, cough; skin diseases including eczema, wounds, abscess, acne, boils, scabies, dermatitis, rash, sores, scar, and warts, mucosae tumors and other ailments such as fever, paralysis, epilepsy, convulsions, heart problems, hypertension, kidney disorders, gout, rheumatic pain, conjunctivitis, and measles. This species has been extensively investigated as a source of natural pharmacologically active compounds with potential antimicrobial, anticancer, antipyretic, anti-inflammatory, antioxidant, analgesic, anti-diarrhoeal, antihypertensive and anti-oedematogenic activities. Phytochemical screenings on the plant have revealed the presence of various pharmacologically active principles of medical importance including tannins, flavonoids (acacetin, apigenin, isovitexin, and pellucidatin), cardiac and xanthone (Patuloside A) glycosides, alkaloids (secolignans, tetrahydrofuranlignans, peperomins A, B, C, and E, sesamin, and isoswertisin), saponins, inulins, terpenes, phenolic compounds, phytosterols (stigmasterol, sitosterol, and campesterol) and other steroids, and resins. *P. pellucida* also contains several essential oils, mainly dillapiole, β -caryophyllene, and carotol. The acute toxicity results revealed that this plant might be considered as a non-toxic plant with high therapeutic index. Much additional work is needed to open new biomedical application of these compounds.

Keywords: *Peperomia pellucida* (L.) Kunth, Pepper elder, shiny bush, ethnopharmacology, phytochemical, dillapiole.

INTRODUCTION

The Asian region of the world enriches with the vast diversity of herbal medicinal plants rich in ethnopharmacological properties that are widely used in different traditional medicinal systems; known as indigenous or folk medicine. The practice of traditional medicine is very popular and widespread in China, Japan, India, Pakistan, Thailand, and Sri Lanka and herbal medicinal preparations are more in demand. Majority of the people in developing countries of Asia and Africa utilize medicinally valuable plants on a regular basis for the primary health care¹. Ethnopharmacological knowledge on these plants has been used for the discovery, synthesis, and development of novel allopathic medicines. Therefore, it is essential to research on herbal medicinal plants to ensure their better utilization, conservation and to save them from extinction, overexploitation and negative consequences of climate changes²⁻³.

Peperomia pellucida (L.) Kunth, also known by the common names pepper elder, shiny bush, silver bush, rat-ear, slate pencil plant, clearweed and man to man⁴⁻¹⁰ which belongs to the family Piperaceae^{8,9,11-14}, is a common annual weed native to tropical North and South America¹⁴⁻¹⁶. In Sanskrit, this plant is known as “Toyakandha or Varshabhoo”¹⁷. The name had been derived from the Latin per (through) and lucidus (clear), referring to the somewhat translucent appearance of this plant¹⁸. It is now pantropic in distribution and is abundantly available in Sri Lanka

and locally known as “Diya Thippili” or “Wathura Gas”^{4,19}. Although this plant is considered as a weed, it has been used by Ayurvedic and traditional physicians in Sri Lanka⁴. It has been utilized in folk medicine for many years worldwide and much research have been devoted. This review focused to summarize updated available evidence on the ethnobotanical uses, phytochemical constituents, pharmacological and toxicological studies of *P. pellucida*.

TAXONOMICAL CLASSIFICATION AND BOTANICAL DESCRIPTION OF *P. PELLUCIDA* (L.) KUNTH

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida (Dicotyledonae)
Sub-class: Magnoliidae
Order: Piperales
Family: Piperaceae (Pepper family)
Genus: *Peperomia* Ruiz & Pav
Species: *pellucida*
Botanical name: *Peperomia pellucida* (L.) Kunth
Former botanical name: *Piper pellucidum* (L.)^{6,9,10,17-18,20-21}

P. pellucida is an annual or short-lived perennial, entirely delicate, fleshy and glabrous herb usually growing to a length of about 15-45 cm^{13,16}. Stems are translucent pale green¹⁷, erect or ascending or decumbent, freely branched^{12-13,18-20}, internodes usually 3-8 cm long and hairless¹⁷. Petioles are 1-2 cm long¹². Its

light-green leaves are alternate throughout^{13,19}, well-spaced and succulent¹⁶. Stipules are absent¹⁸. The leaf blade is broadly ovate or ovate-triangular to deltate (heart shaped), 1-3.5 cm length, length ± equal to the width, cordate at the base with a sinus 1–2 mm deep, thinly membranous, both surfaces glabrous, translucent, palmately 5-7-veined^{5,12,20}. It has very small bisexual flowers growing in the form of cord-like spikes. Spikes are slender, solitary, terminal or leaf-opposed (at the opposite side of leaves), and arising from the leaf axils. Mature fruiting spikes are 2-6 cm long and 1-2 mm in diameter. Flowers are loosely flowered, bracts suborbicular, 0.5 mm wide and short-stalked. A flower has two stamens¹⁸. Anthers are sub-globose. The ovary is ellipsoid. Stigmas are pubescent^{12-13,19}. The fruits are drupe, tiny, dot-like, round to oblong, 0.5-0.7 × 0.4-0.5 mm, ridged, sessile, longitudinally ribbed with the ladder like reticulations; beak minute, conic^{13,17,20}, and first green, blackish brown at maturity^{17,19}. They have one single seed¹⁷ and a mustard-like odor when crushed^{17,22}.

ORIGIN, GEOGRAPHICAL DISTRIBUTION AND HABITAT

P. pellucida is native to tropical North and South America^{7,11-15,17-18,21}. It is now widely distributed throughout the tropics (America, Africa, and Asia) and is often naturalized as a weed and occasionally cultivated^{7,11,14,16,21,23}. It is often epiphytic, terrestrial and occasionally a lithophyte^{9,18}. It grows in clumps, thriving in loose, humid soils^{5,16}, during rainy periods (often in the spring)^{11,16} and a tropical to subtropical climate. Flowering year-round, the plant is found in various shaded and damp habitats within woods, forests, rock crevices, bases of cliffs, sometimes a weed of cultivation; around nurseries and greenhouses and along coastal plain all over Asia and the America near sea level to 200-2000 m^{10,12-14}.

ETHNOMEDICINAL USES OF *P. PELLUCIDA* BY VARIOUS COMMUNITIES AROUND THE WORLD

Leaves and stems of pepper elder are frequently consumed as a spicy leafy vegetable cooked or in salads and condiment in many parts of the tropics. In Africa, it is occasionally cultivated for the food purpose⁷. The whole plant is traditionally prescribed in folk medicine of various countries^{15,16,21,24} and the ethnomedicinal uses are vary depending on the region²⁴. It is sometimes grown as an ornamental container plant⁷.

Ayurvedic and traditional physicians in Sri Lanka have been used this plant for various ailments. The leaves and inflorescence are used in the treatment of diarrhoea, dysentery, nasopharyngeal infections, paralysis, epilepsy, convulsions, skin; mucosae tumors and cancers¹⁹. The entire plant is crushed and rubbed over the burned area to reduce burning sensation and to prevent blisters⁴.

An ethnomedicinal survey conducted in Bangladesh among folk medicinal practitioners has revealed that *P. pellucida* is used in the treatment of gastrointestinal disorders such as dysentery, diarrhoea, stomachache, respiratory tract disorders; asthma, bronchitis, pneumonia, cold, cough, mucus, influenza, and tonsillitis, sore throat and skin diseases including eczema, abscess, acne, boils, scabies, itch, infections, dermatitis, rash, sores, scar, and warts²⁵. The juice of the leaves is being used by the local people of Bangladesh to relieve a cough and fever, as a remedy for colds, diarrhea, heart problems, hypertension²⁶ and in the treatment of excited mental disorder^{23,27}. In India, the whole plant is used to treat a cough, kidney disorders (dysuria, urinary retention, and urinary tract infections), and general weakness²⁸.

The decoction of the roots is used for tumors by the Mog communities of Tripura State, in northeast India²⁹.

Southeast Asians use the crushed mixture of this plant with water to cure haemorrhage in wounds²⁶, as a traditional wound healing medicine as well as a wound dressing material^{24,30} and to control abdominal pain²⁶. *P. pellucida* has been recognized as one of the top ten herbal medicines approved by the Department of Health in the Philippines, due to its variety of valuable medicinal properties³⁰. The wine infusion or decoction of the whole plant is taken orally for gout and kidney troubles and applied externally as a rinse against complexion problems. The warmed leaves are applied to sores and boils^{7,31} and according to the Manila Medical Society, it is used to relieve arthritic pains, but it may cause Central Nervous System (CNS) depression²⁷. In Indonesian traditional medicine, this plant is incorporated in the treatment of wounds, boils, abscesses, pimples, abdominal pain, colic, gout, rheumatic pain, fatigue, kidney disease, furuncles, eye inflammation (conjunctivitis), dengue³², and as an antihypertensive³³. The crushed leaves are used to treat dizziness or headaches if the patient has a fever²⁸. In Malaysia, the plant is known as 'ketumpang air' and it has been used for treating various ailments such as abdominal pain, indigestion, abscess, acne, boils, colic, gout, headache, renal disorders, breast cancer, impotence, measles, mental disorders, smallpox¹⁶, fatigue, and rheumatism²⁶.

Many countries in tropical America used this plant in folk medicine. Fresh juice of leaves and stems is used to treat conjunctivitis in South America^{17,30}. In Brazilian folk medicine, the whole herb is used as a diuretic, cough suppressant and an emollient, to control cardiac arrhythmia^{30,34}, to treat abscesses, furuncles, skin sores and conjunctivitis^{24,30,35}. In Northeastern Brazil, the whole plant is also used to lower the cholesterol levels in the blood (hypocholesteremic agent)²⁴, to cure haemorrhage, fever, abdominal pain, boils, renal disorders, rheumatic pain, mental disorder, eaten as a salad for the treatment of gout and arthritis²². The whole plant is crushed, mixed with water, heated and then administered orally to stop haemorrhages by Altenos Indians in Bolivia^{1,23,30}. The solution of the fresh juice of leaves and stem is used against conjunctivitis in Surinam⁷. In the Amazon region of Guyana, the plant has been used as a cough suppressant, emollient, diuretic, in the treatment of cardiac arrhythmia, proteinuria, and hypercholesterolemia³⁵⁻³⁶.

P. pellucida had been reported in Nigeria and other West African countries as being effective and commonly used to manage various ailments by traditional health practitioners³⁷. It is one of the most prominent plant species incorporated into the commonly used recipes in the treatment of measles^{1,36} and hypertension^{5,33} in Nigeria. The infusion added with milk is ethnomedicinally described to boost the immune system of sick people²³. The aerial parts are used generally as a tonic for healthy well-being⁵ and is employed in the treatment of diabetes, abscesses, furuncles, skin sores, conjunctivitis⁵, abdominal pain, acne, boils, colic, fatigue, gout, headache, renal disorders, rheumatic pain, breast cancer, impotence, female sterility, mental disorders, cardiac arrhythmia, and small pox^{7,36}. In Nigeria and Congo, it is used as an ingredient of an infusion for treating convulsions⁷. An infusion of the plant or a maceration, mixed with salt and palm oil, is taken against a cough in Congo⁷. The aqueous extract is commonly used in Cameroonian traditional medicine for the management of fracture¹¹.

In addition to above, the plant species has a history of other ethnomedicinal uses which include in the treatment of malaria and as a facial rinse for acne and complexion problems³⁰. However, there has not yet been validated clinical data with

regards to *P. pellucida* dosing but the patients with known hypersensitivity reactions to any of the components of the plant species are contraindicated to its use. Nursing mothers have also been contraindicated due to pharmacologically active components of this plant interfere with prostaglandin synthesis³⁶.

PHARMACOLOGICAL ACTIVITIES OF DIFFERENT EXTRACTS OF *P. PELLUCIDA*

This species has been extensively investigated as a source of natural pharmacologically active compounds with potential antimicrobial, anticancer, antipyretic, anti-inflammatory, antioxidant, analgesic, and anti-oedematogenic activities.

Antimicrobial Activity

P. pellucida has shown a broad spectrum of antibacterial activity against gram-positive bacteria; *Staphylococcus aureus*, *Bacillus subtilis*^{13,22,36} and gram-negative bacteria; *Escherichia coli*^{13,22,36,38}, *Pseudomonas aeruginosa*^{13,22,30,36,38}, *Klebsiellae pneumoniae*, *Salmonellae typhi*^{36,38}, *Enterobacter aerogenes*²², *Edwardsiella tarda*, *Flavobacterium* sp., *Aeromonas hydrophila*, *Vibrio cholera*, *Vibrio alginolyticus*, and *Vibrio parahaemolyticus*³⁸. The aqueous and ethanol extracts of the leaves have shown no anti-Methicillin Resistant *Staphylococcus aureus* (anti-MRSA) activity on clinical MRSA isolates³⁹. In addition, this plant extracts have shown antifungal activity against *Candida albicans*, *Rhizopus stolon*, *Aspergillus niger*, *Penicillium notatum*³⁶, and *Trichophyton mentagrophyte*⁴⁰. Another study has revealed the potential of the macerated methanol extract of this plant as an antimalarial against *Plasmodium falciparum* using Desjardin method⁴¹.

An antibacterial study performed using agar-well diffusion method for the aqueous and ethanol leaf extract of *P. pellucida* has reported that the ethanol extract had shown its highest inhibitory activity on *Proteus mirabilis* and *Pseudomonas aeruginosa* while water extract had shown its highest inhibitory activity on *E. coli*⁴². N-hexane, ethyl acetate, and ethanol extracts of *P. pellucida* whole plant that grows around Ekiti State, Nigeria had exhibited antimicrobial activity against *E. coli*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Ethanol extract had exhibited the least potency whilst the N-hexane extract had exhibited the strongest potency with the zone of inhibition 10-12 mm at the concentration of 25 µg/mL²³.

According to the results of a study done by Zubair et al; 2015, the inhibition of bacterial growth of all strains by the hexane, chloroform, ethyl acetate, ethanol, and water extracts of leaves of *P. pellucida* was dose-dependent as evident by the higher zone of inhibitions at higher concentrations. The antibacterial activity had been compared with the 10 mg/mL standard antibiotic penicillin. Hexane extracts had appeared to be the most effective extract. None of the water extracts had shown any antibacterial activity. Chloroform extracts were inactive against all the gram-positive bacteria tested (*Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus cereus*). The antibacterial activity of the extracts was more prominent on the gram-negative bacteria (*E. coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens* and *Salmonella typhi*) than the gram-positive bacteria²⁶. Plant extracts often contain polyphenols and flavonoids which could be the antimicrobial components as suggested by Zubair et al; 2015.

These previous studies have shown the potential usefulness of *P. pellucida* in the treatment of various pathogenic diseases which in the future can be developed as a potential antimicrobial agent.

Anticancer Activity

Peperomin E isolated from this plant had shown anticancer activity/growth inhibitory effects on the cancer cell lines HL-60 (human acute promyelocytic leukemia), MCF-7 (human breast adenocarcinoma), and HeLa (human cervical cancer). The compound 7,8-*trans*-8,8'-*trans*-7',8'-*cis*-7,7'-bis(5-methoxy-3,4-methylenedioxyphenyl)-8-acetoxymethyl-8'-hydroxymethyltetrahydrofuran had exhibited estrogen-like properties in MCF-7 cell line^{30,43}. Anticancer activity of *P. pellucida* leaf extract had also been observed through Colorimetric MTT (tetrazolium) assay against MCF-7 cell line with the half maximal inhibitory concentration (IC₅₀) of 10.4 ± 0.06 µg/mL³⁸.

Antipyretic Properties

Intra-peritoneal administration of petroleum ether and ethyl acetate soluble fractions of ethanol extract of the leaves had shown a significant reduction in the elevated body temperature of rabbits and their antipyretic effects were comparable to that of a standard antipyretic drug, aspirin. This study supports the claims of *P. pellucida* by traditional medicine practitioners in the treatment of fever as an antipyretic remedy⁴⁴.

Antioxidant and Anti-Inflammatory Properties

Antioxidant activity of the crude extracts of this plant had been determined using 2,2-diphenyl-picrylhydrazyl (DPPH) radical scavenging assay^{30,38,45}. Another study had determined the high antioxidant activity of *P. pellucida* even at low concentrations using the scavenging effect on DPPH, hydroxyl radical and ferric thiocyanate compared to the antioxidant standards; butylated hydroxyl anisole (BHA), ascorbic acid, and α -tocopherol³⁶.

Petroleum ether, chloroform, and methanol extracts of this plant had shown antioxidant activity using DPPH assay and anti-inflammatory properties using the Carrageenan-induced rat hind paw oedema method. And the total phenolic content of the methanol extract (6.93 %) had shown the highest free radical scavenging activity⁴⁵. The potent antioxidant activity of the crude methanol extract of this plant was due to its ability to elevate superoxide dismutase and catalase and lower thioltransferase and thioredoxin reductase activities in rat liver under oxidative stress⁴⁶. Oral administration of the plant extract in rats had been confirmed to interfere with the synthesis of prostaglandin, thus acting as an anti-inflammatory and analgesic agent²².

Phongtongpasuk & Poadang; 2014, had conducted a research to investigate the effect of two extraction techniques; maceration and reflux and three extracting solvents; methanol, butanol, and ethyl acetate on the yield and antioxidant activity of *P. pellucida*. The results have shown that the methanol extract by reflux method offered the highest extraction yield. Ethyl acetate extract by reflux method had the highest total phenolic contents and the highest antioxidant activity evaluated by DPPH assay. The antioxidant activity was drastically different and depended upon the extracting solvent and extraction method used⁴⁷. Mohamad et al; 2015, had shown that different drying methods used in their study did not affect the antioxidant and antimicrobial activity and chemical constituents of this plant extracts. Hence expensive drying methods are not compulsory, and it is economically beneficial.

A study had shown that *P. pellucida* has a phenological cycle of approximately 100 days. Researchers had tested the anti-inflammatory potential of the aqueous extract during the four distinct development phases (Complete development, the

beginning of bloom, complete bloom, and seed set) to detect differences in its potency. Aqueous extracts had significant anti-inflammatory activity during phenophases 1 and 2 of winter and spring. Depending on the plant's phenophase there was variation in the potency of oedema inhibition³⁵.

An experimental design had been conducted for the ethanol extract of *P. pellucida* using the enzyme xanthine oxidase and xanthine as the substrate. Inhibition of xanthine oxidase had determined enzymatically with the IC₅₀ of 19.5 ppm. IC₅₀ of allopurinol was 1.99 µg/mL. They have proved that the ethanol extract of *P. pellucida*, has efficacy to reduce levels of uric acid excess by inhibiting the action of the enzyme xanthine oxidase⁴⁸. Hence *P. pellucida* had efficacy to reduce levels of uric acid excess and this claims the ethnomedicinal use of this plant in the treatment of gout.

The high antioxidant activity of *P. pellucida* at low concentrations stipulates that it could be very useful in the treatment of ailments resulting from oxidative stress and further corroborates the ethnomedicinal uses.

Fracture Healing Effects

Orally administered aqueous extract of the whole plant of *P. pellucida* had shown fracture healing effects in female Wistar rats (drill-hole injury model). The aqueous extract had increased bone calcium levels at the lowest dose (100 mg/kg) but maintained this parameter at a normal range at the high dose (400 mg/kg) in fractured rats. Alkaline phosphatase and phosphorus concentrations reduced significantly ($p < 0.01$) at the dose of 400 mg/kg as compared to fractured rats. Radiological tests had revealed a dose-dependent formation of a highly dense and compact fibrocartilaginous callus at the level of the fracture gap. The mineral content of the plant extract had revealed the presence of calcium, phosphorus, magnesium, sodium, and potassium. The aqueous extract of *P. pellucida* had accelerated bone healing due to the considerable mineral content of the extract. These results claim its incorporation into traditionally used recipes in the treatment of bone fractures¹¹.

Antidiarrhoeal Activity

Plant extracts at a dose of 250 mg/kg and 500 mg/kg had shown antidiarrhoeal activity by inhibiting castor oil induced intestinal accumulation of fluid in male and female white albino mice. Literature had documented that antidiarrhoeal and antidysenteric properties of medicinal plants were due to flavonoids, alkaloids, tannins, saponins, and sterols. Tannins, sterols, and alkaloids present in the leaves might be responsible for the antidiarrhoeal activity of *P. pellucida*²⁶.

Central Nervous System (CNS) Depressant Effects

Diazepam-induced sleep, nikethamide-induced toxicity, light-dark test and force swimming test had been performed in mice for petroleum ether and ethyl acetate fractions of ethanol extract of leaves. Results of this study revealed that it contained psychoactive substances which are CNS depressant in nature. The folk medicinal uses of *P. pellucida* for convulsions, in the treatment of the excited mental disorder and its CNS depressant effects, agree with their experimental results. CNS depression had been reported as the neurotoxic effects of styrene isolated from this plant²⁷.

Antidiabetic Activity

Antidiabetic activity of ethanol extract of *P. pellucida* had been investigated in alloxan-induced diabetic albino male rats. Ethanol extract at the dose 1000 mg/kg had shown the better reduction of blood glucose level than the dose 500 mg/kg⁵

Cytoprotective Effect

The ethanol extract of the aerial part of *P. pellucida* had produced significant dose-dependent inhibition of gastric mucosal damage induced by cytodestructive agents (80 % ethanol, 25 % sodium chloride, 0.6 M hydrochloric acid, 0.2 M sodium hydroxide and 30 mg/kg indomethacin) at all doses (10, 30, 100 and 300 mg/kg) in the experimental models of rats. The result suggested that *P. pellucida* possesses anti-ulcer properties as claimed by the ethnomedicine. The findings have justified the traditional use of the plant to treat abdominal pain. Therefore, we can postulate that this plant may have cytoprotective factors based due to the reduction of total lesion area when induced with necrotizing agents¹⁶.

Immunostimulatory Effect

A study has shown the huge potential of *P. pellucida* leaf extract as a natural immunostimulant in controlling motile aeromonad septicemia due to *Aeromonas hydrophila* in red hybrid tilapia, *Oreochromis* sp. The significantly higher value of antibody response to *A. hydrophila* in fish which had been determined by enzyme-linked immunosorbent assay and significantly lower percentage cumulative mortality of fish received medicated feed compared to fish did not receive medicated feed ($p < 0.05$), had been observed. Hence, this plant extract can be incorporated into the fish feed to manage fish health for aquaculture uses⁴⁹.

In Vitro Thrombolytic Activity

The results of a study conducted in Bangladesh to determine in vitro thrombolytic activity revealed that the activity of various extracts had been found in the range of 10.87-55.56 %. The ethanol soluble fraction had exhibited the highest percentage lysis of the clot, hence the highest thrombolytic activity comparable to the standard drug, streptokinase among the hexane soluble fraction, chloroform extract, and aqueous soluble fraction²⁶.

Antihypertensive Activity

Kurniawan et al; 2016, had isolated and determined the chemical structure of the flavonoid (3',4'-Dihydroxy-3-5-dimethoxyflavone-7-O-β-rhamnose) which was responsible for the Angiotensin-converting enzyme (ACE) inhibitory activity from the methanol extract of the aerial part that claims the traditional use of this plant as an antihypertensive. The IC₅₀ value for the in vitro ACE inhibitory activity was 7.72 µg/mL. They had suggested this compound inhibits the enzyme activity by competing with the substrate for the active site³³.

A dose-dependent reduction in systolic, diastolic, mean arterial pressure and heart rate had been observed in Sprague-Dawley rats following intravenous administration of *P. pellucida* aqueous plant extract (10-30 mg/kg) and displayed moderate inhibition of CYP3A4 enzyme activity. Their results suggested that the dose-dependent hypotensive, bradycardic and vasorelaxant effects of this extract were mediated through Nitric oxide-dependent mechanisms. The impact on CYPs enzyme activities indicates unlikely adverse drug effect when *P. pellucida* is consumed with other medications reliant on CYP3A4 metabolism⁸.

Cholesterol Reduction Effects

Isolation of styrene, campesterol, stigmasterol, and β -sitosterol from this plant had been reported. Cholesterol biosynthesis and cholesterol absorption had been reduced by increased sitosterol, campesterol, and stigmasterol levels²⁷. This claims the traditional use of this plant as a hypocholesteremic agent.

ACUTE TOXICITY STUDIES OF *P. PELLUCIDA*

The acute toxicity results of *P. pellucida* revealed that this plant might be considered as a non-toxic plant with high therapeutic index²⁷. Oloyede et al; 2011 had reported that the methanol, hexane, and ethyl acetate fractions of methanol extract of leaves were toxic while the most polar fractions butanol and aqueous fractions were non-toxic by performing the brine shrimp lethality test. Patuloside A isolated from this plant have shown cytotoxic properties to brine shrimp naupli³⁰. Observations of a toxicity study of methanol extract for 14 days (at the dose 500, 1000, 2000, and 4000 mg/kg) had shown that there was no mortality and no symptoms of toxicity on the skin and hair, defecation, feed intake, respiratory system and in behavior between control and the test group of rats. Histopathological observation showed no specific abnormalities in heart, liver, and kidney²⁸.

PHYTOCHEMICALS PRESENT IN *P. PELLUCIDA*

Preliminary and qualitative phytochemical screening on the plant *P. pellucida* have revealed the presence of various pharmacologically active principles of medical importance including tannins^{5,22-23,26,28,36-37}, flavonoids^{5,22-23,26,28,37}, cardiac, xanthone and other glycosides^{5,22-23,37}, alkaloids^{22-23,36-37,41}, saponins^{22,37,41}, inulins³⁷, terpenes, phenolic compounds, phytosterols^{30,37,41} and other steroids^{28,36,41}, resins and carbohydrates³⁶.

New structures of the pharmacologically active principles had been elucidated based on chromatographic and spectroscopic methods mainly by Nuclear Magnetic Resonance (NMR) and Mass Spectroscopy (MS) and evaluation of their biological activities have been reported in the literature. The phytochemicals present in the plant were alkaloids, namely, secolignans, tetrahydrofuranlignans, as well as, highly methoxylated dihydronaphthalenone, peperomins A, B, C, and E, sesamin, and isoswertisin. *P. pellucida* also contained several essential oils, mainly dillapiole, β -caryophyllene and carotol that have high larvicidal activities. Other compounds are flavonoids such as acacetin, apigenin, isovitexin, and pellucidatin, substituted styrenes and anthraquinone. Phytosterols such as stigmasterol, sitosterol, and campesterol had been successfully isolated from dichloromethane extract of the plant^{8,11-15,23,30,34,41,43}.

Phytol had been identified as the major bioactive compound and 2-Naphthalenoldecahydrohexadecanoic acid, methyl ester and 9,12-Octadecadienoic acid (Z, Z)-methyl ester had been identified as the other phytochemicals presented GC/MS^{38,49}. Bayma et al; 2000, had isolated a novel dimeric ArC2 compound named Pellucidin A, together with the known phenylpropanoid dillapiole from the methanol extract of aerial parts of *P. pellucida*. The isolation and characterization of the compounds from hexane and ethyl acetate fraction of ethanol extract had resulted in three compounds named stigmasterol, analogue pheophytin, and β -sitosterol-D-glucopyranoside³².

Another study has reported that thirty-two compounds had been identified by using GC/MS technique from the ethanol extract of the whole plant. Apinol was found to be the major component

followed by (3-Methoxy-nitrophenyl) acetic acid, methyl ester, Phytol, n-Hexadecanoic acid, E-2-Tetradecen-1-ol, 5H-Cyclopropa(3,4)benz(1,2-e)azulen-5-one, 4,9,9a-tris(acetyloxy)-3-[(acetyloxy)methyl], Stigmasterol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, Campesterol, α -Sitosterol, 9,12,15-Octadecatrienoic acid, (Z,Z,Z), Z,Z-2,5-Pentadecadien-1-ol and 3-Hydroxy-4-methoxycinnamic acid⁵⁰.

A xanthone glycoside isolated from this plant named Patuloside A, and arylpropanoids had demonstrated weak antifungal and antibacterial activity while peperomins had exhibited anticancer activity^{15,30,43}. Dillapiole and Pachyophyllin from the chloroform extracts of air-dried leaves had been elucidated by NMR were active against the fungi *Trichophyton mentagrophyte*⁴⁰.

A study on the nutritional and mineral profile of this plant done in Malaysia using atomic absorption spectrometry had determined that *P. pellucida* be rich in crude carbohydrate, protein, and total ash contents. A high-value mineral composition comprises calcium, iron, and potassium as the main elements. They suggested that this plant would serve as a good source of protein and energy as well as micronutrients in the form of a leafy vegetable for human consumption¹⁵.

A commonly used medicinal plant over long durations containing high concentrations of natural radionuclides can cause health problems. Sussa et al; 2013, had conducted a study to determine the natural radioactivity in a sample of *P. pellucida*. The level of radionuclides determined in this study presented the same order of magnitude or slightly higher concentrations than that vegetable foodstuff, tea and herbal medicines concentrations reported in the published literature²⁴.

CONCLUSION

This review summarized updated available evidence on the taxonomy, ethnobotanical uses, phytochemical constituents, pharmacological and toxicological studies of the valuable plant *Peperomia pellucida* (L.) Kunth. This is widely used in different traditional medicinal systems for various ailments such as gastrointestinal disorders, respiratory tract disorders, skin diseases, neurological disorders, heart problems, kidney disorders, rheumatic pain, conjunctivitis, and in the management of fractures. This species has been extensively investigated as a source of natural pharmacologically active compounds with potential antimicrobial, anticancer, antipyretic, anti-inflammatory, antioxidant, analgesic, antidiarrhoeal, antihypertensive and anti-oedematogenic activities. Phytochemical screenings on the plant have revealed the presence of various pharmacologically active principles of medical importance including tannins, flavonoids, glycosides, alkaloids, saponins, terpenes, phenolic compounds, phytosterols and other steroids. *P. pellucida* also contains several essential oils, mainly dillapiole. This review will be useful for further studies on this plant. More research is needed to isolate and characterize bioactive constituents and establish clinical studies, to explore the potential uses of *P. pellucida* that may contribute to drug development.

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Cite this article as:

A.A.M.D.D.N. Amarathunga and S.U. Kankanamge. A review on pharmacognostic, phytochemical and ethnopharmacological findings of *Peperomia pellucida* (L.) Kunth: Pepper elder. Int. Res. J. Pharm. 2017;8(11):16-23 <http://dx.doi.org/10.7897/2230-8407.0811211>

Source of support: Nil, Conflict of interest: None Declared

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