

Peperomia pellucida (L.) Kunth: Traditional medicinal and its bioactivity

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Abstract

Peperomia pellucida (L.) Kunth (Piperaceae) has been long used as food ingredient and traditional medicine. This study aims to explain botany, utilization and bioactivity of *P. pellucida*. The method used in this study is library research on various research results published online, especially on Google Scholar, using the keywords *P. pellucida*, uses *P. pellucida* and bioactivities *P. pellucida*. That information is synthesized which explain the benefits and bioactivity of *P. pellucida* in a comprehensive manner. The *P. pellucida* is an annual herb that easily found in surrounding environment, especially in humid places as a wild plant. *P. pellucida* is very potential as a source of protein and its rich in minerals such as potassium, calcium and iron as the main elements. In traditional medicine *P. pellucida* is used to treat headaches, kidney disease, fever, and wound hypertension, boils, acne, abscesses, stomach pain, colic, gout, kidney, rheumatic pain, headache, fatigue, malaria, treat bleeding, fever, lower cholesterol, cough suppressant and diuretic. The *P. pellucida* has activity as antihypertensive, antidiabetic mellitus, antiosteoporosis, antimicrobial, analgesic, antioxidant. Peperochromen-A compounds have anti-diabetic activity and flavonoids as anti-hypertensive and anti-microbial. Bioactivity of *P. pellucida* as anti-microbial and hypertension can be developed as a nutraceutical.

Keywords: *Peperomia pellucida*; Anti-microbial; Anti-hypertensive; Peperochromen-A

1. Introduction

Peperomia pellucida (L.) Kunth (Piperaceae) is a species have been used as food and traditional medicine [1], by local Indonesian known as *sirih cina* or *suruhan*. This herb is easily found in the surrounding environment, especially in humid places as a wild plant. Some ethnic groups in Indonesia, especially the Sundanese, use it as *lalaban* (a vegetable consumed in fresh) or in the form of stir fry. *P. pellucida* has been traded in the market with the selling price offered ranging from 30,000-50,000 IDR/ kg [2]. Ooi et al [3] reported *P. pellucida* is potential as a source of protein and its rich in minerals such as potassium, calcium and iron as the main elements [3,4] so its suitable for use as food to increase bone density and bone healing [4]. Besides being used as food, *P. pellucida* also used as a traditional medicine. *Peperomia pellucida* has been widely used to treat headaches, kidney disease, fever, and hypertension [5], wounds, ulcers, acne, abscesses, abdominal pain, colic, gout, kidney, rheumatic pain, headaches, fatigue, malaria [6], treat bleeding, fever, lower cholesterol, cough suppressants and diuretics [7]. The use of *P. pellucida* as a traditional medicine is related to its bioactivity.

Leaves of *P. pellucida* have activity as anticancer, antioxidant, antimicrobial [8,9], anti-inflammatory, analgesic [8,10], antipyretic, anti-edematogenic [8], antitumor [9] and hypoglycemic [10]. The ethanolic extract of *P. pellucida* showed antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* with prominent average inhibition of 15.43 ± 0.67 mm and 13.22 ± 0.34 mm, respectively [1]. Kartika et al [11] and Kartika et al [12] stated that *P. pellucida* has the

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potential to use water extract of *P. pellucida* as an alternative source of antiosteoporosis agents. When explored further the bioactivity of *P. pellucida* as an antimicrobial is more prominent than the others. This shows that *P. pellucida* has the potential to be developed as a food preservative as well as to overcome digestive tract disorders caused by microbes [13].

P. pellucida bioactivity is thought to be related to the content of its secondary metabolites. Phytochemical of *P. pellucida* contained alkaloids, flavonoids, glycosides, terpenoids and steroids [1]. The essential oil in the *P. pellucida* is mainly sesquiterpenes followed by phenylpropanoids, although the its content varies in different organs. The main essential oil in the *P. pellucida* leaves is gurjunene, 1,10-di-epicubenol, (E)-caryophyllene and dillapiole. The essential oil of stem is carotol, dillapiole, trans- β -guaiene and (E)-caryophyllene [14]. *P. pellucida* volatile oil is dominated by sesquiterpenoid group (reaching 87.5% of the total volatile oil), while monoterpenoid is only 2.9%. α -farnesene was the most dominant compound followed by bisabolene, bergamoten, 1,4-cadinadiene, copaene and isosativene from the sesquiterpenoid group and Terpinen-4-ol and neril acetate were components major monoterpenoids [15] Peperochromen-A compounds have antidiabetic activity [16]. The bioactivity of *P. pellucida* as an antihypertensive is associated with its flavonoid content [5]. Until now, in-depth studies on *P. pellucida* are still limited, especially in the form of reviews. This study aims to explain the relationship between *P. pellucida* utilization and its bioactivity so that its use can be increased as a food ingredient or traditional medicine.

2. Methods

The method used in this research is library research on various research results published online, especially on Google Scholar. Some of the keywords used are *P. pellucida*, uses *P. pellucida* and bioactivities *P. pellucida*. The information obtained is synthesized so that it can explain the benefits and bioactivity of *P. pellucida* in a comprehensive manner.

3. Results and discussion

3.1. Botany of *P. pellucida*

Description is a fleshy and glabrous annual herb with a height of up to 40 cm. Stems are erect at first, then decumbent, usually branched, roots emerging from nodes or nodes. Segments or intermodal's up to 50 mm long. No stipules. Leaves simple, alternate, petiole up to 20 mm long; broad blade ovate, ovate-elliptical, or ovate-triangular, to 3.5 cm both long and broad, fleshy, webbed when dry, base heart-shaped, rounded to pointed (Figure 1), apex acute or blunt, nerves main 5-7. Flowers arranged in spikes, terminal or axillary from upper nodes, solitary, 2–7 cm long; stalk 5–13 mm long, 0.5 mm in diameter, flowering part 2–5 cm, glabrous. Flowers bisexual, not concave, loose, 0.4–1 mm apart, orbicular bracts, 0.3–0.4 mm long by 0.2–0.3 mm wide, anthers oblong to sub-globose, ovary oval or ellipsoid, longer than stamens, pubescent stigma. Seeds, sticky, globose, 0.5–0.6 mm long by 0.2–0.3 mm wide, papillae; one seed [17,18].



Figure 1 The sirih cina (*Papaeromia pellucida*). A. Habitus. B. The leaves are oval-triangular in shape. C. Branches that support leaves and inflorescence.

This species is native to tropical North and South America. Currently, it has naturalized throughout the Old World. It grows in gardens, grassy but shady areas, roadsides, nurseries, rock crevices, or as a weed in cultivation. It prefers to grow in disturbed habitats. It produces flowers from April to July. In Indonesia it has been found in Sumatra, Java, also in Papua New Guinea. This species grows from the lowlands to an altitude of about 1000 m above sea level [17].

3.2. Uses and Bioactivities

The use of natural materials to treat various disease disorders is considered safer than synthetic drugs, therefore the exploration of natural ingredients with medicinal properties continues to be carried out. The *P. pellucida* has activity as antihypertension, antidiabetic mellitus, antiosteoporosis, antimicrobial, analgesic, antioxidant will be discussed further.

3.2.1. Anti-hypertension

Hypertension is a circulatory system disorder that causes blood vessel pressure to be above normal. The drugs trademarks of antihypertensive such as captopril and amlodipine. Two active angiotensin-converting enzyme inhibitors have been isolated and purified from *Peperomia pellucida* which are used as antihypertensives in traditional medicine, and support their use as angiotensin-converting enzyme-inhibiting drugs [5]. Plants used to treat hypertension are plants that produce angiotensin-converting enzyme (ACE) inhibitor compounds [5,19,20] known as hypotensive plants [5]. The *P. pellucida* extract works as an ACE inhibitor by competing with the active site of the substrate [19].

Ethyl acetate extract fraction of *P. pellucida* at a dose of 50 mg/kg BW has an ACE inhibitory effect similar to captopril so that it can reduce blood pressure, angiotensin II levels and plasma renin concentrations. The bioactivity of *P. pellucida* as an antihypertensive is associated with its flavonoid content [5]. Based on the docking results, polyphenolic compounds from *P. pellucida* have active potential as ACE inhibitors, but have lower affinity than captopril. Based on the interaction of the ACE binding site, 5,6,7-trimethoxy-4-(2,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one showed the most similar interaction with the captopril ligand. *Peperomia pellucida* n-hexane and ethyl acetate extracts contained 2,3,5-trimethoxy-9-(12,14,15-trimethoxybenzyl)-1H-indene and pellucidine A which showed inhibition of angiotensin-converting enzyme activity, with IC50 values 72 M (27.95 g/mL) and 11 M (4.4 g/mL respectively). [21].

3.2.2. Anti-diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder that results in glucose levels above normal referred to as hyperglycemia. Diabetes mellitus is characterized by hyperglycemia and also carries a risk of kidney disease [22]. The *P. pellucida* has traditionally been used as an herbal remedy to lower blood sugar [16]. The *P. pellucida* extract significantly reduced the histologic abnormalities of renal tubular and glomerular cells in alloxan-induced diabetic rats [22]. Metformin is a of the trademarks that is widely used as a DM drug [23]. Plants used to treat diabetes mellitus are plants that produce compounds that affect insulin action or enzymes involved in converting carbohydrates into glucose or which have a hypoglycemic effect. The use of *P. pellucida* as an anti-diabetes mellitus has been reported by Sheikh et al [10] and Kanedi & Mumtazah [22]. The antidiabetic bioactive compounds of *P. pellucida* is Peperochromen-A [16].

The *P. pellucida* methanol extract has antidiabetic activity [23]. Short-term treatment with *P. pellucida* extract had no effect on the ratio of body weight to organ weight; however, significantly reduced liver weight. Administration of *P. pellucida* methanol extract reduces serum cholesterol, triglyceride and phospholipid levels [23]. The blood glucose levels of hyperglycemic Wistar mice given ethanol extract and hexane *P. pellucida* at a dose of 40 mg/kg BW decreased blood glucose levels by 54.57% and 51.25% respectively and with positive control [24]. Administration of *P. pellucida* extract at a dose of 40 mg/kg BW at the 120th minute gave significant results and was significantly different from the negative control group and not significantly different from glibenclamide at a dose of 0.45 mg/kg BW [25].

3.2.3. Anti-osteoporosis

Osteoporosis is a disorder of bone metabolism, in which the rate of bone formation is lower than bone resorption, due to an imbalance in bone remodeling. *Peperomia pellucida* is consumed as a vegetable and used in traditional medicine for fracture healing [4]. Osteoporosis is one of the main health problems, especially in the elderly [12,26]. Osteoporosis is a disorder of bone metabolism that causes fractures that have a negative impact on quality of life [27]. The aqueous and ethanol extract of *P. pellucida* accelerated bone healing *in vivo* [26]. Ethanol extract of *P. pellucida* at a dose of 100 mg/kg had a preventive effect on osteoporosis-induced ovariectomy mice [27]. The *P. pellucida* extract has been shown to contain *in vivo* estrogenic-like effects, thus functioning as an anti-osteoporosis agent [11]. *P. pellucida* has promising anti-osteoporosis activity due to its estrogenic activity, and the compounds responsible for this activity were found to be lignan and phenylpropanoid derivatives [26].

The *P. pellucida* has anti-osteoporosis agent activity has been reported by Kartika et al [12], Kartika et al [26] and Putri et al [27]. One of the functions of the hormone estrogen is to maintain bone density. The *P. pellucida* extract (n-hexane, ethyl acetate, ethanol and aqueous extract) showed estrogenic activity because it contained quercetin, stigmasterol (n-hexane and ethyl acetate extract), apigenin and apigenin (water extract). Apigenin was detected to be present in the ethanol and aqueous extracts of *P. pellucida* which is thought to be related to its bioactivity as anti-osteoporosis [26]. Apigenin and apigenin produce estrogenic activity, while quercetin and stigmasterol can produce estrogenic and antiestrogenic activity [12]. Rats given *P. pellucida* 100 mg/kg ethanol extract showed improvement in trabecular bone dimensions compared to the ovariectomized control group [27]. The methanol and ethyl acetate *P. pellucida* extracts contained phenylpropanoid and two lignan derivatives, namely, 6-allyl-5-methoxy-1,3-benzodioxol-4-ol, pachyostaudin B, pellucidine A, dillapiole, and apiol. The methanol fraction of ethyl acetate extract *P. pellucida* produced the highest estrogenic activity, whereas pachyostaudin B and pellucidine A had partial agonist activity. Several compounds (dillapiole derivatives and pellucidine A) also have antiestrogenic activity properties. The methanol fraction of *P. pellucida* has higher estrogenic activity compared to others [11].

3.2.4. Antioxidant

The antioxidant activity of *P. pellucida* can be measured using the following methods: scavenging effect on 2,2-diphenyl-1-picrylhydrazyl radical (DPPH), hydroxyl radical and iron thiocyanate method [28]. Antioxidant activity was found to be correlated with total phenol content but not with total flavonoid content. Gamma irradiation can be used as a method of preserving *P. pellucida* herb powder [29]. Among the different extraction solvents, ethyl acetate extract had the highest total phenolic content which correlated with antioxidant activity evaluated by DPPH test [30]. The *P. pellucida* extract fraction had antioxidant activity when compared with the standard antioxidants: butylated hydroxyl anisole (BHA), ascorbic acid and -tocopherol used in the test [28].

The antioxidant activity of *P. pellucida* can be measured using the following methods: scavenging effect on DPPH, hydroxyl radical and iron thiocyanate (Oloyede et al 2011). Antioxidant activity was found to be correlated with total phenol content but not with total flavonoid content. Gamma irradiation can be used as a method of preserving *P. pellucida* herb powder [29]. Among the different extraction solvents, ethyl acetate extract had the highest total phenolic content which correlated with antioxidant activity evaluated by DPPH test [30]. The *P. pellucida* extract fraction had antioxidant activity when compared with the standard antioxidants: BHA, ascorbic acid and -tocopherol used in the test [28].

3.2.5. Anti-microbial

Microbes are the cause of various diseases in humans or are also known as microbial pathogens. *P. pellucida* leaves are traditionally used to treat diarrhea due to its antimicrobial activity [31]. Some bacteria can also cause infections on the facial skin, causing acne such as *Propionibacterium acnes* [32]. Some of the pathogenic bacteria in food are *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *Salmonella typhimurium* [33].

P. pellucida has been reported to inhibit the growth of various types of microbial such as *E. coli*, *S. aureus* [28,33,34], *Pseudomonas aeruginosa* [28,35] *Bacillus subtilis*, *Klebsiellae pneumoniae*, *Salmonella typhi*, *Candida albicans*, *Rhizopus stolon*, *Aspergillus niger*, *Penicillium notatum* [28], and *Propionibacterium acnes* [32], *Pseudomonas aeruginosa* [35]. *B. cereus*, and *S. typhimurium* [33]. The essential oil *P. pellucida* showed strong antibacterial activity against *Escherichia coli*, *Enterobacter cloacae*, *Mycobacterium smegmatis*, *Listeria ivanovii*, *S. aureus*, *Streptococcus uberis*, and *Vibrio parahaemolyticus* [34].

The bioactivity of *P. pellucida* extract as an antimicrobial is influenced by various factors such as concentration, compounds used for extraction, organs used, and types of microbes. The ethanolic extract of *P. pellucida* leaves has an inhibitory ability against acne-causing bacteria (*Propionibacterium acnes*) which varies and is directly proportional to the concentration and is classified as having a strong inhibitory power [32]. Aerial methanol extract of *P. pellucida* as a strong inhibitor against *Bacillus cereus* with minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values are 3.91 mg/ml and 7.81 mg/ml, respectively [33]. The ethanolic extract of *P. pellucida* had a higher inhibitory action against *S. aureus*, *B. subtilis*, *P. mirabilis* and *P. fluorescens* [31]. Phytol is the main compound in plant extracts followed by 2-Naphthalenol, decahydro, Hexadecanoic acid, methyl ester and 9,12-Octadecadienoic acid (Z, Z), methyl ester which is thought to be related to its antimicrobial bioactivity [36].

The essential oil from *P. pellucida* leaf extract was bactericidal at 0.20 mg/mL against *S. aureus* while 0.15 mg/mL against *L. ivanovii* was lower than that of the stem [34]. The ethanolic extract of *P. pellucida* inhibited the growth of *P. acnes* (which causes acne) similar to gentamicin (positive control) [8]. Ethanol was better than water extract as a solvent for *P. pellucida* leaf extraction because it showed the highest inhibitory activity on *Proteus mirabilis* and *P. aeruginosa*

while water was the best solvent for *P. pellucida* extraction because it showed the highest inhibitory activity on *E. coli* [7]. Compounds from dichloromethane extract *P. pellucida* contain dillapiole, caryophyllene oxide and stigmaterol [35] which are thought to be related to their bioactivity.

3.2.6. Anti-Cancer

The *P. pellucida* leaf extract had anticancer activity against the human breast adenocarcinoma cell line (MCF-7) with an IC₅₀ value of 10.4±0.06 g/ml. Phytol is the main compound in plant extracts followed by 2-Naphthalenol, decahydro, Hexadecanoic acid, methyl ester and 9,12-Octadecadienoic acid (Z, Z), methyl ester. The *P. pellucida* leaf methanol extract has enormous potential as a drug, especially in the treatment of breast cancer [36]. Antiproliferative activity of the two extracts was found in the sequence ethanol extract > water extract *P. pellucida* [9].

4. Conclusion

- *P. pellucida* is an annual herb that is easily found in damp places and is used as a vegetable. In traditional medicine *P. pellucida* is used to treat headaches, kidney disease, fever, and wound hypertension, boils, acne, abscesses, stomach pain, colic, gout, kidney, rheumatic pain, headache, fatigue, malaria, treat bleeding, fever, lower cholesterol, cough suppressant and diuretic.
- *P. pellucida* has activity as antihypertensive, antidiabetic mellitus, antiosteoporosis, antimicrobial, analgesic, antioxidant.
- *P. pellucida* have Peperochromen-A compounds have anti-diabetic activity and flavonoids as anti-hypertensive and anti-microbial.

Compliance with ethical standards

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