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REVIEW ARTICLES

A Review on *Christia vespertilionis*: A New Emerging Medicinal Plant

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A Review on Christia vespertilionis: A New Emerging Medicinal Plant

SUMMARY

Christia vespertilionis belonging to the Fabaceae family is a hidden gem that is emerging as a medicinal plant in Malaysia and better known as the butterfly wing plant. In recent times, the ornamental plant's pharmacological activities explored by many researchers with multiple research on-going. This plant is rich in flavonoids, phenols, sterols, fatty acids and sesquiterpenoid. It has diverse medicinal effects including anticancer, antitumor, anti-plasmodial, antiproliferative, antidiabetic and antioxidant activities. This review aimed to summarise the therapeutic potential of this plant and its scientific findings that may expand the scientific and commercial potential applications. All possible scientific data of C. vespertilionis was collected from Google Scholar while the structures were obtained from Pubchem and Chemspider while some were sketched using the ChemDraw program.

Key Words: *Christia vespertilionis, Butterfly Wing, Rerama, medicinal plant, pharmacology, phytochemistry*

Christia vespertilionis üzerine bir derleme: Yükselen Tıbbi Bir Bitki

ÖZ

Fabaceae familyasına ait olan Christia vespertilionis, Malezya'da tıbbi bir bitki olarak ortaya çıkan ve daha ziyade "Kelebek Kanadı" bitkisi olarak iyi bilinen gizli bir mücevherdir. Son zamanlarda, bu süs bitkisinin farmakolojik aktiviteleri, birçok araştırmacı tarafindan devam eden çoklu araştırmalarla araştırılmıştır. Bu bitki flavonoitler, fenoller, steroller, yağ asitleri ve seskiterpenoit bileşikleri bakımından zengindir. Antikanser, antitümör, antiplazmodiyal, antiproliferatif, antidiyabetik ve antioksidanlar gibi çeşitli tıbbi etkileri vardır. Bu derleme, bu bitkinin terapötik potansiyelini ve bilimsel ve ticari potansiyel uygulamalarını genişletebilecek bilimsel bulgularını özetlemeyi amaçlamıştır. C. vespertilionis'in tüm olası bilimsel verileri Google Scholar'dan toplanırken, yapılar Pubchem ve Chemspider'den elde edilirken, bazıları ChemDraw programı kullanılarak çizilmiştir.

Anahtar kelimeler: *Christia vespertilionis, Kelebek Kanadı, Rerama, tıbbi bitki, farmakoloji, fitokimya*

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INTRODUCTION

The critical role of plants to human lives is undeniable to date. Since ancient times, nature has been the primary source of food and medicines corresponding to various pharmacological conditions. In recent times, multiple drugs that are being used for treatment are based on plant-derived while some are produced synthetically. Plant phytoconstituent comes in diverse groups, and multiple pharmacologically functions. Malaysia is widely distributed with such plants that have been extensively used as a traditional remedy. *Christia vespertilionis* or butterfly wing plant which locally referred as Rerama is a newly emerging plant with distinctive medicinal values (Dar et al., 2017; Singh, 2015; Dash, 2016; Bunawan et al., 2015).

Initially, the genus was documented as *Hedysarum* in Flora Cochinchinensis by João de Loureiro, and the species was identified as *Hedysarum vespertilionis* and later accepted as *Christia vespertilionis* (Whiting, 2007). The genus *Christia* is an ornamental legume that belongs to the Fabaceae family consisting of various species distributed in tropical and subtropical Asia including Taiwan, Indonesia, Vietnam, Laos, India, China, Cambodia and Malaysia. Commonly, the genus *Christia* is called the island pea. *Christia* contains about 13 species identified in tropical Asia and five species discovered in China (USDA, 2006; Whiting, 2007; Lee et al., 2020).

Christia species are typically diffuse herbs or subshrubs containing trifoliate and simple leaves on the same plant, arranged alternately with stipule-like structure. This genus includes stipels and segmented loments folded and enclosed in the calyx (Keng et al., 1993). They have small flowers in white and axillary panicles or racemes. The flowers have membranous and bell-shaped calyx that enlarges upon maturation and five lobes of ovate-lanceolate. The central-obtuse petals come with unique crease and wing-like leaves which has round and blunt apices. The morphological investigation of the *Christia* pollen grains showed that the grains are tricolpate and medium-sized. The colpi are medium with about 0.6 to 0.8 times length of the polar axis and 0.1 to 0.3 times the width of the equatorial diameter that narrows slightly to rounded ends. The pollen grains shapes varied from spheroidal to subprolate and elliptic or rhombic in equatorial view while in polar view it is semi-angular. The colpus membrane is granulated, and its margin is undifferentiated from mesocolpium, while the end apertures vary from small to medium size with 0.1 to 0.3 times the length of the polar axis (Chen et al., 1993; Ye and Ohashi, 2002; Boo et al., 2003; Wu e al., 2003; Liston, 2004; Whiting, 2007).

Although it is more likely used for decorative purposes, its medicinal values are typically applied in folk medicines. To utilize its health benefits, multiple types of research using this plant are still on-going, and its complete potentials are yet to be discovered. This review aimed to summarize the existing studies done using this plant that will provide data to researchers on the prospect the plant is yet to be utilized and information on its current medicinal values.

BOTANICAL CHARACTERISTICS OF *CHRISTIA VESPERTILIONIS*

Christia vespertilionis (L.f.) Bakh.f. (synonyms: *Hedysarum vespertilionis*, *Laurea vespertilionis*) belongs to the Fabaceae family and known by the name Mariposa, Red butterfly wing and Rerama in Malay due to the unique shape of its leaves that resembles butterfly wings. It is widely distributed in Asian countries, including Malaysia, Vietnam, Thailand, Indonesia, Cambodia, Myanmar, and China (Bunawan et al., 2015). It is a non-climbing perennial herb, famous as an ornamental plant thus cultivated in most gardens in Asian countries. Besides that, the plant has a high tolerance to drought and nitrogen-fixing ability. Typically, the species can be found along the roadsides, inhabiting dry and grassy areas as well as sandy soils. The plant can grow from 60 to 120 cm tall and comes in two colour variations, which are green and red (Dash, 2016). Generally, the stems are slender containing trifoliate leaves, where the juvenile leaves have purple tint while matured ones are dark green with stripes of pale green with prominent veins. *C. vespertilionis* is usually propagated by seed under full sun with high humidity zone, moist media at the temperature of 21°C (Barham, 1996; Smitha & Jain, 2019). The most effective and economical propagation technique suggested were using seeds and semi-woody cuttings that allows *C. vespertilionis* to propagate easily (Shah et al., 2019). Its pollen grains are about 33.0 μm in polar axis, and 30.0 μm in equatorial diameter. The sculpture of mesocolpium is variable within one flower where it can be either microrugulate or granulate. The foot layer is discontinuous, and the infratectum is indistinct (Ye and Ohashi, 2002). The botanical classification of the *Christia vespertilionis* is listed in Table 1 below.

Table 1: Botanical classification of *Christia vespertilionis*

Kingdom	Plantae
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Rosidae
Order	Fabales
Family	Fabaceae – Pea family
Genus	Christia
Species	*vespertilionis* (L.f.) Bakh.f. – East Indian island pea
Synonyms	*Hedysarum vespertilionis, Laurea vespertilionis*
Vernacular name	Red Butterfly Wing (English) Rerama (Malay)

TRADITIONAL USES

Despite being an ornamental plant, this herbaceous shrub was utilised as a remedy for various medical conditions. Generally, the whole plant is used to treat snake bites and tuberculosis. Other traditional method includes the use of its crushed leaves are applied topically treat scabies and to heal bone fractures. Besides that, the leaves mixed with water to prepare decoction to treat bronchitis, colds muscle weakness, inflamed tonsils and to improve blood circulation (Bunawan et al., 2015; Dash, 2016; Ariff et al., 2019).

PHYTOCHEMICALS DISTRIBUTION

Previous studies have reported the phytoconstituents present in *C. vespertilionis* plant parts include phenols, alkaloids, triterpenes, fatty acids, alkanes, and long-chained alcohols (Bunawan et al., 2015; Dash, 2016; Ariff et al., 2019; Smitha & Jain, 2019). About seven tentative compounds with potential anticancer activity were identified using liquid chromatography-tandem with mass spectrometry (LCMS/MS) namely, denbinobin, 5,7-dihydroxy-chromone, rhein, kaempferol, sanleng acid, wedelolacetone and quercetin (Lee et al., 2020). Meanwhile, in another study using gas chromatography-mass spectrometry (GC-MS) analysis, about 26 compounds were identified from *C. vespertilionis* leaves methanolic extract. Some of the most prevailing compounds listed in the study include phytol, 10-undecenoic acid, 6-methylheptyl-2-propenoate, 2-(2-benzothiazolylthio)-1-(3,5-dimethylpyrazolyl)-ethanone and tetrahydro-2-methyl-thiophene as the most abundant compound with 61.77% (Zahidah et al., 2020). All compounds that previously identified in *C. vespertilionis* are tabulated below (Table 2).

Table 2: Phytoconstituents identified in *Christia vespertilionis*

Compound	Chemical class	Uses	References
Palmitine Corynoxidine Chloroquine	Isoquinolone alkaloid Aminoquinoline	Antiinflammatory, antimalarial Anti-acetylcholinesterase	Huang et al. (2012); Mishra et al. (2015)
Pheophorbid-α	Pigment (chlorophyll derivative)	Antioxidant, chemo preventive	Zepka et al. (2019)
7-isopropylidene-1-methyl-1, 2, 6, 7, 8, 9- hexahydronaphthalene (christene)	Sesquiterpene	Anti-plasmodial	Upadhyay et al. (2013)
Artemisinin Zerumbone		Antimalarial Antiproliferative, antioxidant, antiinflammatory, anticancer	Mojab (2012); Rahman et al. (2014); Thirunavukarasu et al. (2019)
Nicotinamide	Pyridine carboxamide	Antioxidant, neuroprotective agent, histone deacetylase inhibitor, antiinflammatory	Thirunavukarasu et al. (2019)
2'- hydroxydecanylpentadec-5, 8, 10, 12-tetraenoate (christanoate)	Oil	None reported	-
Ursolic acid methyl ester Oleanolic acid methyl ester Erythrodiol	Pentacyclic triterpenes	Antiinflammatory, anticancer, antidiabetic, antioxidant, antibacterial effects	Mlala et al. (2019)
2'-hydroxy genistein, Orobol 2, 3- dihydro-2'-hydroxy genistein	Isoflavonoids	Immunosuppressive, antiinflammatory, anticancer	Chang (2014)
Quercetin-3-*O*-glucoside Catechin-3-*O*-β-D glucoside	Flavonoid glycosides	Antioxidant, antidiabetic	Murugesu et al. (2018)
Stigmasterol, β-sitosterol acetate β-sitosterol	Sterols	Antidiabetic, antiinflammatory, anticancer	Murugesu et al. (2018); Ogbe et al. (2015)
Geraniol	Monoterpenoids	Antimicrobial, antioxidant, anti-inflammatory	Chen & Viljoen (2010)
Linoleic acid 10-undecenoic acid	Fatty acids	Precursor - biosynthesis of prostaglandins and cell membranes cytotoxic, anticancer, antioxidant	Ramsden et al. (2012); Narra et al. (2017)
Denbinobin	Phenanthrene	Anticancer	Song et al. (2012); Lee et al. (2020)
5,7-dihydroxy-chromone	Chromones	Anticancer	Yagura et al. (2003); Lee et al. (2020)
Kaempferol Quercetin	Flavonol	Antidiabetic, antioxidant	Murugesu et al. (2018)
Rhein	Anthraquinone	hepatoprotective, nephroprotective, anti-inflammatory, antioxidant, anticancer, and antimicrobial	Zhou et al. (2015)
Sanleng acid	Organic acid	Anticancer	Lee et al. (2020)
Wedelolacetone	Coumestan	Anticancer	Sarveswaran et al. (2012); Lee et al. (2020)
Phytol	Diterpene alcohol	Antiparasitic, antiinflammatory	de Moraes et al. (2014); Olofsscon et al. (2014)

BIOLOGICAL ACTIVITIES OF THE PLANT

Antioxidant Activity

Medicinal plants contain antioxidant compounds ubiquitously in various abundancy, which contributes to the plants' pharmacological activities. The 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity of the plant extract was measured using UV-visible that showed 49.76%, which is near to the predicted value of 50.62% using Response Surface Methodology (RSM) (Ariff et al., 2019). Another study measured the total phenolic and DPPH radical scavenging activity of *C. vespertilionis* powder extracted from aqueous-methanol (80%) and hydrolysed using HCl and NaOH. The outcome of the study showed that the total phenolic content of 9.13 ± 0.13, 4.94 ± 0.042 and 3.16 ± 0.28 mg of GAE/g meanwhile the DPPH assay exhibited percentage of inhibition of 54.52, 59.76, 54.99% and its IC_{50} value of 42.59, 39.54, and 38.13 mg/mL (Jusoh & Haron, 2019). Another screening study using different solvent extracts (hexane, hexane: ethyl acetate, ethyl acetate, ethyl acetate: methanol), of which ethyl acetate: methanol extract exhibited highest DPPH scavenging activity with the lowest IC50 value of 0.549 ± 0.02 mg/mL. Meanwhile, the hexane: ethyl acetate extract measured the highest ferric reducing power (FRAP) value of 271.67 ± 0.93

AAE μg ascorbic acid/g (Shukri et al., 2019). In recent times, the ethanolic and aqueous extract has shown potential antioxidant values with the total phenolic (251.33 and 162.03 GAE mg/g) and total flavonoid (95.39 and 42.35 QE mg/g) values, respectively (Mutalib & Latip, 2019).

Recently, Lee et al. (2020) have reported on the total phenolic content (TPC) of the *C. vespertilionis* root extract and its fractions. The ethyl acetate extract measured the highest TPC of 192.12 g GAE/g while one of its fractions, F4 showed TPC much higher than its crude with 330.92 g GAE/g. Besides that, the highest free radical scavenging activity was observed in the ethyl acetate root extract and its fraction, F6 with the IC_{50} values of 70.16 ± 1.49 and 76.71 ± 0.29 g/mL, respectively. Apart from that, the antioxidant capacity was also investigated using beta-carotene bleaching assay which indicates the discoloration of beta-carotene that results in due to the formation of hydroperoxyls upon thermal exposure is affected by the antioxidants present along with it. Of all the extracts analyzed, ethyl acetate extract of the root demonstrated good inhibition of the beta-carotene oxidation with 59.52%. In comparison, F4 of its fraction accounted for 83.68% inhibition, both at low concentration. The results indicate that the presence of prominent antioxidant compounds in the *C. vespertilionis* root extract and its fractions corresponds to the TPC analysis as well.

Antiplasmodial activity

The ability of the medicinal herbs to counter parasites majorly plasmodial contributes to the antimalarial effect. Plasmodial parasites typically cause a malarial fever that leads to an increased mortality rate in ancient times. The use of medicinal plants is practice since then to overcome this condition (Ahmed et al., 2010; Bethel et al., 2019). *C. vespertilionis* is such a plant that has been reported to possess effective antiplasmodial activity which contributes to its antimalarial activity. The cyclohexane extract of the plant was used to analyse its antiplasmodial activity against chloroquine-resistant *Plasmodium falciparum* of FcB1/Colombia strain measured the IC_{50} value of 10.8 μg/mL (Nguyen-Pouplin et al., 2007).

Another study investigated its antiplasmodial activity using multi-solvent extraction of its root, stem, and leaves. The study concluded that aqueous methanolic extract of stem showed the most significant effect against *Plasmodium falciparum* NH-54, with the IC_{50} of 7.5 μg/mL. This followed by the methanolic leaves extract, which measured the IC_{50} of 32.0 μg/mL. All the extracts were combined and further investigated for its antimalarial effects via *in vivo* technique against *Plasmodium berghei* infected mice. The results showed significant suppression (87.8%) of parasitemia compared to the control (chloroquine) upon eight days of treatment. In order to justify their findings, the combined extract was subjected to fractionation and isolation that retrieved 15 compounds, of which one novel compound identified as 7-isopropylidene-1-methyl-1,2,6,7,8,9-hexahydronaphthalene (Christene), a sesquiterpenoid possesses significant antiplasmodial activity with the IC_{50} of 9.0 μg/mL. The presence of potential phytoconstituents in the plant extract contributes to its anti-plasmodial and antimalarial activity (Dash, 2016; Upadhyay et al., 2013). Recently, Zahidah et al. (2020) reported that the methanolic extract of *C. vespertilionis* leaves displayed a moderate antimalarial activity with an IC_{50} value of 43.87 ± 2.04 μg/mL with some of the compounds corresponding to the activity (Table 2).

Antidiabetic Activity

Various medicinal plant leaves are infused in a drink or prepared as a decoction as a remedy for antidiabetic activity (Ismail et al., 2018). Likewise, *C. vespertilionis*, which claimed to possess antidiabetic effects, was investigated by assessing its α-glucosidase inhibitory activity using its leaves extract, where the hexane: ethyl acetate extract exhibited the lowest IC_{50} value of 0.195 mg/mL. The research team have reported the presence of various compounds that may have contributed to its activity. The outcome of the study suggested that the leaves of the plants can manage hyperglycemia via inhibition of α-glucosidase (Arifin et al., 2019).

Antitumor and Antiproliferative Activities

A tumor is accumulations of cells or mass of tissues that resemble swelling which can be either benign or turn cancerous. However, benign tumors may cause trouble when they enlarge to the extent that they press on the vital blood vessels or nerves, which often requires surgery for tumor removal. Antitumor potential plants may help to ease such conditions along with antiproliferative effect, which will inhibit the growth of the tumor. The previous study suggested that *C. vespertilionis* has significant effects on the inhibition of tumor growth and improved survival time of mice induced with S180 and H22 tumor cells. Upon treatment with the dosage of 12 g/kg, the extract showed inhibition of 54.42% and 60.77% and the life span was improved by 82.13% and 83.10% for both S180 and H22 tumor cells, respectively. Besides that, there were no abnormal changes in the immune functions and hematopoietic system of the treated mice (Wu et al., 2012).

Another antitumor study carried out using human medullary thyroid carcinoma (MTC-SK) and human small intestinal neuroendocrine tumor (SI-NET) cell lines (KRJ-I). Cell morphology upon treatment with ten µg/mL of *C. vespertilionis* plant aerial part extracted with ethyl acetate showed significant antiproliferative and pro-apoptotic effects. After 48 hours of treatment with the extract to MTC-SK cells, multicellular aggregation (diameter: ~300 µm) with the appearance of more single cells compared to the control cells which aggregates twice as large as of the treated cells (diameter: 800-900 µm). In contrast, the KRJ-I cells showed the reduced formation of aggregation with mostly dissociated into single cells. Besides that, both the cell lines were observed to have condensing chromatin, shrinking cells and apoptotic bodies upon treatment for 48 and 72 hours. However, no significant changes occurred in the control cells of both cell lines. The apoptotic pathway was induced via increased caspase 3/7 activity in both cell lines compared to the control cells within the first 24 hours of the treatment. The outcome indicates that *C. vespertilionis* may function as an anticancer for the remedy of neuroendocrine tumors (Hofer et al., 2013).

Anticancer Activity

The anticancer potential of *C. vespertilionis* has been studied using various cancer cells. One of the studies have investigated the viability of the ethanolic extract of *C. vespertilionis* leaves against multiple cell lines and the effectiveness of combination treatment with the standard drug, cyclophosphamide. The extract has showed potential viability against HaCaT (keratinocyte), MCF-7 (breast cancer) HepG2 (liver carcinoma), CRL 2522 (fibroblast), and WRL68 (normal liver) cell lines with the IC_{50} value of 1.22, 1.74, 1.63, 1.51 and 1.93 mg/mL. Besides that, the combination treatment of cyclophosphamide with the ethanolic extract showed synergism with the combination index (CI) value of 0.466. The research team suggested that the presence of isoorientin as the most prominent compound may have contributed to the activity. Besides, the compound has been previously reported induce HepG2 apoptosis via stimulation of reactive oxygen species (ROS) formation, which eventually leads to cellular damage. Additionally, the compound has shown an antiproliferative effect on colorectal cancer cells via alteration of cell pathways and apoptosis. This indicates that the plant extract has the potential to be developed as an anticancer agent (Mutalib & Latip, 2019).

The anticancer effect of *C. vespertilionis* root extracts (ethyl acetate and chloroform) was investigated against two cell lines namely, hormone receptor-positive human breast adenocarcinoma (MCF-7) and triple-negative human breast adenocarcinoma (MDA-MB-231). The extracts displayed dose-dependent cytotoxicity effects on the observed cell lines with the IC_{50} value of 11.34 ± 1.20 and 29.58 ± 3.80 µg/mL against MDA-MB-231 for both ethyl acetate and chloroform root extracts, respectively. Meanwhile, ethyl acetate exhibited the lowest IC_{50} value of 44.65 ± 5.78 µg/mL for MCF-7 cell line, followed by chloroform extract with 54.55 ± 9.51 µg/mL. The results obtained probably due to the different apoptosis mechanism corresponding to the bioactive compounds present in the extract. The study suggested that the presence of flavonoids may predominantly be metabolized via the CYP1A1-mediated pathway in MCF-7 while MDA-MB-231 was metabolized by CYP1B1-mediated pathway. Besides that, previous studies have displayed the presence of triterpenes causes apoptosis in breast cancer cells, which involves the P53-dependent and P53-independent signaling in both MCF-7 and MDA-MB-231, respectively. The study concluded that the ethyl acetate extracts of *C. vespertilionis* roots displayed a promising antioxidant and anticancer effect against breast cancer cell line (Chen et al., 2003, Razak et al., 2019, Kim et al., 2018; Lee et al., 2020).

TOXICITY STUDY

As much as the medicinal plants exert beneficial pharmaceutical effects, some of it may also exhibit specific toxic effects depending on the type of toxicant presence in it and its abundancy. Therefore, it is equally crucial to investigate the toxicity level of the medicinal plants' extract being studied for pharmacological functions. In a subacute oral toxicity study using ethanolic extract of *C. vespertilionis* leaves at the dosage of 75, 125 and 250 mg/kg for 28 consecutive days. The serum biochemical and hematological variables showed no significant changes in both the treated and control rats. However, from the histopathological investigation of the kidney and liver, no significant lesions were observed in the kidney tissues of all treated groups meanwhile mild to a moderate lesion of hepatic necrosis were found in all three dosages, respectively. Apart from that, mild hepatic degeneration and eventual hepatitis were observed in all three groups. The plant may contain toxicant(s) that may have caused these observation or compounds interacting antagonistically (Nurul et al., 2018).

CONCLUSION

Christia vespertilionis plant contains beneficial phytoconstituents that may have contributed to it pharmacological activities that make it a potential remedy for various conditions and can be further explored for its application in the pharmaceutical industry. Technically, there is more research gap that can be fulfilled using the plant.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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