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Journal home page: <http://www.pharmasm.com>**PHARMACOLOGICAL ACTIVITIES OF *BLUMEA BALSAMIFERA* L.DC: AN OVERVIEW**

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**ABSTRACT**

The main components of sambong (*Blumea balsamifera*) are listed in this article. The whole plant and its crude extracts, as well as its isolated constituents, display numerous biological activities, such as antitumor, hepatoprotective, superoxide radical scavenging, antioxidant, antimicrobial and anti-inflammation, anti-plasmodial, anti-tyrosinase, platelet aggregation, enhancing percutaneous penetration, wound healing, anti-obesity, along with disease and insect resistant activities. Although many experimental and biological studies have been carried out, some traditional uses such as rheumatism healing still need to be verified by scientific pharmacological studies, and further studies including phytochemical standardization and bioactivity authentication would be beneficial.

**KEYWORDS:** Traditional Chinese Medicines; *Blumea balsamifera*; sambong; herbal authentication; phytochemistry; biological activities.

**INTRODUCTION**

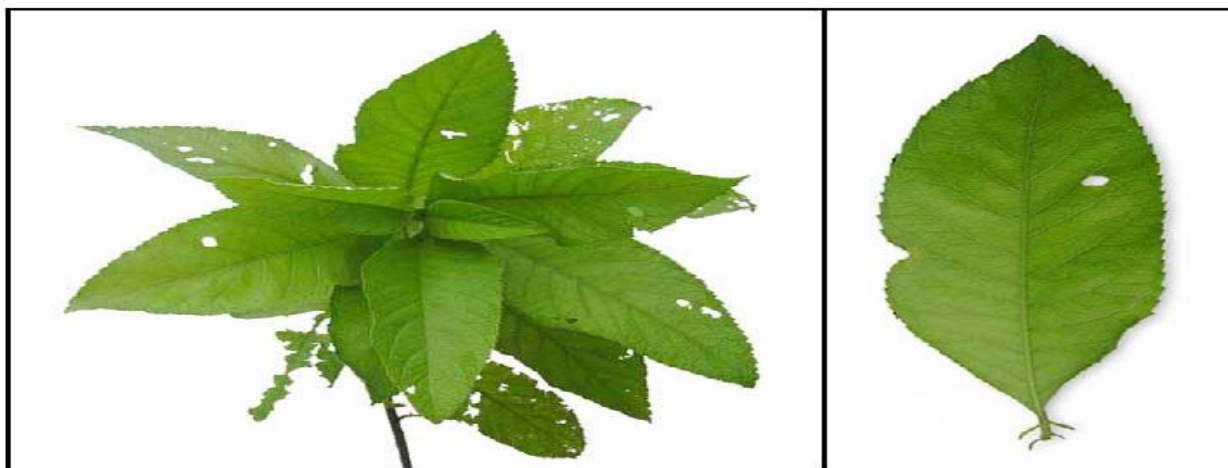
Nowadays, herbal medicines are widely consumed and their sales have been rising significantly all over the world. According to the reports of the World Health Organization (WHO), to treat diseases over 80% of the populations in developing countries mainly rely on herbs, which are considered to be safer and more effective than synthetic drugs. <sup>[1-3]</sup>

*Blumea balsamifera* (L.) DC. (Asteraceae), also known as sambong, has been used as medicine for thousands of years in Southeast Asia countries, such as China, Malaysia, Thailand, Vietnam, and Philippines. <sup>[4-5]</sup> Sambong is the most important member of the genus *Blumea* and is an indigenous herb of tropical and subtropical Asia, especially in China. The whole plant or its leaves were used as a crude Chinese traditional medicinal material to treat eczema, dermatitis, beriberi, lumbago, menorrhagia, rheumatism, skin injury, and as an insecticide. <sup>[6]</sup>

In this review, botanical descriptions, herbal authentications, and phytochemical constituents of *B. balsamifera* are covered. In addition, the previous in vitro and in vivo studies conducted on its biological activities are reviewed, concentrating on antitumor, hepatoprotective, superoxide radical scavenging, antioxidant, antimicrobial, anti-inflammation, antiplasmodial, antityrosinase,

platelet aggregation, wound healing, anti-obesity, disease and insect resistant activities as well as enhancing percutaneous penetration.

### PHARMACOGNOSY OF *BLUMEA BALSAMIFERA*



- ▶ **Synonym** - *B.densiflora* Hook. f. in part.
- ▶ **Family** - Compositae; Asteraceae.
- ▶ **Habitat** - Subtropical Himalayas, Nepal, Sikkim, Assam and Khasi Hills at 700-1350 m.
- ▶ **English** - Ngai Camphor.
- ▶ **Ayurvedic** - Kukundara, Gangaapatri.
- ▶ **Unani** - Kakarondaa.
- ▶ **Action** - Tranquilizer (used in excitement and insomnia), expectorant, sudorific. Given in intestinal diseases, colic, diarrhea. Essential oil from leaves - hypotensive.
- The plant is a source of Ngai or Blumea Camphor. Camphor occurs in all parts of the plant, but is generally extracted from leaves. Ngai Camphor oil consists almost entirely of l-borneol. It is redistilled to obtain the refined camphor for use in medicine. The dried leaves contain sesquiterpene lactones. These lactones exhibit antitumour activity against Yoshida sarcoma cells in tissue culture. The plant exhibits moderate antibacterial activity against *E.coli*.<sup>[7]</sup>
- As a fumigation it is much used in the Phillipines Island for rheumatism and headache.<sup>[8]</sup>

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### General Botanical Description

According to the description of Flora Republic Popularis Sinicae and Chinese Materia Medica *B. balsamifera* is a perennial herb or subshrub, which rises about 1–3 meters in height. Its stem is strong and taupe, and erects with taupe, longitudinal edges. Its upper internodes are covered by dense tawny nonglandular hair. Its leaves, when triturated, send out a unique, cool aroma, which can make people feel refreshed. The leaves are wide ovoid or oblong-lanceolate in shape at the bottom, 22–25 cm in length, 8–10 cm in width. Its base is attenuated with petiole, narrow linear appendants of 3–5 pairs on both sides, pubesced above, slight brown or thick yellow-white silky-villous, highlighted below midrib, with lateral veins of 10–15 pairs. The leaves at the top are oblong-lanceolate or ovate-lanceolate in shape, 7–12 cm in length, 1.5–3.5 cm in width, with an acuminate apex, a slightly acuminate base, without petiole or with a short petiole with narrow linear appendants of 1–3 pairs, entire or with thin serration or pinnatopectinate. The flowering period almost covers the whole year. *B. balsamifera* often grows in forest edges, under forests, river beds, valleys, or grasslands, and the altitude is 600–1000 m. In addition to its various Chinese locations it is also distributed in India, Pakistan, Burma, Indo-China Peninsula, Malaysia, Indonesia and Philippines.<sup>[9]</sup>

- ▶ **Pharmacognostic nature :** *B. balsamifera* is a perennial herb, which grow about 1–3 meters in height. Its stem is strong and taupe, and erects with taupe, longitudinal edges. Its upper internodes are covered by dense tawny nonglandular hair. Its leaves having unique, cool arom. leaves are wide ovoid in shape at the bottom, 22–25 cm in length, 8–10 cm in width.
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### Phytochemistry

- There are more than 100 volatile or non-volatile constituents isolated from sambong, including monoterpenes, sesquiterpenes, diterpenes, flavonoids, organic acids, esters, alcohols, dihydroflavone, and sterols. The study of the plant mainly focused on volatile oils and flavonoids, it possessed various bioactivities in vivo and in vitro.<sup>[9-10]</sup>

### Volatile Constituents

- The volatile constituents for the largest amount of the constituents in *B. balsamifera*, which are major active constituents containing terpenoids, fatty acids, phenols, alcohols, aldehydes, ethers, ketones, pyridines, furans, and alkanes. The most important constituent is L-borneol. natural borneol, different extraction methods have been used to extract the volatile constituents from *B.*

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balsamifera. Steam distillation (SD), simultaneous distillation and extraction (SDE), and CO<sub>2</sub> supercritical extraction were the most common methods in the extraction of volatile oils. [11-16]

Volatile oil in *B. balsamifera* is a yellow oily liquid with a unique aroma.

### **Non-Volatile Constituents**

#### **Flavonoids Constituents**

- Flavonoids, flavanone and chalcone constituents, are the major non-volatile constituents of *B. balsamifera*. ultrasonic extraction methods of total flavonoids of *B. balsamifera* were studied. [17] It was found that 30% ethanol was suitable extraction solvent with solid/liquid ratio of 1/300. It was extracted by ultrasonic frequency (85 Hz), each time for 30 min, where extraction yield was 208.6 mg/g. *B. balsamifera*, flavonoids recognized for their medicinal properties and the investigation, validation, standardization of the local plant have been developed as an herbal medicine.

#### **Sterols**

- A small number of sterols were isolated from *B. balsamifera*. obtained colorless acicular as well as sheet crystals from *B. balsamifera* by silica gel column chromatography, where crystals identified to be stigma sterol and  $\beta$ -sitosterol by TLC and melting point measurement. [18]

#### **Sesquiterpene Lactone (SLs)**

- Sesquiterpene lactones (SLs) are a group of common chemicals in many Asteraceae plants. They were famous because they had cytotoxic and potential to be tumor inhibitors. In sambong a member of Asteraceae family, there were three sesquiterpene lactones, Blumealactone A, Blumealactone B, and Blumealactone C. isolated them by extracting its dried leaves with 90% ethanol. [19-20]

#### **Other Constituents**

- There were some other constituents in this plant. found two coumarin constituents, such as umbrelliferone and hydrangetin, in *B. balsamifera* also found a lignans constituent, which was syringaresinol. [12]

### **PHARMACOLOGICAL ACTIVITY OF *BLUMEA BALSAMIFERA***

#### **Anticancer Activity/Hepatoma**

Norikuraa T (2008) : Study of methanolic extract of *Blumea balsamifera* induced growth inhibitory activity in rat and human hepatocellular cells without cytotoxicity in rat hepatocytes used as cell model. suggest a possible therapeutic potential in hepatoma cancer patients and the depletion of cellular APRIL (proliferation related ligand) may be an important mechanism in the growth inhibitory effect of the extract. [21]

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Toshio Norikura (2008) : Study of *B. balsamifera* extract induced growth-inhibitory activity in rat and human hepatocellular carcinoma cells without cytotoxicity. Findings suggest a possible therapeutic role for the *B. balsamifera* methanol extract in treatment of hepatoma cancer patients.<sup>[22]</sup>

Hiroo Hasegawa (2006): Study shows combined treatment with a dihydroflavonol extracted from *Blumea balsamifera* exhibited the most striking synergism with TRAIL (tumor necrosis factor [TNF]-related apoptosis-inducing ligand) and suggests a new strategy for cancer therapy.<sup>[23]</sup>

### **Skin Wounds Healing**

Yuxin Pang (2017) : Study evaluated the effects of total flavonoids from *Blumea balsamifera* on skin excisional wound on the back of Sprague-Dawley rats. Study postulates all the ingredients in the total flavonoid sample may exert a synergetic effect on wound curing and that the flavonoids were the main active constituents that contributed to the excisional wound healing. Mechanisms of wound healing were attributed to wound contraction, capillary regeneration, collagen deposition, and re-epithelialization.<sup>[24]</sup>

Yuxin Pang (2014) : Study evaluated the effectiveness of volatile oil from *Blumea balsamifera* leaves on wound healing in mice. Results showed promotion of capillary regeneration, blood circulation, collagen deposition, granular tissue formation, epithelial deposition and wound contraction. Wound healing mechanism may be related to the induction of SP (neuropeptide substance P) secretion and the proliferation and differentiation of mesenchymal cells.<sup>[25]</sup>

### **Anti-Tyrosinase / Anti-Cancer Activities**

N. Saewan (2011) : An ethylacetate extract of leaves yielded nine flavonoids. The anti-tyrosinase activity of dihydroflavonols and flavonols were stronger than arbutin. In cytotoxicity evaluation, compounds 2,4 and 9 were active against KB cells. Compound 9 showed strong cytotoxicity against human lung cancer cell lines and moderate toxicity against oral cavity (KB) cancer cell lines.<sup>[26]</sup>

### **Calcium Oxalate Crystal/Stone**

Charlimagne M(2017) : Study showed *B. balsamifera* extract increased the crystallization rate of calcium. The increased crystallization rate would favor the formation of smaller crystals that are easily eliminated from the urinary system.<sup>[27]</sup>

Charlimagne M(2017) : Study evaluated the effect of BB extract on morphology of calcium oxalate crystals. Results showed decreased crystal size, shifted crystal phase from COM to COD and prevention of aggregation of calcium oxalate crystals.

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Charlimagne M (2016) : Sambong tea is believed to aid in the treatment of kidney stones. Study evaluated the effect of *Blumea balsamifera* tea in the nucleation of calcium oxalate crystals. Results showed decrease in induction time associated with increase nucleation rate with the formation of large number of smaller stones that are easier to eliminate by urination. [28]

Fernando Rico ( 1992) : In vitro study shows sambong to be a promising chemolytic agent for calcium stones. Results showed statistically significant stone dissolution of a 1 cm stone sample. A 40 mg/day dose showed maximum therapeutic effects

### **Xanthine Oxidase Inhibition**

Le Nguyen Tu Linh (2017) : Xanthine oxidase is the enzyme responsible for catalyzing the oxidation of hypoxanthine and xanthine to form uric acid. Study of a methanol extract of leaves showed total flavonoid content of 72.7 mg/g dw, promising inhibition of xanthine oxidase activity with IC<sub>50</sub> of 27.6 µg/mL, with a significant decrease in serum urate and reduced xanthine oxidase in the liver.

### **ACE Inhibition Activity**

Gerard Lee Lo ( 2016) : ACE inhibition has been proven to be an effective strategy in the prevention and treatment of hypertension. Study evaluated the angiotensin converting enzyme inhibition activity of sambong tea in a rabbit lung ACE-induced hydrolysis of FAPGG. Results showed sambong tea possess inhibitory activity on rabbit lung ACE. Activity was attributed to flavonoids and terpenoids. [29]

### **Hepatoprotective Activity**

Xu (1998) : demonstrated that oral blumeatin (5,3',5-trihydroxy-7-methoxydihydroflavone) exhibited a significant protective activity against the liver injury caused by paracetamol and prednisolone. Furthermore, Xu and Zhao have shown that five other blumea flavanones possessed protective activity for acute experimental liver injury.

Pu (2000) : Further verified the five blumea flavanones protecting the hepatocytes against lipid peroxidation, which was induced by CCl<sub>4</sub> or FeSO<sub>4</sub>+cysteine. Certain concentration of the five compounds (10–100 µmol/L) inhibited the malonaldehyde production, GSH depletion, and GPT leakage of hepatocytes.

Xu (1994) : Blumea flavanone II showed the strongest activity. They also reported that the blumea flavones had protective effects against acute liver injury induced by different chemicals.

### **Superoxide Radical Scavenging Activity**

Nessa (2004) : The methanol extracts of *B. balsamifera* leaves showed a higher radical scavenging activity than the chloroform extracts. However, the pet-ether extracts had less



activity against nonenzymatically generated superoxide radicals. The capacity of nine kinds of flavonoids (100 mmol/L) of the plant was decreased as follows: quercetin > luteolin > 5,7,3',5'-tetrahydroxyflavanone > blumeatin > rhamnetin > tamarixetin > luteolin-7-methyl ether > dihydroquercetin-4'-methyl ether > dihydroquercetin-4',7dimethyl ether. The flavonoids showed more activity than methylated compounds. [30]

### **Antioxidant Activity**

Nguyen (2012) : Demonstrated the methanol extracts of *B. balsamifera* (collected in Lam Dong province) with strong xanthine oxidase inhibitory activity with an IC<sub>50</sub> value of 6.0 µg/mL. They also verified the seven compounds of *B. balsamifera* methanol extract in Vietnam, which exhibited significant xanthine oxidase inhibitory activity. Three compounds among them, such as (2R,3S)-(-)-4'O-methyldihydroquercetin, quercetin, and quercetin-3,3',4', showed a higher potent inhibitory activity, with their IC<sub>50</sub> values ranging from 0.23 to 1.91 mmol/L, as compared to that of the positive control allopurinol (IC<sub>50</sub> of 2.50 mmol/L). [31]

Nessa (2010): It had found that the methanol extract of *B. balsamifera* exhibited a higher xanthine oxidase inhibitory activity as compared to that of the chloroform and pet-ether extracts. [32]

### **Anti-Microbial Activity**

Uthai Sakee (2014) : Reported the essential oil of *B. balsamifera* to have a minimum inhibitory concentration (MIC) of 150 µg/mL and 1.2 mg/mL against *Bacillus cereus*, *S. aureus* and *Candida albicans*, respectively. Furthermore, the hexane extract inhibited *Enterobacter cloacae* and *S. aureus*. These results suggested that the extracts of *B. balsamifera* possessed an activity against certain kinds of infectious and toxin-producing microorganisms. It could potentially be utilized to prevent and treat microbial diseases. [33]

### **Anti-inflammatory Assays**

Johanna G. Bantol (2017) : Study evaluate the in vitro anti-inflammatory activity on hexane extract of *Blumea balsamifera* leaves through albumin denaturation inhibition, HRBC membrane stabilization, and protease inhibition assays. The results showed that in all anti-inflammatory assays, 100 mg/mL hexane extract had the highest % inhibition and % stabilization. The hexane extract of *Blumea balsamifera* leaves have a potential anti-inflammatory activity in the assays, HRBC membrane stabilization and protease inhibition, in comparison to the aspirin. *Blumea balsamifera* leaves are a potential candidate for anti-inflammatory agent, minimizing side effects from non-steroidal anti-inflammatory drugs (NSAIDs). [34]

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### **Antiplasmodial Activities**

Noor (2017) : According to the traditional efficacy of relieving fever, the methanol extract of *B. balsamifera* from Forest Research Institute Malaysia was investigated for any potential antiplasmodial activity. The extracts of roots and stems exhibited some activity against *Plasmodium falciparum* D10 strain (sensitive strain) with an IC<sub>50</sub> value of  $(26.25 \pm 2.47) \mu\text{g/mL}$  and  $(7.75 \pm 0.35) \mu\text{g/mL}$ , respectively. [35]

### **Apigenin / Aldose Reductase (AR) Inhibitory Activity**

Dong Gu Lee ( 2012) : Study evaluated fractions of *Blumea balsamifera* for their ability to inhibit aldose reductase activity in rat lenses. Apigenin, identified from the active EtOAc fraction, exhibited high AR inhibitory activity. Results suggest a useful natural source for a novel AR inhibitory agent against diabetic complications. [36]

### **Anti-Diabetic / Antioxidative Activity**

Kalyan Roy (2013) : Study evaluated the antidiabetic and in vivo antioxidant property of hydro-ethanolic extract of leaves of *B. balsamifera* in streptozocin induced diabetic rats. Results showed significant reduction in blood glucose. There was also significant alteration in elevated lipid profile along with serum marker enzymes. Antioxidant potential was evidenced by significant increase in GSH and CAT measurements. [37]

### **Platelet Aggregation Activities**

Xu (1994) : The concentration of  $1.26 \mu\text{mol/L}$  blumeatin displayed a significant promoting activity on the rat and human platelet aggregation caused by arachidonic acid, 5-hydroxytryptamine, and epinephrine. However, concentrations of  $0.315$  and  $2.52 \mu\text{mol/L}$  inhibited platelet aggregation. It suggested that the effects of blumeatin on the platelet aggregation were dependent upon the concentration used. The injection of *B. balsamifera* extracts decreased the blood pressure, expanded the blood vessels, and inhibited the sympathetic nervous system in order to address the high pressure and insomnia. The infusion of the plant also had the function of diuresis. [38]

### **Enhancing Percutaneous Penetration Activity**

Chen (2009) : The L-borneol, as the main effective compound of *B. balsamifera*, showed a percutaneous penetration enhancer effect. The essential oil camphor and 1-menthol of the plant specifically promoted the percutaneous absorption of nicotinamide. [39]

### **Anti-Arthritic / Antioxidative Activity**

Yan Xia (2014) : Study evaluated the effect of an ethyl acetate fraction of BB residue on rats with adjuvant arthritis immunized through Freund's complete adjuvant (FCA). Results showed



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high dose BBE could significantly ameliorate joint swelling and arthritis index, effectively inhibit synovial hyperplasia, down-regulate the levels of MDA, NO, OH, ALP, AST, ALT, NAG, SA, IL-1, IL-6, TNF $\alpha$  and up-regulate serum levels of SOD and GSH. <sup>[40]</sup>

### **Anti-Obesity Activity**

Mae Genevieve G. Cheung (2016) : Study evaluated the effectiveness of aqueous and ethanolic leaf extracts of *Blumea balsamifera* in reducing obesity on diet-induced obese Sprague-Dawley rats. Investigation about the in vivo anti-obesity effect of the aqueous and ethanolic leaf extracts of *Blumea balsamifera* on diet-induced obese Sprague-Dawley rats. <sup>[41]</sup>

### **Angiogenic Property**

Jemisha Mistry (2015) : Study reported that angiogenic property of aqueous extract from *Blumea balsamifera* leaves has been examined on in vitro shell less chick (*Gallus gallus*) embryo cultures. <sup>[42]</sup>

## **CONCLUSION**

The survey and summary of the extensive studies revealed that *B. balsamifera* was an essential and valuable medicinal plant used for folk treatments such as treating eczema, dermatitis, beriberi, lumbago, menorrhagia, rheumatism, skin injury, or used as insecticide. As a traditional medicine, the biological and pharmacological studies of the plant materials, crude extracts, and isolated chemical constituents of *B. balsamifera* offered experimental and scientific proofs for its various traditional uses. The pharmacological studies focused on studying the anti-microbial and anti-inflammatory effects, antiplasmodial effects, platelet aggregation, wound healing, and disease and insect resistant activities, all of which confirmed the plant's traditional uses. Moreover, some new pharmacological uses were discovered, such as antitumor, hepatoprotective, superoxide radical scavenging, antioxidant, antityrosinase, enhancing percutaneous penetration, and anti-obesity activities.

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