REVIEW ARTICLE

A review on medicinal benefits of *Persicaria minor*

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Abstract:

Herbal plants have been documented to treat various types of disorder such as cold, fever and sore throat. Due to the revolution of treatment, chemical drugs have been developed to treat patients. However, prolong administration of chemical drugs has been claimed to contribute various side effects among chronic patients. *Persicaria minor,* locally known as *kesum*, is currently being used as a traditional remedy instead of using it as an additional aromatic flavor in food. The main focus of this study is to summarize the recent findings on medicinal benefits of the leave extract of *P. minor*. Several studies have demonstrated the ability of this plant in inhibiting the growth of common infection organisms including *S. aureus*, reducing oxidative stress in the body as well as its anti-proliferative property for cancer and tumor development. The plant extract also helps to protect cell tissues from abnormal conditions including ulcer. Furthermore, other studies also stated that the plant can reduce high blood pressure by inhibiting the activity of angiotensin-converting enzyme (ACE), enhance wound healing process and increase vitamin A in blood. Therefore, it can be stated that *P. minor* has many medicinal values, making it a strong potential therapeutic agent that can be used as an alternative for the current chemical drugs.

Keywords: Anti-proliferative, antimicrobial, antioxidant, *kesum*, *Persicaria minor*

1. INTRODUCTION

Since ancient times, herbal plants have been used to provide nutrition to humans and animals. It is also believed that plants are used as therapeutic to treat various chronic disorders or diseases such as cancer, diabetes, fever, arthritis and cough owing to the huge number of phytochemical compounds discovered from them [1]. In developing countries, herbal medicinal plants are still used as normal bases to maintain good health [2]. It has been also found that medicinal plants contain bioactive property that possesses antioxidant, anti-inflammatory, antivenom, antimicrobial, and antitumor characteristics [3]. Over the years, many studies have shown a great interest to further study on plants and their value that can provide benefits to the world especially in pharmaceutical industry. Current common drugs produced by pharmaceutical industry such as aspirin and atropine have their origin from traditional medicines, which mostly from natural resources [4].

In Malaysia, there are a variety of vegetables and herb plants that are being consumed by the local people as side dishes. The term that is widely used is ‘ulam’, which can be consumed raw or soaked in hot water. Many studies have indicated that these plants have high content of carbohydrates, minerals, vitamins and proteins [5]. Some of the plants are often used in cooking due to their aromas and flavors including *daun kesum* or *Persicaria minor*. *Persicaria minor* is an herbaceous plant that grows in Southeast Asia including Thailand, Vietnam and Laos. In Thailand, it is known as ‘’Pakpaw’’, whereas in Vietnam, it is called ‘’rau ram’’. In Malaysia, Brunei and Singapore, this plant is called *daun kesum* and sometimes *daun laksa*. This plant is mostly used in cuisine to give aromatic flavor to the food [6]. Traditionally, *P.minor* is used to cure digestive disorders and dandruff problems [7].

People with health-related problems across the globe have been rising every day. Prolonged administration of chemical drugs can cause chronic side-effects on certain internal organs including the liver. Increasing liver detoxification activity can further induce increased liver function biomarkers such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyl transferase (GGT) [8]. Numerous studies have presented that certain *P. minor* phytochemical compounds are able to give advantages to the pharmaceutical industry. It is necessary for the industry to develop a form of drug extracted from natural resources that has been known to have less side effect on patient. *Kesum* plant has several sub-species variants including *Persicaria hydropiper*, *Persicaria odorata* and *Persicaria minor*. There is, however, a lack of reviews on *P. minor* medicinal benefits compared to other sub-species. Hence this study aims to summarize the available information on the evidence for medicinal benefits of *P. minor.*

2. PHYTOCHEMICAL COMPOUNDS IN *Persicaria minor*

Kesum or scientifically called *P. minor* is categorized under the Polygonaceae family (Table 1). Its other commonly used name is Vietnamese coriander [9]. The plant is also synonym as *Polygonum minus*. The shape of its leaves can be described as green in color with long and sharp edge of the leaf ranging from 1.5 to 2 cm in width and 5.0 to 7.0 cm in length as shown in Figure 1 [6].

Table 1. The taxonomy of *P. minor*.

Kingdom	Plantae
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Order	Polygonales
Family	Polygonaceae
Genus	*Polygonum*
Species	*minus* Huds.

Figure 1. Morphology of *P. minor* plant and leaf.

Several studies have demonstrated that there are high phytochemical compounds that can be found in *P. minor* [10]. Phytochemical compositions that can be found in the plant are flavone, methyl flavonol, decanal, dodecanal, 1-decanol, 1-dodecanol, undecanal, tetradecanal, 1-undecanol, nonanal, 1-nonanol and β-caryophyllene [11]. According to Baharum et al. [12], decanal and dodecanal are the major aldehydes that give the unique flavor of *kesum*.

Many studies mentioned that *P. minor* is rich with phenolic and flavonoid. According to Hassim et al. [13], the highest polyphenol content can be obtained from the methanol extract of the leaf portion (645.60 ± 166.68 mg GAE/100 g). This finding is supported by the study of Zakaria et al. [14], which stated that the pure extract of *P. minor* possesses the highest phenolic content of 1388.19 ± 111 mg GAE/100 g, which is higher than that of *bawang putih*, *ulam raja* and *pegaga*. Furthermore, the plant can still show high phenolic content even though from the plant extract with medium polarity of solvent, which is 70% ethanol and 30% water [15]. In terms of total flavonoid content (TFC), Abdullah et al. [16] demonstrated that the methanol extract of *P. minor* extract contains the highest TFC value, which is 53.19 ± 0.71 mg GAE/g, followed by ethyl acetate (47.22 ± 0.71 mg GAE/g), water (43.65 ± 0.36 mg GAE/g) and hexane (10.18 ± 0.20 mg GAE/g), respectively.

3. MEDICINAL USES OF *Persicaria minor*

3.1. Antimicrobial Activity

Bacterial infection is one of the most common types of disease that can infect animals instead of humans. According to the Center for Disease Control and Prevention (CDC), fever, vomiting, nausea, fatigue, diarrhea, loss of appetite and sore throat are the common symptoms of having an infection. If the infection is not properly treated, it can develop into severe state like sepsis, which is a lethal life-threatening condition [17]. Early and proper treatment using antimicrobial drug can avoid it from getting worse. Many studies mentioned that traditionally used herbal plants have antibacterial capacity. Numerous plants have been proven to inhibit various types of bacteria that cause common infections, which include *Staphylococcus aureus*, *Streptococcus agalactiae*, *Bacillus subtilis* and *Helicobacter pylori* [18].

Many recent studies have suggested that *P. minor* extract contains antimicrobial compound. Moreover, several studies have documented that *P. minor* was able to inhibit *Staphylococcus aureus*, *Escherichia coli*, *Escherichia faecalis*, *Staphylococcus epidermidis* and *Bacillus subtilis*. Plus, the essential oil of *P. minor* was able to inhibit the growth of *S. aureus*, *E. coli*, *B. subtilis* and *S. agalactiae* [19]. This is supported by a study conducted by Hassim et al. [13] demonstrating that the methanol extract of *P. minor* showed large inhibition zone of gram-positive bacteria such as *S. aureus* and *B. subtilis*, as well as gram-negative bacteria including *E. coli*. Essential oil and methanol extract may have the same phytochemical compound extracted from the plant *P. minor*.

Another study conducted by Hassan et al. [20] showed that the aqueous extract of the plant was able to inhibit the growth of *Salmonella typhimurium* and *Serratia marcescens* at the initial concentration of 250 mg/ml. They demonstrated that the plant extract exhibited 9.0 mm and 9.5 mm in diameter of inhibition zone on *S. typhimurium* and *S. marcescens*, respectively, at 500 mg/ml concentration. S. *typhimurium* and *S. marcescens* are the common microorganisms that cause gastroenteritis and urinary tract infection. Based on these findings, it can be suggested that the aqueous extract of the plant has a potential to treat infectious diseases, which shows a need for further study to be done.

P. minor has been traditionally used as a remedy for many disorders including as anti-dandruff. *Pityrosporum ovale* has been identified as one of the yeasts that cause of dandruff formation and hair shredding [21]. According to Hadiarti [22], shampoo formulated with ethanol extract of *P. minor* was able to inhibit the growth of *P. ovale* with 2.61 cm of clear zone. The concentration of the plant extract gives high impact on the antifungal activity. *Candida albicans* is one of *Candida spp* that cause candidiasis and dermatitis. According to study done by Korulkin and Muzychkina [19], the essential oil of *P. minor* was able to inhibit the growth of *C. albicans*, which exhibited 12 ± 0.2 mm clear zone of the organism. This was due to the presence of aldehyde

compound (75.43%) in the highest percentage in the essential oil of the plant followed by terpenoid (13.19%), alcohol (8.07%) and acid (0.83%) [23]. Aldehyde compound is believed to play a significant role as antifungal property.

The plant extract of *P. minor* is also able to cure dermatophytosis and ringworm infection that is commonly caused by *Trichophyton rubrum* [24, 25]. To support the statement, a study conducted by Dewi et al. [26] presented that the ethanol extract of *P. minor* was able to inhibit the growth of *T. rubrum* effectively at concentration of 20% and above. The clear inhibition zone at concentration of 20% was 14 ± 1.63 cm, indicating that the fungus is sensitive to the plant extract. The antifungal activity may be suggested to be caused by the synergism effect of the phytochemical compounds in the ethanol extract of the plant such as alkaloids, flavonoids, phenols, triterpenoids, tannins and saponins [27, 28]. According to Dewi et al. [26], alkaloid is responsible for inhibiting the DNA and RNA polymerase in the organism; flavonoids and saponins are responsible for interrupting the cell membrane permeability of the organism while triterpenoid is responsible for inhibiting the organelles function of the organism.

P. minor also can be used as an antiviral against certain viruses. The phytochemical compound of the plant extract that has antiviral property may protect cell tissues from Herpes Simplex Virus-1. According to Wahab et al. [29], the plant extract is able to protect cells from attachment of the virus and avoid the viral from entering the cells. The possible reason for the finding is due to the antiviral mechanism of the plant extract that may have interrupted or altered the binding site of the virus on the surface of the cell membrane. HSV-1 virus is able to attach to cells due to presence of HSV-bind receptor called nectin-1 found on the cell surface [30]. Hence, this finding may suggest that the plant extract can avoid the infection of virus.

Another study showed that the plant extract of *P. minor* was able to treat the infection of Human Immunodeficiency Virus-1 (HIV-1) by disrupting its internal enzyme. According to a study conducted by Ahmad et al. [31], a compound known as Polygonumins A (Figure 2) isolated from the plant was able to inhibit protease activity of β-glucosidase in the HIV-1 virus. The compound isolated from the plant possesses good antiviral activity making it able to inhibit 56.51 ± 0.13% of the virus [31]. This is because the compound has a similar structure to Vanicoside A (Figure 3), which is known for its function to act as β-glucosidase inhibitor [32].

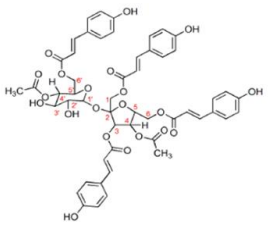

Figure 2. Polygonumins A.

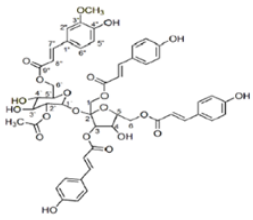

Figure 3. Vanicoside A.

3.2. Antioxidant Activity

Free radicals such as reactive oxygen species and reactive nitrogen species are generated from the human body via various endogenous systems. The balance between of free radicals and antioxidant is necessary to the body, whereas excess production of free radicals can cause the development of oxidative stress that can lead many unpleasant effects such as the formation of tumor and cancer [33]. Antioxidant is one of the secondary metabolisms of plant that are essential for defense, development and growth of the plant while primary metabolism of plant is important for its maintenance such as sugar, amino acid and fatty acid [34]. Antioxidant is the defense mechanism capable of combating oxidative stress. It can be generated endogenously or through diet rich with antioxidant such as fruits and vegetables [35].

Plant extract of *P. minor* has high antioxidant activity. This can be proven from many studies done to determine its antioxidant activity. According to Zakaria et al. [14], the plant has a good ability to scavenge DPPH when the IC50 of the activity is high, which is 84.45 ± 7.33%. This is supported by other studies showing that the methanol extract of the plant produces good DPPH radical scavenging activity [13, 16]. Ferric reducing antioxidant power (FRAP) is also one of the assays used to determine the antioxidant activity of the plant. According to Abdullah et al. [16], methanol extract of the plant has the highest FRAP activity of 1728.33 ± 0.96 μmol Fe^{2+}/g extract. This is supported by Khalid and Babji [36], which stated that the plant extract possesses high ferric reducing power at 63.61 ± 0.73 μmol Fe^{2+}/g.

The antioxidant activity of *P. minor* has been also determined using in vivo study. The plant extract was able to reduce increased superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase in hepatoxicity induced Sprague Dawley rats and protect red blood cell (RBC) destruction induced by hydrogen peroxide (H_2O_2), which is the cause of oxidative stress in the RBC [10, 37]. Superoxide dismutase is one of the antioxidant enzymes that serve to catalyze the superoxide radicals produced by various metabolism processes endogenously and formed into hydrogen peroxide and oxygen (O_2). Besides, there was a study stating that superoxide and hydrogen peroxide also play important role in maintaining organism and cellular function if well-regulated [38].

Aging is one of the reactions caused by many factors, but oxidative stress has been recognized to play a massive role in the aging process [39]. Elastase enzyme is one of the factors responsible for accelerating the aging process by breaking down elastin protein responsible for giving elastic property to connective tissues [40]. A recent study done by Hussin et al. [41] discovered the anti-aging activity of *P. minor* when the plant extract was able to inhibit elastase enzyme activity by 57.61 ± 0.95%, which indicates a good anti-aging activity compared to quercetin that acted as control (52.94 ± 1.18%). The reason was due to presence of these compounds; quercetin, quercetin-3-O-rhamnoside, myricetin derivatives, catechin, isorhamnetin, astragalin and apigenin that are believed to suppress the activity of elastase enzyme [41].

3.3. Effect on Normal and Abnormal Cell

There are several studies demonstrated the high potential of *P. minor* leaf to fight against cancer and tumor cells of mammary gland. This is due to the presence of flavonoid content in the plant that indicates potential of the plant in anti-proliferative and cytotoxicity activity towards the cancer and tumor cells [42]. According to study conducted by Korulkin and Muzychkina [19], the flavonoid content extracted from *P. minor* and other Polygonum L. plants showed that the compound was able to induce apoptosis to the Human's Oral Cavity Carcinoma cell (HSC-2), salivary glands tumor cell (HSG) and normal fibroblasts of human's gums (HGF). The flavonoid compounds from the plant are believed to play significant role in possessing high antitumor activity, which include leukoanthocyanins complex, anthocyanins complex, myricetin and quercetin [19].

Other studies have displayed that the plant extract of *P. minor* has anti-proliferative activity when the extracts of methanol, hexane and ethyl acetate of the plant were not stimulating any growth of colon cancer (HCT116) while the methanol and aqueous extracts encouraged the formation of normal colon cell (CCD841) in healing process in dose-dependent manner [16]. However, according to Abdullah et al. [16], the water extract of the plant also possesses unpleasant effect in which the study demonstrated that it contributed to the growth of the colon cancer cells (HCT116) as well as normal colon cancer (CCD841) with cell viability to 134% and 157%, at 167 μg/mL and 333 μg/mL, respectively. These results remained unclear as they may indicate the presence of proliferative compound extracted from aqueous solvent; thus, further study needs to be done.

The effectiveness of the plant extract against cancer is supported with a study conducted by Ahmad et al. [31] where the novel compound, Polygonumins A found in the plant, was able to treat leukemia, colorectal and breast cancer. The study showed cell viability inhibition to colon cancer cell HCT116, leukemic cell (K562) and breast cancer cell (MCF7) with IC50 of 3.24 μg/ml, 2.25 μg/ml and 2.87 μg/ml, respectively.

There were many studies done on the ability of *P. minor* to protect normal cells from drug toxicity. According to Rashid et al. [37], the essential oil of *P. minor* was able to protect hepatocyte from the overdose of cisplatin drug. This can be proven when 400 mg/kg ethanol extract of *P. minor* has significantly reduced the AST, ALT and serum bilirubin of the Sprague Dawley rats compared to cisplatin-induced groups. This indicates that the phytochemical compounds in the essential oil of the plant help in reducing the workload of the liver to detoxify the drugs [43]. Other studies also demonstrated that the plant extract helps to protect hepatocyte from the toxicity of paracetamol and carbon tetrachloride. According to Thanapakiam et al. [44], the aqueous extract of the plant showed hepatoprotective activity against the toxicity of liver induced by paracetamol. The methanol extract of the plant has also showed hepatoprotective activity against liver toxicity induced by carbon tetrachloride [45]. These findings are supported by a study conducted by Christapher et al. [46] where the methanol extract of the plant extract was able to prevent hepatoxicity of paracetamol and carbon tetrachloride.

There was a study that demonstrated the ability of *P. minor* to protect stomach cells from developing ulcer. According to Christapher et al. [6], the methanol extract of the plant was able to decrease the pH of the stomach of Wistar albino mice, which is 1.81 ± 0.11. The total acidity of the rat stomach from the gastric juice treated with the plant extract was lowered (29.83 ± 3.03 mEq/L) compared to control group (73.83 ± 6.41 mEq/L). Ulcer in the stomach is usually formed from the absence or lack of mucous membrane, which is the protective layer of the stomach wall. Thus, the stomach acid is directly in contact with the stomach cells, leading to the formation of ulcer [47].

3.4. Other Medicinal Benefits

Pain is one of the responses felt by humans and animals, which is also a protective function that may co-indicate the severity of disease or disorder suffered by patients [48]. Currently, the administration of morphine as a painkiller in treating patients is commonly used in hospitals. There were many studies demonstrated that various plants have analgesic property that can replace the usage of morphine. In agreement with this, a study has been conducted showing that *P. minor* can reduce pain by acting as analgesic [6]. In addition, the aqueous and methanol extracts of *P. minor* leaves have showed significant analgesic effect against acetic acid writing, tail immersion and formalin induced pain methods in Wistar rat model. Moreover, it can reduce inflammation in tissues. This is because the presence of 7-methylenedioxy-5, 3´, 4´, 5´-tetramethoxyflavone and 6, 7-4´, 5´-dimethylenedioxy-3, 5, 3´-trimethoxy flavone compounds that are believed to possess analgesic and anti-inflammation properties [49]. *P. minor* is also able to enhance the activity of wound healing of the skin. In line with this, a study conducted by Korulkin and Muzychkina [19] showed that the plant extract was able to heal the flat dermal wounds in 17.9 ± 0.3 days, indicating a healing process that only took less than 18 days compared to untreated wounds that averagely took 20 days to heal.

P. minor also helps in reducing high blood pressure in hypertension patients. According to Khalid and Babji [36], the aqueous extract of the plant was able to inhibit angiotensin-converting enzyme (ACE) activity. The antihypertensive activity of the plant was determined at 89.13 ± 5.42% of ACE inhibition. Based on the result, it indicates that the formation of angiotensin II can be lowered due to receptor for angiotensin I enzyme attached on ACE enzyme, which is inhibited by the antihypertensive compound of the plant extract. Low level of angiotensin II causes the blood vessel to relax and reduces the blood pressure to normal level, increase the passes of salts through the kidneys and brings water into the urine [50, 51].

On top of that, *P. minor* is also able to help patients with deficiency of vitamin A. This is because the plant contains beta carotenoid, which is responsible for increasing vitamin A in human's blood by converting into retinol that takes place in the liver [52]. According to Othman et al. [53], the high-performance liquid chromatography (HPLC) analysis showed that the plant has three compounds of carotenoid namely lutein, α-carotene and β-carotene with concentrations of 4.16 ± 0.11 μg/g, 0.71 ± 0.08 μg/g and

2.53 ± 0.25 μg/g, respectively. These carotenoids can be readily used as retinols, which are the vitamin A when the substances are metabolized in the liver. Usually, patients with liver damage caused by alcoholism can develop vitamin A deficiency syndrome. In agreement with that, a recent study conducted by Nagel et al. [54] showed that patients with liver cirrhosis may suffer vitamin A deficiency due to the inability of the organ to convert β-carotenoid into retinol.

4. CONCLUSION

In overall, this review has explained the diverse phytochemical compounds in *P. minor* that provide many benefits especially in the aspect of pharmacological activities. The plant that has been used for many years and widely found in the Southeast Asian area has been observed with the ability to act as antimicrobial against infection, reduce oxidative stress and protective effect to cell tissues from developing into cancer, help to reduce pain, reduce blood pressure and combat vitamin A deficiency. Therefore, it is suggested that future researchers should plan and conduct more *in vivo* studies as this plant has a high potential to be explored for its therapeutic activities in treating a wide range of disorders or diseases.

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