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Blumea balsamifera Linn DC: A review on traditional uses, phytochemical composition and pharmacological properties

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Blumea balsamifera (Linn) DC from Asteraceae family is well known medicinal plant in South East Asia and China. The plant locally known as sembong (Malaysia, Vietnam & Indonesia), capa (Malaysia), sambong (Philippine), sombong (Indonesia) and ainaxiang (China). This plant has been used traditionally for centuries to treat many illnesses. The present review article illustrates the recent studies on phytochemisty and pharmacological properties of *B. balsamifera*. More than 100 compounds have been identified from this plant and most of the compounds are flavonoids and essential oil. Pharmacological studies on the plant extract and isolated compounds (volatile and non-volatile) focuses on antioxidant activity, anticancer, anti-lithiasis, antimicrobial, wound healing and anti-obesity. Compiled data of traditional uses, phytochemistry and pharmacologic property of *B. balsamifera* revealed that this plant is robust and has high potential to be developing as alternative medicine.

Keywords: *Blumea balsamifera*, asteraceae, sembong, anti-lithiasis, wound healing.

INTRODUCTION

According to WHO, more than 80% of the world population still depends on medicinal plant as the source of their primary healthcare. In terms of economic value, medicinal plant account for more than US$4 billion market value (Mohd 2017; Azemin and Mohd 2015). This value is expected to increase to US$7 billion in 2027 with the annual growth rate of 5.5% (WHO, 2002).

Blumea balsamifera (L.) DC. (Asteraceae) is one of the promising medicinal plants. Locally known as *sembung, sambong* or *capa*, this plant is originated from subtropical and tropical Asia (Pang et al., 2014, Nessa et al., 2005) including Malaysia, Taiwan, Myanmar, South China, Thailand, Indonesia, India and the Philippines (Shirota et al., 2011). This plant is an erect, softly hairy, half woody stem shrub with strong aromatic properties (Figure 1A). The leaves are simple, alternate with toothed margin. The blade is broad, elongated oblong with 7-20 cm long, and appendaged base. Base of the leaf is attenuated with petiole and narrow linear appendants of 3 to 5 pairs on both sides, pubescence above, slight brown or thick yellow-white silky-villous, highlighted below midrib, with lateral veins of 10-15 pairs. The flowers are yellow with loose flower head scattered along leafy panicles (Fig. 1B). The discoid flower has two types; first type, the central flower consists of few large flower with campanulate corolla. The peripheral flower is tiny, numerous, with tubular corolla; Anther cells tailed at base. Fruits or known as achene are 1-seeded, dry, 10-ribbed, with hairy at top. *B. balsamifera* plant is able to grow up to 3 m high depending on the locality. This plant is normally found along the forest edges, under forests, flood plain, roadsides, lowlands, valleys, river beds, and mountainous areas (Yuan et al. 2011).

In this review, the uses of this plant in traditional system of medicine are described. The phytochemical composition and identified compound from studies around the world are compiled. Meanwhile, reported pharmacological properties from *in vitro* and *in vivo* studies are also covered.

Figure 1: *Blumea balsamifera* plant (A) and flower (B). Locality- Kuala Berang, Terengganu, Malaysia.

Traditional Uses

B. balsamifera has been used in traditional medicine by several community including Chinese minority groups for the treatment of stomach pains, respiratory infections, and for rheumatism (as aromatic bath) (Ragasa et al. 2005). The leaves infusion is used as aromatic bath for women who just giving birth. Roots and leaves are used for fevers and reduced the body temperature (Byeoung et al*.,* 2012). Besides that, sembung roots and leaves are also used as herbal medicine treatment for lumbago, eczema, beriberi, dermatitis, skin injury, menorrhagia, rheumatism, and as an insecticide (Burkill 1966). The Pharmacopoeia of the People's Republic of China stated that *B. balsamifera* as the only plant source for Aipian with a consistent efficacy which could clear heat, relieve pain and induce resuscitation (Pang et al*.* 2014). For colds and coughs treatment, sembung can be drink as a tea (Henry et al*.* 2018). According to Sakee et al*.*2011, in Thailand and Chinese, leaves of *B. balsamifera* are used to treat septic wounds and other infections. The roots and leaves of *B. balsamifera* have also been used for the treatment of rheumatism, arthritis, and gynecologic diseases (Xu et al. 2012). In Malay traditional medicine, the leaves of sembong are taken with food as stomachic. The decoction of roots is used for indigestion, beri-beri and fever (Burkill, 1935). Decoction of the leaves is consumed to treat heavy menstrual bleeding. The boiled leaves also taken to treat lower back pain, joint pain and bathe after childbirth (Burkill, 1935). In Philippines, its primary uses are as diuretic, common cold, urolithiasis, treat urinary track infections, high blood pressure and sometime as an astringent for wounds (Rico, 1992).

PHARMACOLOGICAL PROPERTIES

Anticancer

There were several *in vitro* studies reported anticancer activity for *B. balsamifera*. Ng et al. (2010) determined cytotoxicity activity of methanol extract against various cancer cell lines by MTT assay. It was found that no regular or acute cytotoxicity on T-47D, HepG2, CCD-18Co, NCI-H23 and HCT-116. In addition, six out of nine isolated flavonoids possess cytotoxicity against NCI-H187, MCF-7, and KB cell lines (Saewan et al. 2011).

Hasegawa et al. (2006) isolated and tested dihydroflavonol from *B. balsamifera* showed potent synergism with TRAIL in treatment of the TRAIL-resistance ATLL cell line KOB. With combination treatment, resulted in apparent apoptosis. Treatment with dihydroflavonol isolated from *Blumea* has increased the level of TRAIL-R2 promoter activity and surface protein expression in a p53-independent manner. *B. balsamifera* extract was also effective against human hepatocellular carcinoma cells (Merina et al. 2012). This data suggest that combination treatment with dihydroflavonol from *B. balsamifera* and TRAIL would be a strategic move for cancer therapy.

A study showed sembung extract inhibits the activity in human and rat hepatocellular carcinoma cells without causing cytotoxicity. This finding shed some light on the possible therapeutic effect of *B. balsamifera* extracts onto hepatoma cancer patients (Norikura et al. 2008). Methanol extract of B. balsamifera was able to cause the induction of cell cycle arrest at GI phase via decreases in expression of cyclin-E and phosphorylation of retinoblastoma (Rb) protein in both dose and time dependent manners. There was also a significant reduction of the level of a proliferation related ligand which stimulates tumor cell growth as a result of *B. balsamifera* extract.

Antioxidant

It is pivotal to evaluate antioxidant activity for medicinal plant as free radicals are the source of various malady (Ahmad et al. 2015). *B. balsamifera* extracts (leaves) using various solvent was tested for antioxidant and exhibited various capacity in scavenging free radicals. These studies revealed that flavonoids from *B. balsamifera* showing interesting antioxidant activity especially in scavenging superoxide radicals (Neesa et al. 2003; 2004). Neesa et al. (2004) have isolated and characterized eleven flavonoids (velutin, ombuin, tamarixetin, blumeatin, luteolin, luteolin 7-methylether, quercetin, 5,7,3',5'-tetrahydroxy flavanone, rhamnetin, dihydroquercetin-7,4'-dimethylether, dihydroquercetin-4'-methylether) from the leaves of *B. balsamifera* and tested for their free radical scavenging activity, DPPH. It was revealed that flavonoids from this plant are potent antioxidants, comparable in activity with tocopherol and the widely used synthetic antioxidants BHT and BHA. The antioxidant activities of flavonoids were decrease in order of quercetin > rhamnetin > luteolin > luteolin-7- methylether > blumeatin > 5,7,3',5'-tetrahydroxy flavanone > tamarixetin > dihydroquercetin-4'-methylether > dihydro quercetin-7,4'-dimethylether (Neesa et al., 2004).

Nguyen et al. (2004) carried out xanthine oxidase inhibitory activity of methanol extracts of Vietnamese *B. balsamifera* (collected from Lam Dong province). Strong xanthine oxidase inhibitory activity was found with an IC_{50} of 6.0 μg/mL. In addition, seven compounds were identified from the methanol extract. Three of the compounds possess IC_{50} of 0.23 to 1.91 mmol/L, as compared to that of allopurinol (IC_{50} of 2.50 mmol/L), a standard compound in xanthine oxidase inhibitory activity. Those three compounds are quercetin, (2R,3S)-(−)-4'-O-methyl-dihydroquercetin, and quercetin-3,3',4', showed higher inhibitory activity.Corroborated with this finding, Nessa et al. (2010) have also found that the methanol extract of Malaysian *B. balsamifera* possess higher xanthine oxidase inhibitory activity as compared to that of the pet-ether and chloroform extracts. Wang and Yu, (2018) found that the antioxidant activity of the essential oil of *B. balsamifera* from China had DPPH free radical scavenging activity at IC_{50} of 28.22 g/L.

These reports suggest that *B. balsamifera* leaves extracts may provide a new source of natural food antioxidants.

Antimicrobial

Three different extracts, hexane, dichloromentane, methanol together with essential oil of *B. balsamifera* was tested against various bacteria and fungi using the disc diffusion method. Essential oil have shown to have the most potent antimicrobial activity especially against *S. aureus* and *B. cereus* (clinical isolates) with good clear of 19 to 12 mm of inhibition zones and against fungi *C. albicans* (Sakee et al. 2011; Wang and Yu, 2018). Moreover, hexane extract appeared to have the broadest spectrum of activity, capable of inhibiting two strains of *S. aureus* and two strains of the Gram-negative bacterium *E. cloacae* (Sakee et al. 2011).

Jiang et al. (2014), found that the volatile oil in *B. balsamifera* has obvious inhibitory activity on the experiment fungal strains of eight kinds of plant pathogenic fungi, and among them, the antibacterial activity on *Rhizoctonia solani* Kühn, *Rhizoctonia solani* AG1-IA, and *Sclerotinia sclerotiorum* are relatively strong with minimum inhibitory concentration (MIC) value for all is 0.195 μL/mL. Chen et al. (2009; 2010) agreed that the essential oil from *B. balsamifera* responsible for antifungal activity.

Antiplasmodial

B. balsamifera extract has also shown antiplasmodial activity. The methanol extracts of roots and stems of *B. balsamifera* showed activity against *Plasmodium falciparum* D10 strain (sensitive strain) with an IC_{50} value of (26.25 ± 2.47) μg/mL and (7.75 ± 0.35) μg/mL, respectively (Upadhyay et al. 2013; Noor et al. 2007).

Abdillah et al. (2015) said the extracts *B. balsamifera,* showed good antiplasmodial activity with ED_{50} of 101-250 mg/kg body weight.

Wound Healing

According to Krishna et al. (2015), varying concentrations of *B. balsamifera* leaves decoction showed different effects on deep wounds of mice. The faster the wound healing was found when greater the concentration of *B. balsamifera* leaves was used. There was significant difference in the effect of *B. balsamifera* leaves decoction and Betadine in the number of days of wound healing in mice especially in the redness and swelling. Essential oil of *B. balsamifera* leaves was diluted with 10% ethanol and applied topically once daily to wound of adult male and female rats of Sprague Dawley (220-250g) had promoted significantly ($p<0.05$) burn-wound healing (>90% complete healing) compared to control group (burn ointment) after 21 days of treatment (Fan et al. 2015).

In the same study (Fan et al. 2015), rats with different concentration *B. balsamifera* oil (BBO) showed that BBO is capable in accelerating the burn-wound healing via anti-inflammatory response. This study also show the decreasing of inflammatory factors, IL-1 and TNF-α in rats after BBO treatment especially at fifth day after burn. Observation after day 9 of burn injury, more collagen fibers and fibroblasts cells observed.

Evaluation of healing process on Sprague-Dawley rat skin wounds treated flavonoid-rich leaves extract from *B. balsamifera* showed a very encouraging results. After 7 days of treatment, the wound was contacted with collagen deposition, capillary regeneration, and re-epithelization was observed (Pang et al. 2017). Biochemical analysis revealed, those alterations were associated with expression of transforming growth factor-β1 (TGF-β1), enhanced expression of vascular endothelial growth factor (VEGF), and CD68 antigen in rat wound tissues. In another study, BBO was applied topically onto wounded Kun-Ming mice. Similar results obtained, where collagen deposition, enhanced angiogenesis, additionally induced epithelial deposition and formation of granular tissue was observed (Carvalho et al. 2018).

Anti-Obesity

Kubota et al. (2009) found that lipid accumulation and glycerol-3-phosphate dehydrogenase (GPDH) activity was suppressed by treatment with *B. balsamifera* extract. The suppression took place without causing cell cytotoxicity in adipocytes and preadipocytes of 3T3-L1. The expressions of key adipogenic transcription factors, including CCAAT element binding protein (C/EBPs), leptin and peroxisome proliferator-activated receptor (PPAR)γ, was significantly affected by *B. balsamifera* extract treatment. It can be suggested that the possible mechanism of *B. balsamifera* extract as anti-obesity is through blocking the adipogenesis by decreasing key adipogenic transcription factors in preadipocytes of 3T3-L1 cells. This also suggests that *B. balsamifera* extract may possess anti-inflammatory, antiatherogenic, and antidiabetic effects through up-regulation of adiponectin in 3T3-L1 adipocytes.

Anti-lithiasis

Some studies explored the growth modifying properties of herbal treatment to urinary calculi (Rodgers et al. 2014). A decoction of the leaves of *B. balsamifera* is reported to have anti-lithogenic effects (Rico, 1992). *B. balsamifera* extract be able to alter the morphology of calcium oxalate crystals (Montealegre et al. 2017), the pivotal mechanism for anti-lithiasis agent. The crystal size was shifted from calcium oxalate monohydrate (COM) phase to calcium oxalate dehydrate (COD) phase. This scenario prevents the crystals from aggregated. By using modeling Ca^{2+} concentration in solutions, the effect of *B. balsamifera* extract on the crystallization of calcium oxalate was established. This shows that the extract is capable of increased the rate of crystallization where it would favour the formation of smaller crystals that are easily eliminated from the urinary system (Montealegre et al. 2017; Nancollas and Gardner 1974)

Agriculture pest management

The use of *B. balsamifera* extract for agriculture pest pathogen was investigated by several group (Gao 2007; Luo et al. 2004; Wang et al. 2012; Chu et al. 2013). Acetone extracts of *B. balsamifera* are shown to inhibit the growth of agriculture fungi pathogen such as *Colletorichum musae*, *C. capsici*, *C. gloeosporioides*, *Pryicutaria oryzae*, *Fusarium oxysporum*, and *F. oxysporum* f. sp. with more than 90% inhibition rate (Luo et al. 2004). Meanwhile, Gao (2007) reported the volatile oil of *B. balsamifera* inhibited *F. graminearum*, *Aeromonas hydrophila*, and *Magnaporthe grisea*. Wang et al. (2012) reported the extract of *B. balsamifera* leaves showed a 60.8% insecticidal activity against the adult of spiralling whitefly, *Aleurodicus disperses*, a white sap-sucking insect.

Besides that, Chu et al. (2013) reported that the essential oil of *B. balsamifera* possess fumigant toxicity against the maize weevils, such as *Sitophilus zeamais*. The crude oil also induced the fatality of *Sitophilus zeamais* adults. Taking together, the findings show that the both extract and essential oil of *B. balsamifera* possess the potential to be develop new plant-based insecticides.

Others pharmacological activity

Other pharmacological activity is summarized in Table 1.

Table 1: Others pharmacological activities of *B. balsamifera*.

No.	Activity	References
1	Anti-inflammatory	Chen et al. (2010)
2	Antityrosinase	Saewan et al. (2011)
3	Platelet Aggregation	Xu et al. (1994)
4	Enhancing Percutaneous Penetration	Fu et al. (2013)
5	Antihyperglycemic	Xia et al. (2014)
6	Aldolase reductase inhibitory activity	Dong et al. (2012)
7	Gastric ulcer	Nugroho et al. (2016)

PHYTOCHEMICAL ANALYSIS

There have been more than 100 volatile or non-volatile constituents isolated from *B. balsamifera,* including monoterpenes, sesquiterpenes, diterpenes, flavonoids, organic acids, esters, alcohols, dihydroflavone, and sterols. (Pang et al. 2014; Neesa et al. 2004; Neesa et al. 2010; Fujimoto et al. 1988; Barua et al.1992), as well as essential oils (Osaki et al. 2005; Du et al. 2009; Sakee et al. 2011; Ruangrungsi et al.1981).

Barua et al. (1992) described the isolation of two new unusual flavanones, (2R,3R)-5'-methoxy-3,5,7,2'- tetrahydroxyflavanone, (2S')-5,7,2',5'-tetrahydroxyflavanone and a rare flavonol, 7,5'-dimethoxy-3,5,2'- tetrahydroxyflavone, from the chloroform extract of *B. balsamifera*.

Ruangrungsi et al. 1981, have isolated d-carvotanacetone, 1-tetrahydrocarvone, a mixture of butyric, isobutyric, u-octanoic acids and an unidentified phenol. Subsequently, *l*-borneol, fenchone, 1,8-cineol, two carvotanacetone derivatives , a diester of coniferyl alcohol, some polyacetylenes and thiophene derivatives, campesterol, stigmasterol , sitosterol, xanthoxylin, erianthin and 5,3',4'-trihydroxy-3,6,7-trimethoxyflavone, other unidentified flavonoids, coumarins and triterpenes , and myristic acid have been isolated from *Blumea* species.

Chen et al. (2009) carried out separation by repeated column chromatography (including SiO_2 and Sephadex LH-20) and preparative reverse-phase HPLC afforded ten new sesquiterpenoid esters, from the CH_2Cl_2 fraction. 13 known flavonoids are, 3,5,3′,4′-tetrahy droxy-7-methoxyflavone, 5,7-dihydroxy-3,3′,4′-trimethoxyflavone, davidigenin, ayanin, davidioside, catechin, dihydroquercetin 7,4′-dimethyl ether, blumeatin, dihydroquercetin 4′-methyl ether, 3,5,3′-trihydroxy7,4′-dimethoxyflavone , 5,7,3′,5′-tetrahydroxyflavanone, luteolin, and quercetin, from the EtOAc fraction.

Volatile compounds

Most of the isolated compounds from *B. balsamifera* was characterized by gas chromatography mass spectrometry (GC-MS). Alcohols and terpenoids were the main volatile compounds and the terpenoids accounted for a considerable proportion was found. The volatile components in leaves of *B. balsamifera* have been identified and major active constituents containing terpenoids, fatty acids, phenols, alcohols, aldehydes, ethers, ketones, pyridines, furans, and alkanes. Several volatile oils are contained in the leaves and branchlets of *B. balsamifera*, which are the key crude materials of refined borneol. Volatile oil in *B. balsamifera* is a yellow oily liquid with a unique aroma. (Pang et al. 2014, Chen et al. 2009)

Wang et al. (2014), had extracted essential oil of *B. balsamifera* by improved hydrodistilation (IHD), simultaneous distillation extraction (SDE) and hydrodistillation-solvent extraction (HDSE) and analyzed by gas chromatography-mass spectrometry (GC-MS). As a result, (-)-borneol, a bicyclic monoterpenoid alcohol was obtained in very high percentage (82% in IHD, 45% in HDSE and 44% in SDE).

Bhuiyan et al. (2010) reported that the volatile oils of *B. balsamifera* mainly contained monoterpenes and sesquiterpenes, such as L-borneol, 10-epi-γ-eudesmol, γ-eudesmol, β-eudesmol, α-eudesmol, limonene, L-camphor, palmitic acid, and D-camphor. Meanwhile, Chen et al. (2010) identified blumeaenes A-J, sesquiterpenoid esters. GC-MS analysis of essential oil of *B. balsamifera* leaves revealed the presence of 50 components, contributing to 99.07% of the oil. The dominant components in the oil from leaves were borneol (33.22%), caryophyllene (8.24%), ledol (7.12%), tetracyclo[6,3,2,0,(2.5).0(1,8) tridecan-9-ol, 4,4-dimethyl (5.18%), phytol(4.63%), caryophyllene oxide(4.07%), guaiol (3.44%), thujopsene-13 (4.42%), dimethoxy-durene (3.59%) and γ-eudesmol (3.18%).

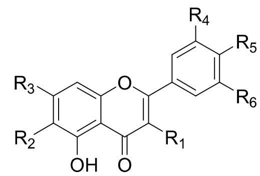
Hao et al. (2000) have qualitatively and quantitatively analyzed the volatile oil of *B. balsamifera* growing in Guizhou Province. A total of 28 constituents were identified in this study, including: L-borneol, β-caryophyllene, camphor, γ-eudesmol, 1-octen-3-ol, trans-β-ocimene, and 1,3,4,5,6,7-hexahydro-2,5,5-trimethyl-2H-2,4a-ethanonaphthalene.

Flavonoids

Flavonoids group of compounds, including flavonoid, flavanone and chalcone constituents, are the major non-volatile constituents of *B. balsamifera*. The activity of compounds in *B. balsamifera* greatly depended upon the nature of the substitution in the flavonoids. The compounds having the hydroxyl groups at C-5 and C-7 and the double bond between C2 and C3 in the ring C displayed stronger XO inhibitory activity than those of the other compounds. All isolated flavonols possessed stronger activity than that of the positive control allopurinol and the presence of methoxyl groups at C-3, C-7, C-3′/C-4′ instead of hydroxyl group in 6 showed slightly improved activity. Among the five flavanones, compounds having a hydroxyl group at C-3 displayed strong activities with IC_{50} values smaller than that of 5 without the hydroxyl group at C-3. In addition, the presence of an -OH group at C-3 showed more potent activity (Nguyen et al. 2012). Some of the flavanoids are shown in Table 2 (flavones and flavonols) and Table 3 (flavanones and flavanonols)

Ming et al. (2010), have isolated thirteen flavonoid compounds from the aerial parts of *B. balsamifera*. Their structures were identified as 5,7-dihydroxy-3,3′,4′-trimethoxy flavone, 3,5,3′,4′-tetrahydroxy-7-methoxyflavone, davidigenin , catechin , ayanin, davidioside, dihydroquercetin-7,4′-dimethylether, blumeatin, dihydroquercetin-4′-methylether, 3,5,3′-trihydroxy-7,4′-dimethoxyflavone, 5,7,3′,5′-tetrahydroxyflavanone, luteolin, and quercetin. Meanwhile, Nessa et al. (2004) isolated several flavonoid including blumeatin, velutin, tamarixetin, dihydroquercetin-7,4'-dimethyl ether, ombuine, rhamnetin, luteolin-7-methylether, luteolin, quercetin, 5,7,3',5'-tetrahydroxyflavanone, and dihydroquercetin-4'-methyl ether.

Table2: Some flavonoid (flavones and flavonols) isolated from *Blumea balsamifera*

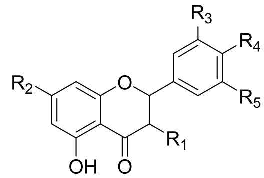


Flavones and Flavonols

R1-H, R2-H, R3-OMe, R4-H, R5-OH, R6-H: 4”,5-Dihydroxy-7-methyletherflavone
R1-H, R2-H, R3-OH, R4-OH, R5-OH, R6-H: Luteolin
R1-H, R2-H, R3-OMe, R4-OH, R5-OH, R6-H: Luteolin-7-methylether
R1-H, R2-H, R3-OH, R4-OH, R5-OMe, R6-H: Diometin
R1-OH, R2-H, R3-OH, R4-OH, R5-OH, R6-H: Quercetin
R1-H, R2-H, R3-OH, R4-OMe, R5-OH, R6-H: Chrysoeriol
R1-OH, R2-H, R3-OMe, R4-OH, R5-OH, R6-H: 3,5,3’,4’-Tetrahydroxy-7-methoxyflavone
R1-OH, R2-H, R3-OMe, R4-OH, R5-OMe, R6-H: 3,5,3’-Trihydroxy-7,4’-dimethoxyflavone
R1-OH, R2-H, R3-OMe, R4-OH, R5-OMe, R6-H: Ombuine
R1-OH, R2-H, R3-OH, R4-OH, R5-OMe, R6-H: Rhamnetin
R1-OH, R2-H, R3-OH, R4-OMe, R5-OMe, R6-H: Tamarixetin
R1-OH, R2-H, R3-OH, R4-OMe, R5-OMe, R6-H: 3,5,7-Trihydroxy-3’,4’-dimethoxyflavone
R1-OH, R2-H, R3-OMe, R4-OH, R5-OH, R6-H: 3,3’,4’,5-Tetrahydroxy-7-methoxyflavone
R1-OH, R2-H, R3-OMe, R4-OMe, R5-OMe, R6-H: 3,5-Dihydroxy-3’,4’,7-trimethoxyflavone
R1-OMe, R2-H, R3-OMe, R4-OMe, R5-OH, R6-H: 4’,5’-Dihydroxy-3,3’, 7-trimethoxyflavonone
R1-OMe, R2-H, R3-OH, R4-OMe, R5-OMe, R6-H: 5.7-Dihydroxy-3,3’,4’-trimethoxyflavone
R1-OMe, R2-OH, R3-OMe, R4-OMe, R5-OH, R6-H: Chrysoplenol C
R1-OMe, R2-H, R3-OMe, R4-OH, R5-OMe, R6-H: Ayanin
R1-OMe, R2-H, R3-OH, R4-OMe, R5-OH, R6-H: 4’,5,7-Trihydroy-3,3’-dimethoxyflavone

Ali et al. (2005), extracted 3,4',5-trihydroxy-3',7- dimethoxyflavanone from the ligroin extract of *B. balsamifera* leaves. The constituents of 3',4',5-trihydroxy-7-methoxyflavanone and a new bioflavonoid, determined as 3-O-7'-biluteolin, were extracted by acetone.

Table3: Some flavanones and flavanonols isolated from *Blumea balsamifera*



Flavanones and Flavanonols

R1-H, R2-OMe, R3-OH, R4-H, R5-H: Bumeatin (**20**)
R1-H, R2-OH, R3-OH, R4-OH, R5-H, 5,7,3',5'-Tetrahydroxyflavanone (**21**)
R1-H, R2-OMe, R3-OH, R4-OH, R5-H: 3',4',5-Trihydroxy-7-metoxyflavanone (**22**)
R1-OH, R2-OH, R3-OH, R4-OMe, R5-H: Dihydroquercetin-4'-methylether (**23**)
R1-OH, R2-OMe, R3-OH, R4-OMe, R5-H: Dihydroquercetin-7,4'-dimethylether (**24**)
R1-OH, R2-OMe, R3-OMe, R4-OH, R5-H: 3,5,4'-trihydroxy-3',7-dimethoxyflavanone (**25**)
R1-OH, R2-OH, R3-OH, R4-H, R5-OH: 3,3',5,5',7-Pentahydroxyflavanone (**26**)
R1-OH, R2-OMe, R3-OH, R4-OH, R5-H: 3,3',4',5-Tetrahydroxy-7-methoxyflavanone (**27**)
R1-OH, R2-OMe, R3-OH, R4-OMe, R5-H: 3,3',5-Trihydroxy-4',7-dimethyflavanone (**28**)
R1-OH, R2-OH, R3-OH, R4-OMe, R5-H: 3,3',5,7-Tetrahydroxy-4'-methoxyflavanone (**29**)
R1-OMe, R2-OMe, R3-OH, R4-OH, R5-H: 3',4',5-Trihydroxy-3,7-dimetoxyflavanone (**30**)

Sesquiterpene Lactone

There were three sesquiterpene lactones, blumealactone A, blumealactone B, and blumealactone C. isolated from *B. balsamifera* by extracting its dried leaves with 90% ethanol (Fujimoto et al. 1988). These compounds is reported responsible for cytotoxic and potential to be tumor inhibitors (Chadwick et al. 2013; Ghantous et al. 2010)

Sterol

Chen (2009) isolated β-sitosterol, daucosterol, and 5α,8α-epidioxyergosta-6,22-dien-3β-ol from the aerial sections of B. balsamifera collected from Mengla, Yunnan. Zhao et al. (2007) also isolated stigmasterol and β-sitosterol from *B. balsamifera* leaves. Meanwhile, from ethyl acetate and chloroform extract, Liang et al. (2011) obtained seven compounds including sterol daucosterol.

CONCLUSION

B. balsamifera has been featured in most of the herbal compendium around the world such as Malaysian Herbal Monograph, Chinese Materia Medica, Materia Medika Indonesia, WHO Selected Monograph, German Commission E, Vietnamese Herbal Pharmacopeia, ESCORP and several other ayurvedic compendium (Mohd, 2017). From the data compiled in this article, it can be concluded that *B. balsamifera* is a very robust medicinal plant with great potential. There are many traditional uses of this plant including treatment for respiratory infections, antiseptic, wound healing, stomach pains, fever, dermatitis, rheumatoid, joint pain, etc. Phytochemical studies on this also very extensive with more than 100 compounds isolated and identified. These compound mainly flavonoids, terpenes, sterol and volatile oils. Most of these compounds been tested for their pharmacological activities including anticancer, wound healing agent, anti-inflammatory, anti-lithiasis/kidney stone disease, antimicrobial and antioxidant. Based on this information, *B. balsamifera* has all the potential to be developed as an alternative medicine. Future studies on this plant can be focuses on dissecting the mechanisms of action for its therapeutic activities.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

KSM and NAMR contributed equally to the collection of material and drafted the articles. KSM reviewed and approved the final version of the article.

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