



REVIEW ARTICLE

A Comprehensive Review of *Peperomia pellucida*: Chemical Composition, Traditional and Pharmacological Uses, and Potential in Dermatitis Management

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Abstract

Peperomia pellucida has been used widely in ethnomedicine and many studies have been conducted on this plant. Locals have been using this plant in traditional medicine and consumed as food. This review summarized previous studies conducted on this plant, focusing on plant's chemical composition, pharmaceutical and traditional uses, pharmacological activities and dermatitis management. *P. pellucida* contains phytochemical groups, namely alkaloids, tannins, resins, flavonoids, steroids, phenols and carbohydrates, while the nutritional and mineral profile revealed that the plant is rich in crude protein, carbohydrate and total ash content. Traditionally, this plant has been used to treat different medicinal conditions such as conjunctivitis, convulsions, fatigue, fever, headache, gout, rheumatic pains, skin diseases that include dermatitis, acnes and eczema, breast cancer and diabetic. Studies reported that the plant possesses antimicrobial, anticancer, antidiabetic, and antioxidant activities. The natural pharmacological activities and active compounds in *P. pellucida*, namely tannins, saponins and flavonoids have been shown to help in managing dermatitis. This review concludes that *P. pellucida* can be utilized as a promising candidate for developing new therapeutic drug for the treatment of various diseases including dermatitis.

Keywords: Peperomia pellucida, ethnomedicine, dermatitis, alternative therapeutic drug

Introduction

Peperomia pellucida is a common annual weed that are mostly found in North and South America and Asian countries (Kartika et al., 2016; Roslida & Noor, 2009; Ho et al., 2022). They are mostly known as silver bush or shiny bush that belongs to a family of *Piperaceae*. *P. pellucida* is also known by other names in the country where they are found. In Malaysia, it is known as 'Sireh Cina' or 'Ketumpangan Air'. In other parts of the world, it is known as pak-krasang (Thailand), kaca-kaca or surukan (Indonesia), Silverbush, Man-to-Man, Pepper Elder or Rat Ear (North America), Usuba Sunakosho (Japan) and others (Ooi et al., 2012).

Peperomia pellucida grows in a damp, moist places and it grows erect and succulent. The stem is fleshy, round, delicate, and glabrous. The leaves are medium green on the upper surface and whitish green on the lower surface. The leaves are thinly fleshy, broadly ovate, heart-shaped at the base and smooth on both surfaces (Mosango, 2008). *Peperomia pellucida* is grouped under family *Piperaceae* and order Piperales (Mosango, 2008).

Composition of Peperomia pellucida

Peperomia pellucida is a complex mixture of proximate, mineral and chemical composition. Phytochemical studies revealed that *P. pellucida* contains a variety of chemical constituents. Studies revealed the presence of saponins, tannins, flavonoids, essential oils, pellucidin, steroid, alkaloids, cardiac glycosides, inulins, phenolic compounds, resins and carbohydrates (Kartika et al., 2016). A study on the proximate, nutritional and mineral composition of *P. pellucida* revealed that the plant is rich in crude protein, carbohydrate and total ash content. The plant consists of 93.14% moisture content in the fresh whole plant form (Ooi et al., 2012). Even in dry state, moisture content of the whole *P. pellucida* plant still accounts for 8.33%. The moisture content of the plant is contributed mostly by the bulk tissue weight of fleshy and succulent stem. Whereas the protein (10.63%) and lipid (3.24%) contents of *P. pellucida* is comparable to other leafy vegetables, where the protein content ranged from 1 to 7% of fresh weight or 8 to 30% of dry weight basis. *Peperomia pellucida* also contains a high level of total ash content (31.22%). High level of total ash content indicates a high level of minerals content. In the same study, *P. pellucida* is revealed to have high minerals content such as potassium, calcium and iron.

A phytochemical study done by (Oloyede et al., 2011) using crude methanolic extract of *P. pellucida* revealed the presence of alkaloids, tannins, resins, flavonoids, steroids, phenols and carbohydrates. Another phytochemical screening also showed that the methanolic extract of *P. pellucida* contains flavonoid, tannin and steroid. However, in that study, alkaloids, saponins and quinon observed to be absent (Waty et al., 2017). Phytochemical study of *P. pellucida* using an ethanolic extract revealed the presence of several different chemical constituents. They are tannin, saponin, flavonoids, reducing sugar and cardiac glycosides (Awe et al., 2013). Another study to determine the bioactive compounds of *P. pellucida* was done using the gas chromatography-mass spectrum technique (GC-MS). The study using GC-MS identified thirty-two compounds from the ethanolic extract of *P. pellucida* and apiol was found to be major compounds followed acetic acid methyl ester and phytol. All compounds identified were organic compound, sesquiterpene, ether compound, alcoholic compound, palmitic acid, diterpene, linoleic acid, ketone compound, phenolic compound, steroids and others (Narayanamoorthi et al., 2015). Besides, recent study showed that the plant's ethanolic extract consists of refrofactamide B, trihydroxybutyrophenonevelutin, and dehydroretrofractamide C (Gomes et al., 2022).

Pharmaceutical and traditional use of Peperomia pellucida

Peperomia pellucida can be found in various countries and their use varies according to the countries they are found. The leaves and stems are commonly consumed as vegetable or

condiment in many parts of the tropics. Other than being consumed as food, the plants are also traditionally prescribed in folk medicine. The plants have been widely used to treat different medicinal conditions such as conjunctivitis, convulsions, fatigue, abdominal pain (Roslida & Noor, 2009), fever, headache, gout, rheumatic pains, skin diseases (Mollik et al., 2010), breast cancer (Lee et al., 2011) and diabetes (Hamzah et al., 2012). Table 1 shows traditional use of *P. pellucida* worldwide.

Countries	Traditional use	References			
Philippines	Gout, kidney problems, sores, boils, and arthritic pain	Mohamad et al., 2015; Pinarok et al., 2015			
Indonesia	Wounds, boils, abscesses, pimples, abdominal pain, colic, gout, rheumatic pain, fatigue, kidney disease, furuncles, eye inflammation (conjunctivitis), dengue, and antihypertensive medicine	Hartati et al., 2015; Kurniawan et al., 2016			
Malaysia	Abdominal pain, indigestion, abscess, acne, boils, colic, gout, headache, renal disorders, breast cancer, impotence, measles, mental disorders, smallpox, fatigue, and rheumatism	Zubair et al., 2015			
Nigeria	Measles and hypertension	Oloyede et al., 2011; Kurniawan et al., 2016			
Cameroon	Bone fracture	Florence et al., 2017			
Brazil	Haemorrhage, fever, abdominal pain, rheumatic pain, gout and arthritis	Awe et al., 2013			

Table 1.	Traditional	use of Pe	peromia p	oellucida a	as alternative	medicine	worldwide
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Peperomia pellucida is crushed and then mixed with water by the Southeast Asians to treat haemorrhage in wounds. It acts as a traditional wound healing medicine, as a wound dressing material and as an abdominal pain reliever (Mohamad et al., 2015; Sussa et al., 2015). In the Philippines, the Department of Health has recognised and approved *P. pellucida* as one of the top ten herbal medicines because of the variability and valuable medicinal properties (Mohamad et al., 2015). The wine infusion or decoction of the whole plant is taken orally for gout and kidney problems and applied externally as a rinse against complexion problems.

The warmed leaves are applied to sores and boils and according to the Manila Medical Society, it is used to relieve arthritic pains, but it may cause Central Nervous System (CNS) depression (Khan et al., 2008; Pinarok et al., 2015). In Indonesian traditional medicine, *P. pellucida* is used in the treatment of wounds, boils, abscesses, pimples, abdominal pain, colic, gout, rheumatic pain, fatigue, kidney disease, furuncles, eye inflammation (conjunctivitis), dengue, and as an alternative antihypertensive medicine (Hartati et al., 2015; Kurniawan et al., 2016). The crushed leaves are used to treat dizziness or headaches if the patient has a fever (Waty et al., 2017). In Malaysia, the plant has been used in treating various ailments such as abdominal pain, indigestion, abscess, acne, boils, colic, gout, headache, renal disorders, breast cancer, impotence, measles, mental disorders, smallpox, fatigue, and rheumatism (Zubair et al., 2015).

Tropical countries in America have been using this plant in folk medicine. In South America, fresh juice obtained from *P. pellucida* leaves has been used to treat conjunctivitis (Mohamad et al., 2015). In Brazil, the whole plant is used for variety of ailments, including cough suppressant, abscesses, skin sores, conjunctivitis, cardiac arrhythmia and diuretic medicine (Arrigoni-Blank et al., 2002; Sussa et al., 2013) . In North-eastern Brazil, the whole plant is also used to reduce blood cholesterol level, to cure haemorrhage, fever, abdominal pain, rheumatic pain, gout and arthritis (Awe et al., 2013).

P. pellucida has been reported in Nigeria and other West African countries as being effective and commonly used to manage various ailments by traditional health practitioners. It is one of the most prominent plant species incorporated into the commonly used recipes in the treatment of measles (Oloyede et al., 2011) and hypertension (Kurniawan et al., 2016) in Nigeria. The aerial parts are used generally as a tonic for healthy well-being and is employed in the treatment of diabetes, abscesses, skin sores, conjunctivitis, abdominal pain, acne, fatigue, gout, headache, renal disorders, rheumatic pain, breast cancer and cardiac arrhythmia (Hamzah et al., 2012; Oloyede et al., 2011). Cameroonian used the aqueous extract of *P. pellucida* in their traditional medicine to manage bone fracture (Florence et al., 2017). Figure 1 shows the promising application of *P. pellucida* as alternative therapy in management of certain diseases.





Pharmacological activities of Peperomia pellucida extracts

Antimicrobial properties

Extract of *P. pellucida* using different solvents have been tested on many microorganisms to this day. In a report by Akinnibosun et al., (2008), water and ethanolic extracts of *P. pellucida* leaves were found to be effective against *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* at different concentration of leaf extract. However, *E. coli* was resistant to the ethanolic

extract when it was tested with the extract at low concentration. The study also proved that ethanolic extract of *P. pellucida* leaves gave a better antimicrobial effect than water as solvents. The antimicrobial activity of this plant used in this study shows that the plant extracts is a potential source of antimicrobial agent against *E. coli, P. mirabilis and P. aeruginosa* and can be used in the management of nosocomial infection (Akinnibosun et al., 2008).

Another study by Oloyede et al., (2011) described that leaves extract of different solvents of *P. pellucida* possessed antimicrobial activities on both Gram positive and Gram negative bacteria, and fungi. The methanolic extract was active on *Candida albicans* and *Rhizopus stolon* at 25-200 mg/ml which indicates a selective inhibition on fungi. The n-hexane extract inhibited all the microbes at 50 - 200 mg/ml but showed mild activity to *R. stolon* and *Penicillium notatum*. The ethyl acetate extract exhibited a broad-spectrum activity on the entire microorganisms tested at 50 - 200 mg/ml except on *E. coli*. Butanol extract showed moderate activity for all but was particularly active on *Staphylococcus aureus* at 12.5-200 mg/ml. Overall, it showed that the methanolic extract was low in activity compared to the other solvents, while n-hexane, ethyl acetate and butanol extract at concentration of 50 - 200 mg/ml showed a broad spectrum of antimicrobial activity on bacteria and fungi used in this study. Recent study showed that carotene sesquiterpene, namely pellucarotine, isolated from ethanol extract of this plant exhibited potent antimicrobial activity against *C. albicans* at MIC value of 512µg/mL (Ngo et al., 2023).

In another study, *P. pellucida* leaves extract exhibited antimicrobial activity against *S. aureus*, *E. coli*, *P. aeruginosa*, *Klebsiella pneumoniae* and *Salmonella typhi*, in which the methanolic extract showed the least potential as antimicrobial therapy while n-hexane extract showed the strongest potential as an antimicrobial therapy (Idris et al., 2016). Ethanol extract of *P. pellucida* also demonstrated antibacterial activity against pathogens that cause delay in wound healing that include *S. aureus*, *E. coli*, and *P. aeruginosa* at MIC value of 4µg/mL, and has potential as alternative treatment for wound healing as the extract stimulates cell migration to the wounded cell area in vitro (Frankova et al., 2021).

Anticancer properties

Research to evaluate anticancer property of this plant against cancer is scarce and there is a lack of recent study conducted to assess anticancer property of this plant. However, anticancer activity of *P. pellucida* leaves extract was reported in literature data by Lee et al. (2011). In the report, the cytotoxicity of the *P. pellucida* leaves extract against human breast adenocarcinoma (MCF-7) cell line was determined using colorimetric MTT (tetrazolium) assay. The result of the cytotoxicity test against the human breast adenocarcinoma showed that the viability of cancer cells decreased sharply by 72% when concentration of the *P. pellucida* leaves extract was 0.5µg/mL (Lee et al., 2011).

Antidiabetic properties

Antidiabetic property of *P. pellucida* leaves extract was reported by Hamzah et al., (2012). Diabetes mellitus is one of the chronic diseases. It is often associated with hyperglycaemia, hyperlipidaemia, obesity, hypertension, increased oxidative damages, glucosuria and other chronic complications. In the report, *P. pellucida* leaves extract showed an antidiabetic activity by reducing the blood glucose level in diabetic rats to 64% and 68% after treatment with 10% w/w and 20% w/w *P. pellucida*, respectively. Besides, total cholesterol, triglycerides and LDL-cholesterol level were close to normal in diabetic rats treated with diet supplemented with 10% w/w and 20% w/w of *P. pellucida*.

The good cholesterol, namely HDL-cholesterol increased significantly in the diabetic rats when treated with diet supplemented with 10% w/w and 20% w/w of *P. pellucida* compared to the diabetic control rats. Besides, the diabetic rats with *P. pellucida* treatment showed reduction in the

AST, ALT and ALP activities where these liver enzymes have shown higher activity in person with type-2 diabetes mellitus. Therefore, all findings indicate that *P. pellucida* has an antidiabetic property (Hamzah et al., 2012). Methanolic extract of *P. pellucida* (L.) Kunth shows potential as an alternative therapeutic option for glycation-mediated diabetic retinopathy by demonstrating anti-inflammatory effects and restoring cell viability in AGE-stimulated ARPE-19 cells through the JAK-STAT3 pathway (Ho et al., 2024).

Antioxidant properties

Antioxidant is a substance that reduces or stops damage to cells caused by harmful substances called oxidants or also known as free radicals. Oxidants can be found in the environment due to air pollution, cigarette smoke and others. However, they are also produced by our body with sole intention to help our immune system to fight against viruses and microbes. Nevertheless, excessive free radicals in human's body can lead to cancer and heart diseases. In a report by Mutee et al., (2010) antioxidant activities of *P. pellucida* were determined using DPPH scavenging activity assay. DPPH is a stable free radical and accepts an electron or hydrogen radical to become a stable diamagnetic molecule. Results showed that methanolic extract of *P. pellucida* has DPPH scavenging effect in vitro where its scavenging activity was $IC_{50} = 0.083$ mg/mL and was compared to BHT standard where its scavenging activity was $LC_{50} = 0.027$ mg/mL.

In another report, *P. pellucida* leaves extract scavenged DPPH with a 30% inhibition at a concentration of 0.625 part per thousand (ppt). It was also observed that there was a dose-response relationship between *P. pellucida* leaves extract and percent of inhibition of DPPH scavenging activity where the percent of inhibition increased when the concentration of the plant extract used increased (Lee et al., 2011). Antioxidant activity of *P. pellucida* leaves extract was also determined using other methods. They are scavenging effect on hydrogen peroxide (H₂O₂) and antioxidant activity by ferric thiocyanate method (FTC) (Oloyede et al., 2011). In the study, *P. pellucida* leaves were extracted using different solvents such as methanol, hexane, ethyl acetate, butanol and aqueous extract. For hydroxyl radical scavenging activities when compared to standards. Among all the extracts, the one that was better at scavenging activity was the n-hexane extracts. Still, all extracts displayed better activity than the standard used. In FTC method, it was used to determine the amount of peroxide which oxidized ferrous chloride to a reddish ferric chloride pigment. All *P. pellucida* leaves extract showed moderate antioxidant activities in a concentration dependant manner (Oloyede et al., 2011)

Another study by Hamzah et al., (2012) reported the antioxidant properties of P. pellucida leaves extract as it was tested for superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH) and lipid peroxidation in diabetic rats. SOD and CAT are two scavenging enzymes that remove toxic free radicals. In the study, the results showed that SOD and CAT level were significantly increased in diabetic rats treated with supplement diet containing 10% and 20% w/w of P. pellucida leaves extract. Supplementation of 10% and 20% w/w of P. pellucida leaves extract in diabetic rats also significantly increased the level of GSH content compared to control diabetic rats where the level of GSH significantly reduced. Supplementation with 10% and 20% w/w of *P. pellucida* leaves extract also reduced the lipid peroxidation in the diabetic rats treated group thus indicates that P. pellucida leaves extract may inhibit the lipid peroxidation and thereby oxidative damage to tissues in diabetes. Recently, combination of P. pellucida (L.) and Pachyrhizus erosus (L.) extract that is rich in antioxidant compounds such as alkaloids, tannins, flavonoids, and saponins has been demonstrated to exhibit gastroprotective property in rats with gastric ulcer (Pertiwi et al., 2022). In dental research, ethanol extract of P. pellucida was demonstrated to stimulate bone healing process following tooth extraction in rat model through increase in the production of fibroblasts and decrease in polymorphonuclear cells (Kartika et al., 2021).

Peperomia pellucida in dermatitis management

Peperomia pellucida has been mentioned in studies that it is used by the locals to treat dermatitis. Recent study using in silico method also found that compounds from *P. pellucida*, namely procyanidin and acacetin, have anti-aging property to skin via interaction with collagenase, elastase, and tyrosinase (Oyinloye et al., 2023). In general, dermatitis is caused by an imbalance of immune system and a defective skin barrier in which causing opportunistic pathogens to gain entry into our body and caused an inflammation of the skin. Figure 2 shows the promising use of *P. pellucida* in management of dermatitis. *Peperomia pellucida* contains various phytochemical constituents that confer in the pharmacological activities of the plant.



Figure 2. Application of *Peperomia pellucida* in dermatitis management.

Peperomia pellucida has shown a broad spectrum of antibacterial activity against Grampositive bacteria such as *S. aureus*, *Bacillus subtilis* and Gram-negative bacteria such as *Escherichia coli*, *P. aeruginosa*, *K. pneumoniae* and *S. typhi. Peperomia pellucida* leaves extract also has shown an antifungal activity against different types of fungi such as *Candida albicans*, *Rhizopus stolon* and *Penicillium notatum*. Other than that, antioxidant and anti-inflammatory properties of *P. pellucida* also helped in managing dermatitis. It has been confirmed that the plant extract interfered with the synthesis of prostaglandin, thus acting as an anti-inflammatory and analgesic agent (Awe et al., 2013).

The presence of biologically active compounds or secondary metabolites in *P. pellucida* such as tannins, saponins and flavonoid are crucial as they have their own biological functions. Tannin is water-soluble polyphenols with molecular weight that ranges from 500 and 3000, thus giving tannins properties that include the ability to precipitate alkaloids, gelatine and other proteins (Bate-Smith & Swain, 1962). Some studies reported that tannins reduced feed intake, growth rate, feed efficiency, net metabolizable energy, and protein digestibility in experimental animals (Chung et al., 2010; Kumar et al., 2016). However, tannins also have been reported to possess

anticarcinogenic and antimutagenic potentials as well as antimicrobial properties. Tannins have also been reported to exert other physiological effects, such as to accelerate blood clotting, reduce blood pressure, decrease the serum lipid level, produce liver necrosis, and modulate immune responses (Chung et al., 2010). Tannins are astringent, bitter-tasting polyphenols plant that can precipitate proteins (Bele et al., 2010). Therefore, presence of tannins in the plant extract can be pharmacologically used as an astringent where the astringent activity of tannins will precipitate proteins and tissue that will consequently improve the wound healing. The ability of tannins to form a protective layer over the exposed tissue keeps the wound from being infected even more (Ashok & Upadhyaya, 2012). Tannins also have antimicrobial activity as they inhibit the microbial proliferation by denaturation of enzymes that play roles in microbial metabolism (Awosika, 1991).

Saponins are glycosylated compounds that can be found in many types of plants (Mert-Türk, 2006). Saponins can be divided into three major groups, namely steroid, tripernoid and steroidal glycoalkaloid (Aiyer Harini et al., 2013; Barbosa, 2014; Mert-Türk, 2006; Thakur et al., 2011; Wina et al., 2005). Saponins are stored in plant cells as an inactive precursor. However, they are readily converted into biologically active enzymes as an immune response to pathogen (Mert-Türk, 2006). Saponins have been reported to possess antimicrobial, antifungal, antiparasitic and insecticidal properties which plays crucial roles in defending the plant against pathogens (Moses et al., 2014). Other than that, studies also revealed that saponins have biological activities that include antibacterial, antileishmanial, antifungal, antimalarial, antiplasmodial, antiviral, and antitumoral. Saponins also have immunoadjuvant activities (Barbosa, 2014; Dinda et al., 2010). Adjuvant is defined as a substance that helps to accelerate, prolong or increase the cellular or humoral immune response to an antigen. Therefore, saponins in plant extract can help to enhance an immune response. Additionally, saponins are able to permeate cells without destroying the cells morphology, therefore, saponins are used in laboratory applications to treat live cells in order to facilitate peptides or reagents such as antibodies to enter the cells (Awe et al., 2013).

Flavonoids are phenolic compounds which are naturally found in a broad range of fruits, vegetables, grains, roots, stems, flowers and tea (Durgo et al., 2007; Marella, 2017; Nijveldt et al., 2001; Pietta, 2000; Tapas et al., 2008). Flavonoids is nutraceutical, a food or parts of food that provide medical or health benefits that include prevention and treatment of disease (Tapas et al., 2008). Flavonoids contribute to many biological properties such as antioxidant, antiallergic, antiinflammatory, antiviral, antiproliferative, and anticarcinogenic activities, in addition to having effects on mammalian metabolism (Yao et al., 2004).

Peperomia pellucida plant extract also comprises of flavonoids, antioxidant that prevents injury caused by free radicals through suppression of singlet oxygen, inhibition of enzymes that generate ROS, chelating ions of transition metals, which may catalyse ROS production and quenching cascades of free-radical reactions in lipid peroxidation (Mierziak et al., 2014). Flavonoids are also modifiers which modify the body's reaction to allergens and are useful in therapeutic roles (Awe et al., 2013).

Conclusion

This review summarized the phytochemical constituents and pharmacological activity of *P. pellucida* and how the plant is used to treat and manage dermatitis. *Peperomia pellucida* is widely used in different medicinal systems all around the world for various ailments such as skin diseases, diabetes, conjunctivitis, fever, gastrointestinal disorders and in the management of fracture. Although *P. pellucida* also has been investigated as a source of natural pharmacologically active compounds with potential antimicrobial, anticancer, antipyretic, anti-inflammatory, antioxidant, and analgesic activities, further investigations must be undertaken in the future on the medicinal properties of this plant particularly on anticancer property.

Phytochemical screenings on *P. pellucida* also revealed pharmacologically active compounds of medical importance including tannins, flavonoids, glycosides alkaloids, saponins, terpenes, phenolic compounds and others. The natural pharmacological activities and active compounds of *P. pellucida* has helped in managing and treating the dermatitis.

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