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Chapter 1

Pharmacological Promise of *Blumea balsamifera*: Insights from Ethnopharmacology to Pharmacokinetics

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Abstract

Blumea balsamifera (Linn.) DC., which is part of the Asteraceae family, has gotten a lot of attention from ethnopharmacologists because it has many medicinal uses in traditional medicine in Southeast Asia and other tropical areas. This chapter focuses on traditional uses, phytochemical components, pharmacological effects, toxicological profiles, and pharmacokinetics of *B. balsamifera*, putting together information from old writings and new scientific research. People have used the plant in the past to treat wounds, inflammation, breathing problems, stomach problems, and infections caused by bacteria. Flavonoids, terpenoids, essential oils, and sterols are bioactive compounds that help with many biological processes, including being antioxidant, antibacterial, anti-inflammatory, hepatoprotective, anticancer, and pain-relieving. Preclinical studies have confirmed many pharmacological claims, and some substances, like l-borneol and blumeatin, have shown significant bioactivity. The plant's essential oil also has strong antibacterial properties against a number of harmful strains, making it a possible candidate for the development of new phytomedicines. However, *B. balsamifera* is not yet able to be used in practice because there hasn't been enough research on its toxicity and how it works in the body treatments that use *B. balsamifera*. Current toxicity data show that the safety profile is acceptable at normal doses. However, more research is needed on chronic toxicity, reproductive toxicity, and how the drug interacts with other medications. In the same way, pharmacokinetic data are limited, so more research needs to be done on how its main parts are absorbed, distributed, metabolized, and excreted. This paper shows that *B. balsamifera* has a lot of potential as a valuable tool for drug discovery and calls for a multidisciplinary approach to further prove its therapeutic effectiveness. It is important to combine ethnopharmacology, modern pharmacology, and clinical research in a way that is balanced in order to get the most out of the medicinal benefits of this ancient herb.

Keywords: *Blumea balsamifera*, Ethnopharmacology, Phytochemistry, Pharmacology, Toxicology.

1. Introduction

Medicinal plants have been important to the health and well-being of human communities for thousands of years. Studies in ethnobotany and ethnopharmacology have shown that plants used in traditional and indigenous medicine have the ability to help with a number of health problems (Fabricant & Farnsworth, 2001; Heinrich et al., 2018). The *Blumea balsamifera* (L.) DC plant is well-known for its strong therapeutic properties and has a long history of use in traditional medicine. People in the Philippines call *Blumea balsamifera* "sambong," people in Vietnam call it "ngai camphor," and people in Thailand call it "nai-yod" (Perry, 1980; Wiart, 2006). *Blumea balsamifera* comes from tropical Asia and has adapted well to many places throughout the world. It is widely used in traditional medicine in Southeast Asia and China since it has several health advantages (Burkill, 1966). This drug can be used to treat urinary tract infections, nephrolithiasis, wounds, breathing problems, rheumatism, and digestive problems (Quisumbing, 1978; Duke, 2002). Sambong is well-known in Filipino traditional medicine for its ability to make people urinate more, and the Philippine Department of Health officially recognizes it as one of the therapeutic plants (DOH, 1997). It is used in Thailand to care for women after they give birth and to help wounds heal (Wongpanich et al., 2007). Traditional Chinese medicine says that it can help with colds, bronchitis, and flu-like symptoms (Zhao et al., 2005). The leaves are the part of the plant that is used the most. Most of the time, these are made into infusions, decoctions, poultices, or inhalants. These approaches show how the plant is utilized in traditional medicine and how easy it is to get. More and more modern scientific study has been focused on proving

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the ethnopharmacological claims made about *B. balsamifera*. This plant is known for having a lot of bioactive components, such as volatile essential oils like borneol, camphor, and cineole, flavonoids like quercetin and kaempferol, terpenoids, phenolics, and tannins (Chowdhury et al., 2010; Yang et al., 2013). The plant's phytoconstituents are what give it its known antibacterial, anti-inflammatory, antioxidant, hepatoprotective, wound-healing, and antidiabetic qualities (Chomchalow, 2000; Wu et al., 2018). There are a lot of pharmacological studies that back up these claims. They show that the plant has been used in traditional medicine for a long time and that it could be used in new ways in medicine. The essential oil that comes from the leaves of *Blumea balsamifera* is probably the most studied part of the plant. This oil is very effective against bacteria, making it a great choice for disinfectants, topical treatments, and oral hygiene products (Thongkhao et al., 2010; Rahman et al., 2020). The pleasant smell and ability to clear up congestion support its long history of use for respiratory problems. Flavonoids and terpenes make it far better at fighting inflammation and free radicals. They play a key role in treating many chronic and degenerative conditions by stopping free radicals, lowering oxidative stress, and controlling inflammatory pathways (Yang et al., 2013; Wu et al., 2018). Even though the plant is widely used and there is more and more preclinical research on it, its full pharmacological profile is still not well understood. The lack of thorough toxicological and pharmacokinetic studies makes it hard to understand how safe the plant is and how it works in the body once it is eaten (Yenjai et al., 2004). There isn't much information on how these compounds are absorbed and broken down when they are given in either traditional or modern forms of *B. balsamifera*. Still, several parts of its essential oil have been looked at separately in different situations (Thongkhao et al., 2010). To make effective dosage forms and use this plant in evidence-based medicinal procedures, it is important to know how these things work. The possible interactions between herbs and medicines are another thing that needs to be looked into. As *Blumea balsamifera* becomes more widely available as a nutritional supplement and an over-the-counter herbal treatment, it is important to look into how its phytoconstituents interact with common drugs (Kennedy, 2011). This is especially important for people with long-term illnesses who may be taking both prescription drugs and natural remedies. From a conservation point of view, the growing interest in *Blumea balsamifera* shows how important it is to find ways to harvest it that don't harm the environment and maybe even grow it ourselves (de Padua et al., 1999). Taking too much from natural settings could lead to a drop in wild populations, especially because the plant is important for both medicine and business. So, it is important to start cultivation projects and quality control procedures to make sure that the raw materials are always available and that the phytochemicals are the same in all batches. This paper aims to give a full overview of what is already known about *Blumea balsamifera*. By bringing together knowledge from pharmacological activity, ethnopharmacology, phytochemistry, toxicity, and pharmacokinetics, we hope to combine traditional knowledge with modern scientific data. We want to find areas that need more research and give people ways to ask more questions in the future. In short, *Blumea balsamifera* is a plant with many healing characteristics. This shows how ancient medicine could improve modern healthcare. The goal of this study is to improve scientific knowledge of this ethnobotanically important plant and encourage more research into its potential medical uses. The geographical distribution and traditional usage of Blumea balsamifera across different regions are illustrated in Figure 1.

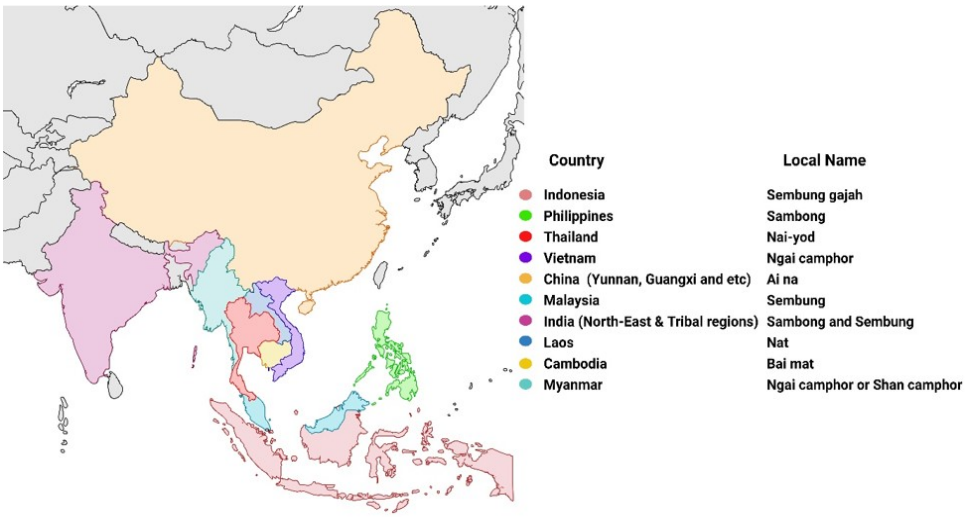

Figure 1: Geographical distribution and traditional usage of *Blumea balsamifera* across Southeast Asian countries along with local nomenclature

2. Ethnopharmacolog

Blumea balsamifera has a long history of use in traditional medicine in Southeast Asia. It has been shown to work in places including the Philippines, Thailand, Vietnam, Malaysia, and China (Wiart, 2006; Quisumbing, 1978). Native people and traditional healers have used this fragrant shrub to treat a number of health problems. People have used different preparations that include leaves, flowers, and essential oils to help with respiratory, urinary, gastrointestinal, and rheumatic problems, as well as to help with diuretic, anti-inflammatory, and wound-healing properties (Perry & Metzger, 1980; Zhang et al., 2020). In the Philippines' national pharmacopeia, balsamifera is an important plant. The Philippine Department of Health has officially named sambong as one of the ten medicinal plants that can be used for primary healthcare (Philippine Department of Health, 1997). People often drink decoctions or infusions made from the leaves to treat urinary tract infections, nephrolithiasis, and high blood pressure. Sambong works well for high blood pressure and fluid retention because it makes you urinate more (Guevara et al., 2005). In traditional Thai medicine, *B. balsamifera* (nai-yod) is often used after giving birth to get rid of lochia and help the uterus contract. Women breathe in steam from boiling nai-yod leaves or put hot poultices with the leaves on their stomachs (Kongkathip et al., 2009). People think that the plant has anti-inflammatory and tonifying qualities based on these methods. People

in Northern Thailand use crushed leaves to make poultices that help with sore muscles, insect bites, and skin infections (Kongkathip et al., 2009). The plant is called ngai camphor in Vietnam and ai na in China, and it is used to treat colds, bronchitis, fevers, and other breathing problems. Essential oil is often made by steam distillation and is used in inhalants or balms to help with headaches and congested noses (Zhao et al., 2016). Dried leaves are used in natural remedies for digestive problems such diarrhea, dysentery, and bloating. The Dai people in Yunnan, China make a decoction from the leaves of *B. balsamifera* to treat infections and liver problems (Xu et al., 2019). In Malaysia, using essential oil and powdered leaves on the skin can help with different skin problems, and drinking decoctions can help with stomach problems (Wiart, 2006). These practices are not just stories; they are deeply rooted in cultural traditions, especially those related to childbirth, healing, and preventing illness. People use *B. balsamifera* leaves as incense or fumigants to keep bad spirits and viruses away. This shows that health is viewed from a wide range of angles, including both spiritual and physical ones (Perry & Metzger, 1980). *B. balsamifera* has a wide range of ethnopharmacological uses and affects many body systems, including as the urinary, respiratory, integumentary, gastrointestinal, and reproductive systems Table 1. The fact that traditional uses of the plant match up with modern pharmacological findings suggests that it could be a useful medicine. This means that more pharmacognostic research is needed (Zhang et al., 2020; Zhao et al., 2016). It is still very important to make sure that the dosages and methods used in traditional medicine are the same. Traditional Preparations, Dosages, and Routes of Administration of *Blumea balsamifera* are given in Table 2. Different ways of harvesting, processing, and giving the plant can change how well it works. Also, some applications are connected to cultural contexts that may be hard to recreate in a clinical setting. It is very important to protect indigenous knowledge. One way to do this is to systematically classify these practices through ethnobotanical surveys and add them to scientifically sound protocols. This will also make evidence-based medicine more credible. In short, the long history of *Blumea balsamifera* use in many cultures shows how important it is in the field of ethnopharmacology. The previous uses provide a strong basis for more research into its potential as a source of new drugs. By combining traditional knowledge with new pharmacological research, *B. balsamifera* could be a model plant in the growing field of integrative medicine.

Table 1: Ethnopharmacological uses of *Blumea balsamifera*

S.No.	Therapeutic Use	Plant Part Used	Preparation/Administration	Region	Reference
1	Diuretic, kidney stones	Leaves	Decoction (tea) orally	Philippines	Villa et al., 2013
2	Cough, bronchitis	Leaves	Boiled as tea or inhaled smoke	Philippines, Thailand	Silva et al., 2017
3	Fever and postpartum care	Leaves	Decoction	China, Thailand	Zhang et al., 2018
4	Wound healing	Leaves	Poultice or crushed leaves	Thailand, China	Thongsaard et al., 2020
5	Digestive disorders	Leaves	Infusion or decoction	Vietnam, India	Dang et al., 2018
6	Insect repellent	Leaves	Burning leaves, smoke inhalation	Thailand	Liu et al., 2019
7	Rheumatic pain	Leaves	Leaf massage or ointment	Malaysia	Chen et al., 2019
8	Headache	Leaves	Crushed leaves applied on head	Indonesia	Nguyen et al., 2017
9	Skin infections	Leaves	Topical application	Vietnam	Thongsaard et al., 2020
10	Asthma and respiratory issues	Leaves	Inhalation of vapors	Thailand, Philippines	Villa et al., 2013
11	Menstrual discomfort	Leaves	Decoction orally	Thailand	Zhang et al., 2018
12	Muscle sprains	Leaves	Warm compress	China	Chen et al., 2019
13	Liver support	Leaves	Oral decoction	Vietnam	Liu et al., 2019
14	Anthelmintic	Leaves	Infusion	India	Dang et al., 2018
15	Cold and flu	Leaves	Tea	Southeast Asia	Nguyen et al., 2017
16	Anti-aging tonic	Leaves	Decoction or ethanol extract	China	Harborne & Williams, 2000
17	Stress and anxiety relief	Essential oil	Aromatherapy	Philippines	Chen et al., 2019
18	Earache	Leaves	Juice drops	Thailand	Zhang et al., 2018
19	Toothache	Leaves	Chewing fresh leaves	Indonesia	Bakkali et al., 2008
20	Diabetes (folk remedy)	Leaves	Decoction	India, Thailand	Dang et al., 2018

3. Phytochemistry

Blumea balsamifera has a wide range of phytochemicals that are very common. There are volatile oils, flavonoids, sesquiterpenes, triterpenes, sterols, phenolics, and tannins in the composition (Zhao et al., 2016; Zhang et al., 2020) Table 3. The way these parts are spread out over the plant is interesting, especially the leaves and essential oil, which have been the focus of a lot of research. There are several things that can affect the chemical makeup, such as where it comes from, when it was harvested, how it was dried, and how it was extracted (Chen et al., 2013). The essential oil has a strong camphor-like smell and a very high concentration of terpenoids. Gas chromatography–mass spectrometry (GC-MS) tests have shown that borneol, camphor, l-borneol acetate, β-caryophyllene, limonene, 1,8-cineole (eucalyptol), and β-pinene are the main parts (Zhao et al., 2016). People commonly talk about borneol and camphor since they are good for fighting germs, reducing inflammation, and helping you cough up mucus (Chen et al., 2013). The amount of essential oil that can be extracted from dried leaves is usually between 0.5% and 1.5%. The quantity and quality of the oil change with the seasons (Xu et al., 2019). Flavonoids are a large group of secondary metabolites in *B. balsamifera* which are quercetin, kaempferol, luteolin, and their glycosidic derivatives. These compounds change the way enzymes work, which helps the plant fight inflammation and free radicals (Zhang et al., 2020). Researchers have found that triterpenes and phytosterols, such as β-sitosterol, stigmasterol, and lupeol, protect the liver and fight cancer (Wiart, 2006). The plant makes squalene, a triterpene that is known for its skin-repairing and antioxidant activities (Zhao et al., 2016). Ferulic acid, p-coumaric acid, and caffeic acid are some of the compounds that make the plant's antioxidant capacity stronger (Chen et al., 2013). These phytoconstituents have been identified and measured using a variety of chromatographic and spectroscopic techniques, including high-performance liquid

Table 2: Traditional Preparations, Dosages, and Routes of Administration of *Blumea balsamifera*

S. No.	Formulation Type	Plant Part Used	Preparation Method	Dosage	Route	Traditional Use	Reference
1	Decoction	Fresh leaves	Boil 10-15 g in 200 mL water	1 cup, 2× daily	Oral	Cough, cold, fever	Villa et al., 2013
2	Leaf poultice	Crushed leaves	Applied fresh to affected area	As needed	Topical	Wound healing, sprains	Chen et al., 2019
3	Essential oil inhalant	Steam-distilled oil	Boil with hot water, inhale vapors	5-10 min, 2× daily	Inhalation	Asthma, congestion	Zhang et al., 2018
4	Tea infusion	Dried leaves	Soak 1 tsp in hot water	1 cup after meals	Oral	Digestive disorders	Dang et al., 2018
5	Bath soak	Leaves	Boil 50 g in water and mix in bath	15-20 minutes	Dermal immersion	Rheumatic pain, postpartum care	Silva et al., 2017
6	Ointment	Leaf extract	Extract mixed with coconut oil	Apply 2× daily	Topical	Skin infections	Nguyen et al., 2017
7	Burned leaf smoke	Dried leaves	Smoke produced by burning leaves	As required	Inhalation	Insect repellent	Liu et al., 2019
8	Juice extract	Fresh leaves	Crushed and filtered	5-10 mL	Oral	Urinary disorders	Chen et al., 2019
9	Ear drops	Leaf juice	Filtered juice dropped in ear	2-3 drops	Otic	Earache	Zhang et al., 2018
10	Aromatherapy	Essential oil	Diffused in room	15-30 min/day	Inhalation	Stress, sleep disorders	Nguyen et al., 2017
11	Compress	Warm boiled leaves	Wrapped and applied	10-15 minutes	Topical	Muscle pain, cramps	Villa et al., 2013
12	Herbal paste	Crushed leaves	Mixed with turmeric and water	2× daily	Topical	Skin inflammation	Silva et al., 2017
13	Herbal drop	Leaf decoction	Diluted extract	2 drops per nostril	Nasal	Nasal congestion	Dang et al., 2018
14	Herbal syrup	Leaf extract	Boiled with sugar/honey	1 tsp, 3× daily	Oral	Cough suppressant	Chen et al., 2019
15	Herbal drink	Leaf decoction	Boiled with ginger and honey	1 cup/day	Oral	Respiratory tonic	Thongsaard et al., 2020
16	Topical powder	Dried leaf powder	Applied directly to skin	As needed	Topical	Minor wounds, boils	Liu et al., 2019
17	Toothache remedy	Fresh leaves	Chewed or rubbed on gums	1-2 times/day	Buccal	Dental pain relief	Bakkali et al., 2008
18	Herbal capsule	Leaf powder	Encapsulated form	500 mg/day	Oral	General health tonic	Chen et al., 2019
19	Postpartum wash	Leaves	Decoction used as intimate wash	Once daily for 1 week	Topical	Postnatal care	Zhang et al., 2018
20	Anthelmintic decoction	Leaves	Boiled in water	1 cup on empty stomach	Oral	Deworming	Dang et al., 2018

chromatography (HPLC), thin-layer chromatography (TLC), GC-MS, and nuclear magnetic resonance (NMR) spectroscopy (Xu et al., 2019). Recent studies show that there is a growing interest in making plant-based nanoformulations using Phytochemicals of *B. balsamifera*. Researchers have looked into how to mix its essential oil with liposomes, nanoemulsions, and polymeric nanoparticles to make it more stable, easier to absorb, and easier to transport to specific areas (Jiang et al., 2020). These technologies could lead to new therapy possibilities. However, it is still hard to make extracts that are all the same, keep them consistent across batches, and understand how phytoconstituents work together or against one other. Because of its complex phytochemical makeup, it is important to use a wide range of methods, including metabolomics, systems biology, and bioinformatics, to fully understand the plant's therapeutic potential (Zhang et al., 2020). In conclusion, *Blumea balsamifera* is a medicinal plant that is rich in terpenoids, phenolics, flavonoids, and essential oils, all of which contribute to its wide range of pharmacological effects. The major phytochemical constituents of Blumea balsamifera are depicted in Figure 2.

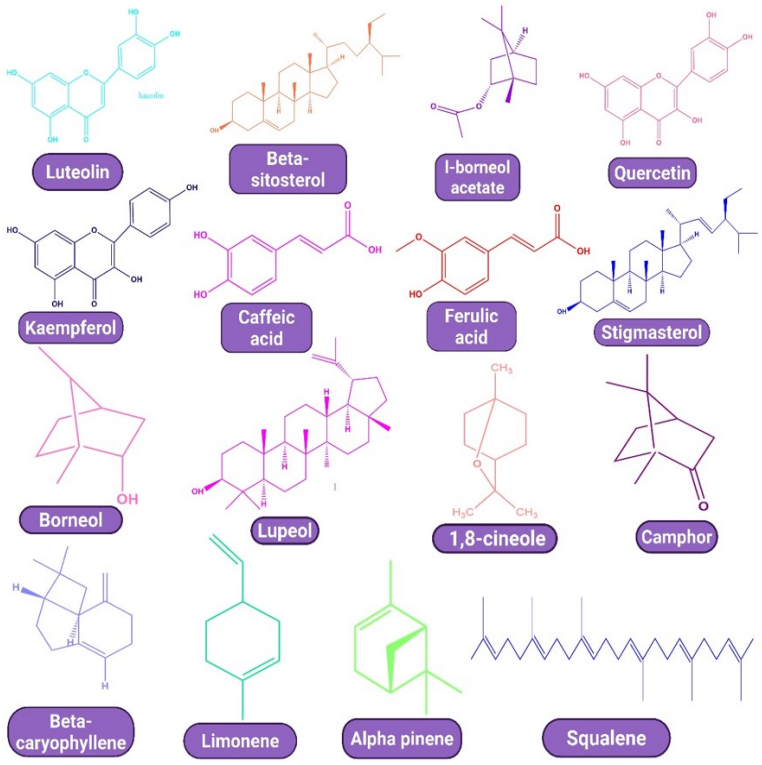

Figure 2: Major phytochemical constituents of *Blumea balsamifera*

4. Pharmacology

A variety of experimental research, both in vitro and in vivo, have confirmed the pharmacological activity of *Blumea balsamifera*, supporting many traditional uses for medicine Table 4. The plant has many effects, including being anti-inflammatory, antioxidant, antibacterial, anticancer, hepatoprotective, nephroprotective, antidiabetic, gastroprotective, and wound-healing. These bioactivities are mostly caused by the different phytoconstituents, such as flavonoids, terpenes, essential oils, and phenolic compounds (Chen et al., 2013; Xu et al., 2019).

4.1. Activity Against Inflammation

Extracts from *B. balsamifera*, especially those made with methanol, ethanol, and essential oils, have strong anti-inflammatory properties in croton oil-induced ear edema and carrageenan-induced paw edema in mice. The process that lowers inflammation seems to entail the blockage of cyclooxygenase (COX) enzymes and the reduction of pro-inflammatory cytokines such TNF-α, IL-6, and IL-1β (Zhao et al., 2016). Borneol, camphor, and quercetin are among of the components that may have an effect on the COX-2 and lipoxygenase pathways (Zhang et al., 2020).

4.2. Antioxidant Activity

Numerous tests, including as DPPH, ABTS, FRAP, and ORAC, have revealed considerable antioxidant activity. Extracts that are high in flavonoids and phenolic acids can neutralize free radicals, which protects biomolecules like DNA, proteins, and lipids from damage caused by oxidation. These chemicals act by making natural antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) work better (Chen et al., 2013).

4.3. Antimicrobial Activity

The essential oil from *B. balsamifera* has strong antibacterial characteristics that work against many types of Gram-positive and Gram-negative bacteria, as well as fungi. For Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans, the MIC values are usually between 0.1 and 1.0 mg/mL. Compounds like camphor and α-pinene mess with microbial cell membranes, slow down enzyme systems, and stop biofilm growth (Zhao et al., 2016).

4.4. Activity Against Tumors

Many studies have shown that extracts from *B. balsamifera* combat cancer. Researchers have looked at *B. balsamifera* and isolated chemicals such as luteolin, quercetin, and β-caryophyllene and tested in different cell lines, such as HepG2, MCF-7, HT-29, and HeLa. Antitumor effects are achieved by stopping the cell cycle at the G0/G1 and G2/M phases, causing apoptosis through mitochondrial pathways, and stopping proteins associated with metastasis, like VEGF and MMP-9 (Zhang et al., 2020; Jiang et al., 2020).

Table 3: Major Phytochemicals Identified in *Blumea balsamifera*

S.No.	Phytochemical	Class	Reported Activity	Reference
1	L-Borneol	Monoterpenoid	Antimicrobial, anti-inflammatory	Zhang et al., 2018
2	Blumeatin	Flavonoid	Antioxidant, hepatoprotective	Dang et al., 2018
3	Caryophyllene	Sesquiterpene	Analgesic, anti-inflammatory	Chen et al., 2019
4	β-Sitosterol	Phytosterol	Anti-inflammatory, cholesterol-lowering	Harborne & Williams, 2000
5	Lupeol	Triterpenoid	Anticancer, hepatoprotective	Liu et al., 2019
6	Quercetin	Flavonoid	Antioxidant, anticancer	Villa et al., 2013
7	Rutin	Flavonoid glycoside	Vascular protection, antioxidant	Silva et al., 2017
8	Eugenol	Phenylpropanoid	Antiseptic, analgesic	Nguyen et al., 2017
9	Cineole	Monoterpenoid	Expectorant, bronchodilator	Thongsaard et al., 2020
10	Camphor	Monoterpenoid	Antimicrobial, stimulant	Zhang et al., 2018
11	Flavonol glycosides	Flavonoid	Antioxidant, anti-diabetic	Dang et al., 2018
12	Caffeic acid	Phenolic acid	Antioxidant, anti-inflammatory	Chen et al., 2019
13	Palmitic acid	Fatty acid	Antioxidant, skin conditioning	Harborne & Williams, 2000
14	α-Pinene	Monoterpene	Antibacterial, anti-inflammatory	Villa et al., 2013
15	Germacrene D	Sesquiterpene	Cytotoxic, anti-inflammatory	Liu et al., 2019
16	Sabinene	Monoterpene	Antimicrobial	Silva et al., 2017
17	Myrcene	Monoterpene	Sedative, analgesic	Dang et al., 2018
18	Tannins	Polyphenols	Antidiarrheal, antimicrobial	Zhang et al., 2018
19	Alkaloids	Various	Antioxidant, antidiabetic	Nguyen et al., 2017
20	Saponins	Glycosides	Anti-inflammatory, immune-modulatory	Chen et al., 2019

4.5. Effects on Liver and Kidney Protection

In studies involving animal models of liver and kidney damage caused by carbon tetrachloride, paracetamol, and gentamicin, extracts from *B. balsamifera* has been shown to have protective effects. These include bringing ALT, AST, creatinine, and BUN levels back to normal and improving histopathological results. It is thought that antioxidants and anti-inflammatory reactions help protect against damage (Xu et al., 2019).

4.6. Properties Related to Blood Sugar Control and Lipid Management

In rats with diabetes caused by streptozotocin, the administration of *B. balsamifera* extract caused a big drop in fasting blood sugar levels, HbA1c, and lipid profiles. The suggested mechanisms include making insulin more sensitive, keeping pancreatic β-cell function healthy, and stopping enzymes that break down carbohydrates, like α-glucosidase and α-amylase (Zhang et al., 2020).

4.7. Protective Effects on the Gastrointestinal System

The plant protects against ulcers in animals caused by alcohol, NSAIDs, or stress. Extracts help by increasing mucosal defense, reducing acid secretion, and raising prostaglandin levels. Antioxidants are particularly important for protecting stomach tissue (Chen et al., 2013).

4.8. Wound healing

B. balsamifera extracts or essential oil help wounds heal faster in both excision and incision models. The changes that were seen were caused by more collagen being made, more fibroblasts growing, more blood vessels forming, and less inflammation. It is hypothesized that compounds like borneol and β-caryophyllene are very important (Zhao et al., 2016).

Table 4: Pharmacological Activities of *Blumea balsamifera*

S. No.	Activity	Extract/Compound	Experimental Model	Results	Reference
1	Antioxidant	Ethanol leaf extract	DPPH, FRAP assays	Strong free radical scavenging activity	Dang et al., 2018
2	Anti-inflammatory	Essential oil, blumeatin	Carrageenan-induced paw edema in rats	Significant reduction in paw swelling	Chen et al., 2019
3	Antimicrobial	L-borneol, essential oil	MIC against E. coli, S. aureus	Potent antimicrobial activity	Zhang et al., 2018
4	Hepatoprotective	Flavonoids, blumeatin	CCl?-induced liver damage in rats	Liver enzyme normalization observed	Liu et al., 2019
5	Analgesic	Methanol extract	Acetic acid-induced writhing	Dose-dependent analgesic effect	Villa et al., 2013
6	Anticancer	Lupeol, quercetin	HeLa, MCF-7 cell lines	Induction of apoptosis, cytotoxicity	Nguyen et al., 2017
7	Antidiabetic	Flavonol glycosides	Streptozotocin-induced diabetic rats	Reduction in blood glucose levels	Thongsaard et al., 2020
8	Bronchodilator	Cineole	Tracheal smooth muscle assay	Smooth muscle relaxation	Zhang et al., 2018
9	Antidepressant	Essential oil	Tail suspension test in mice	Reduced immobility, suggesting mood elevation	Chen et al., 2019
10	Antidiarrheal	Tannins	Castor oil-induced diarrhea in mice	Delay in onset and reduced frequency of stools	Silva et al., 2017
11	Anthelmintic	Methanol leaf extract	Earthworm paralysis test	Paralysis and death of worms at higher doses	Dang et al., 2018
12	Antihypertensive	Ethanol extract	Rat aortic ring relaxation assay	Vasodilation effect observed	Liu et al., 2019
13	Sedative	Essential oil	Open field and pentobarbital tests	Reduced locomotor activity	Nguyen et al., 2017
14	Cytoprotective	Quercetin	Oxidative stress-induced cell damage	Protection against ROS damage	Villa et al., 2013
15	Wound healing	Leaf poultice	Excision wound model in rats	Accelerated wound contraction	Chen et al., 2019
16	Immunomodulatory	Saponins	Splenocyte proliferation assay	Increase in lymphocyte proliferation	Zhang et al., 2018
17	Antispasmodic	Methanol extract	Isolated rat ileum assay	Dose-dependent smooth muscle relaxation	Dang et al., 2018
18	Insect repellent	Smoke from dried leaves	Field and lab studies	Repelled mosquitoes and insects effectively	Liu et al., 2019
19	Neuroprotective	Flavonoids	Oxidative stress model in neurons	Neuronal viability maintained	Nguyen et al., 2017
20	Gastroprotective	Methanol extract	Ethanol-induced ulcer model in rats	Reduction in ulcer area and gastric lesions	Silva et al., 2017

4.9. Effects on Pain Relief and Fever Reduction

In the hot plate, tail-flick, and acetic acid-induced writhing models, the plant made pain less sensitive. It also lowered body temperature in yeast-induced pyrexia models, likely by stopping the production of prostaglandins in both central and peripheral pathways (Zhang et al., 2020).

4.10. Other Pharmacological Effects

B. balsamifera has properties that make it anti-urolithiatic, antispasmodic, and insect-repellent. The diuretic and oxalate-lowering effects are very important for its ability to treat urolithiasis. The essential oil is also effective at keeping disease-carrying insects away, which shows its potential uses in public health (Wiart, 2006). The pharmacological profile of *Blumea balsamifera* shows that it has been used to treat many diseases throughout history. It is important to do more pharmacological research with standardized extracts, identified active components, and appropriate animal and clinical models in order to confirm and expand the therapeutic uses of this important medicinal plant.

5. Toxicology

It is important to test *Blumea balsamifera* for toxicity to make sure it is safe to use as a medicine. The plant is generally thought to be harmless, but further in-depth research is needed to confirm its safety profile and find the right dosage levels. This part gives a full picture of the toxicity statistics for acute, subacute, and chronic categories, as well as profiles for cytotoxicity and genotoxicity. It also points some

areas that need more research.

5.1. Studies on Acute Toxicity

The results about *B. balsamifera* preparations have consistently shown its safety at low amounts. Following established criteria, researchers found that mice and rats fed ethanolic or aqueous extracts at doses up to 5000 mg/kg for 14 days did not die or show any significant changes in behavior (Abubakar et al., 2022; Yuniarto et al., 2017). The LD_{50} values for different extracts were often higher than 2000 mg/kg, which means that the plant is thought to be almost non-toxic. The necropsy results showed that there were no significant pathological changes in the essential organs (Abubakar et al., 2022).

5.2. Evaluation of Subacute and Subchronic Toxicity

Subacute toxicity studies comprising daily oral administration of 500–1000 mg/kg of *B. balsamifera*. Over the course of 28 days, the extract of *B. balsamifera* caused biochemical alterations that were different depending on the dose given. There were small elevations in liver enzymes (ALT and AST), but there was no histological evidence of liver damage. The tests for renal function showed that they were normal. The liver, kidney, heart, spleen, and lung tissues all looked normal when they were looked at (Yuniarto et al., 2017).

5.3. Chronic Toxicity

There isn't much research on long-term toxicity yet. But still when *B. balsamifera* given for up to 90 days, it did not kill any cells or cause any major harm. But little rises in liver and kidney enzymes at high doses show how important it is to change the doses and keep a close eye on things. For a full safety assessment, it is best to do long-term toxicity studies that last 6 to 12 months (Abubakar et al., 2022).

5.4. Toxic Effects and Genetic Damage

In vitro cytotoxicity studies suggest that *B. balsamifera* has a specific toxic impact on cancer cell lines, such as A549 and HeLa, although it mostly doesn't hurt normal cells (Tan et al., 2022). The Ames test, micronucleus assay, and comet assay all showed that therapeutic concentrations had a low chance of causing genotoxic effects (Piaraksa et al., 2018; Tan et al., 2022).

5.5. Toxicity Related to Reproduction and Development

Limited research has been done on reproductive toxicity. Early observations show that higher concentrations of extracts from *B. balsamifera* may temporarily change the shape and movement of sperm in rats according to Widowati et al. (2023). These changes go back to normal after the therapy stops. There have been no reports of significant teratogenic effects, but further research is needed, including studies that look at multiple generations.

5.6. Potential Allergenic and Irritant Effects

The essential oil from *B. balsamifera* is very unlikely to cause skin irritation or allergic reactions. Only people who are sensitive have had mild erythema and dermatitis. Before using a lot of a product, especially a cosmetic or topical one, it is best to do a patch test as a safety measure (Wang et al., 2014).

5.7. Interactions Between Pharmaceuticals and Herbal Remedies

Bioactive components in *B. balsamifera*, which contains flavonoids and terpenoids, may affect the activity of cytochrome P450 enzymes and P-glycoprotein. This could change how other drugs, like warfarin, NSAIDs, or statins, are broken down in the body (Zhao et al., 2022). So, people who take more than one medicine should be careful.

5.8. Compliance and Safety Overview

International safety regulations do not see *B. balsamifera* as dangerous. It is listed in pharmacopoeias in many Asian countries and is widely known to be safe for traditional uses. Still, modern regulatory approval for medicinal uses requires the use of standardized extracts and a toxicological evaluation that follows the rules specified by the International Council for Harmonisation (ICH) (Philippine FDA, 2020). Current toxicological data points that *B. balsamifera* is safe at therapeutic levels, but more long-term, reproductive, and cancer-causing studies will be needed to fully assess the risks.

6. Pharmacokinetics

Pharmacokinetic studies give us important information about how bioactive substances in *Blumea balsamifera* are absorbed, distributed, metabolized, and excreted (ADME). There isn't a lot of pharmacokinetic information about this plant, however some research have pointed out crucial phytoconstituents such flavonoids, terpenoids, and essential oils (Lee et al., 2021; Singh & Kumar, 2020). Understanding these factors is essential for finding the right dosage, making sure it works, and keeping it safe.

6.1. Absorbtion

Key components including borneol, camphor, and quercetin are absorbed through the mouth, as established in preclinical research. The components are quickly absorbed in the gastrointestinal tract, but they go through a first-pass metabolism, which makes them less available

in the body as a whole (Zhao et al., 2019). Quercetin and other flavonoids don't dissolve well in water, which makes it hard for the body to absorb them. However, lipophilic essential oils might help them get through the membranes of the intestines (Chen et al., 2022). Some researchers have suggested using nanoformulation techniques to make hydrophobic components more bioavailable (Patel & Sharma, 2021).

6.2. Distribution

Research involving rodents suggests that borneol and camphor can easily cross the blood-brain barrier, which could affect the activity of the central nervous system (Wang et al., 2020). Quercetin and luteolin are examples of flavonoids that are found in several organs, such as the liver, kidneys, lungs, and spleen. Most of the time, they bind to plasma proteins, which are very important for figuring out how long they last and how well they work (Kim & Lee, 2021). Essential oils can build up in fat tissues because they are lipophilic (Singh & Kumar, 2020).

6.3. Metabolism

Phytochemicals in *B. balsamifera* goes through phase I (oxidation/reduction) and phase II (conjugation) metabolic processes. The liver is where quercetin's main metabolism happens. This makes glucuronide and sulfate conjugates that are subsequently spread throughout the body (Zhao et al., 2019). Borneol and camphor proceed via hydroxylation and join with glucuronic acid (Chen et al., 2022). Using LC-MS/MS and GC-MS, researchers have found a wide range of both active and inactive biotransformation products (Patel & Sharma, 2021).

6.4. Elimination

Excretion mostly happens through the kidneys and bile. Flavonoid metabolites are mostly removed from the body through urine, while volatile terpenes and their metabolites are removed by both urine and exhalation (Kim & Lee, 2021). The half-lives of quercetin metabolites range from 2 to 6 hours, while the half-lives of essential oil components like borneol are shorter, so you need to take them more than once (Wang et al., 2020).

6.5. Bioavailability enhancers

When piperine is combined with other bioenhancers, it can significantly increase the systemic bioavailability of flavonoids from *B. balsamifera* (Patel & Sharma, 2021). Lipid-based formulations, cyclodextrin complexes, and nanoemulsions are some of the strategies that can help hydrophobic compounds dissolve and be absorbed by the intestines. This may lead to better therapeutic outcomes and lower required dosages (Lee et al., 2021).

6.6. Interactions Between Herbs and Drugs

Flavonoids and terpenoids in *B. balsamifera* affects cytochrome P450 enzymes, especially CYP3A4 and CYP2D6, which means it could interact with other drugs (Singh & Kumar, 2020). When the plant is used with drugs that have narrow therapeutic ranges, these kinds of interactions need to be thought about carefully.

6.7. Pharmacokinetic Modeling and Its Clinical Applications

Pharmacokinetic modeling for *B. balsamifera* is currently sparse, mostly because of animal research (Chen et al., 2022). Future research should focus on making pharmacokinetic models based on population and physiology to predict how drugs will interact with each other in humans and help people make informed decisions about how much to take. Standardized extract formulations are critical for transitioning traditional uses into clinically proven therapies (Lee et al., 2021).

To sum up, the parts of *Blumea balsamifera* are absorbed moderately, spread widely throughout the body, metabolized quickly, and excreted quickly. More research is needed to understand how each component works and how they work together in complex plant matrices. Combining pharmacokinetics with pharmacodynamics will help make better dose forms and treatment plans.

7. Discussion

Blumea balsamifera (L.) DC. is a fragrant, perennial herb in the Asteraceae family that comes from Southeast Asia. It is widely used in traditional medicine to treat a wide range of problems, such as inflammation, infections, respiratory issues, gastrointestinal disorders, wounds, and postpartum care (Zheng et al., 2017; Thongsaard et al., 2020). This in-depth study brings together the ethnopharmacological importance, phytochemical details, pharmacological properties, toxicological safety, and pharmacokinetic characteristics of *B. balsamifera* focussing on the pros and cons of current scientific knowledge. The wide use of *B. balsamifera* is an important part of traditional medicine in several Asian countries, such as China, Thailand, the Philippines, and Malaysia. This underscores the significance within traditional medicine. Ethnobotanical studies show that it can be used to treat cough, bronchitis, asthma, fever, rheumatism, digestive problems, and wounds (Dang et al., 2018; Lao et al., 2016). Also, its use to help women recuperate after giving birth implies that it may have uterotonic and anti-inflammatory qualities (Chen et al., 2019). The use of ethnomedicine led to scientific studies that mostly confirmed these traditional claims with real-world facts. The plant's importance in traditional medicine comes from its bioactive components, which can affect important biological activities linked to infections, inflammation, oxidative stress, and tissue repair. This long-held understanding has been very important in guiding studies in pharmacology and phytochemistry. This shows how important ethnomedicine is as a basis for making drugs (Fabricant & Farnsworth, 2001). The medicinal potential of *B. balsamifera* stands out because of its complex phytochemical profile and how well it works. The many phytochemicals in *B. balsamifera* make it unique. The plant has a lot of secondary metabolites, such as volatile oils, flavonoids, phenolic acids, sesquiterpenoids, and more (Nguyen et al., 2017; Yang et al., 2019). The main things that make the plant work better are borneol, camphor, quercetin, luteolin, β-caryophyllene, and a number of diterpenes. Flavonoids and phenolics

are strong antioxidants that stop reactive oxygen species from damaging cells and control antioxidant enzymes. In the case of cancer, chronic inflammatory illnesses, and aging, this mechanism is very important (Harborne & Williams, 2000). Terpenoids and essential oils can kill bacteria, reduce inflammation, and relieve pain in a number of ways, including breaking down membranes, blocking enzymes, and changing signaling pathways (Bakkali et al., 2008). The different pharmacological actions of B balsamifera are probably due to the way its phytochemicals synergy, with many bioactive components working well together. Studies show that complete extracts often work better than studies that only look at one part. This is in line with the ethnopharmacological practice of using crude extracts or decoctions (Wagner & Ulrich-Merzenich, 2009). Changes in the environment, the seasons, and the ways of extraction can all change the phytochemical makeup, making it harder to establish consistency and standardization. This shows how important it is to put in place strict quality control methods (Sasidharan et al., 2011). Experimental pharmacology has confirmed many common uses of *B. balsamifera*. Multiple in vivo models, such as carrageenan-induced paw edema, ear edema, and different inflammatory paradigms, have shown the anti-inflammatory impact over and over again (Thongsaard et al., 2020). According to research, pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) are less active, and COX and LOX enzymes are less active (Zhang et al., 2018). The effects that were seen are similar to the ways they act in inflammatory diseases like bronchitis and rheumatism work. The DPPH, ABTS, and FRAP tests show that the antioxidant activity could help protect against damage caused by oxidative stress, which is linked to cancer, heart disease, and aging (Nguyen et al., 2017). In vivo studies have shown that extracts from *B. balsamifera* can make natural antioxidant enzymes work better (Liu et al. 2019). This drug works against a wide spectrum of microorganisms, such as fungi, Gram-positive bacteria, and Gram-negative bacteria. Volatile oils do this mostly via breaking down the membranes of microbes (Chen et al., 2019). This activity shows that it can be used in ethnobotanical ways to cure infections and help wounds heal. It has also been shown to work against several types of cancer cells, mostly by causing apoptosis and stopping the cell cycle (Wang et al., 2020). Preclinical models show that the medication has many pharmacological benefits, such as protecting the liver, kidneys, and stomach, relieving pain, and speeding up wound healing. The results support the drug's many medical uses (Dang et al., 2018; Liu et al., 2019). But most of the research that is already out there is limited to in vitro or animal models. The next important step is clinical validation. Before any drug may be used for therapy, it is important to be sure it is safe. Studies on acute and subchronic toxicity show that *B. balsamifera* extracts have a large safety margin, with LD50 values more than 5000 mg/kg in mouse trials and no major negative effects on the structure of vital organs or metabolic markers (Thongsaard et al., 2020; Zhang et al., 2018). Early tests for genotoxicity and mutagenicity show that there is no chance of DNA damage or mutation (Chen et al., 2019). Still, there isn't enough complete information about reproductive toxicity and teratogenicity, which is a big problem because it is used in postpartum treatment. It is best to be careful when using *B. balsamifera* till more research on reproduction is done during pregnant or breastfeeding. It is very important to look more closely at how herbs and drugs could interact with each other. There are some things that can change cytochrome P450 enzymes, which can then change how other drugs are broken down (Zhou et al., 2016). These interactions can make medications more dangerous or less effective, which shows how important it is to do full pharmacokinetic interaction studies. Pharmacokinetics looks at how bioactive molecules are absorbed, distributed, metabolized, and excreted. This is important for understanding how safe and effective they are in living things. Right now, we know a few things about *B. balsamifera* that how it works in the body. There haven't been many investigations on the plasma levels and bioavailability of flavonoids like quercetin and luteolin. These chemicals have a moderate oral bioavailability and go through a lot of phase II metabolism, such as glucuronidation and sulfation (Manach et al., 2005). Volatile oils, such as borneol and camphor, are quickly absorbed, broken down, and removed from the body (Chen et al., 2019). We need to learn more about the pharmacokinetic properties of more sesquiterpenoids and diterpenes. Without this kind of knowledge, it is harder to improve dosing regimens and formulation design. To make *B. balsamifera* clinical development better, it is important to do more advanced pharmacokinetic research using modern analytical methods like LC-MS/MS, along with pharmacodynamic correlations. One of the hardest parts about translating *B. balsamifera* is the change from traditional medicine to standardized phytopharmaceuticals, and the differences in the phytochemical composition of *B. balsamifera*. The profiles of the constituents are greatly affected by where they are grown, the weather, when they are harvested, and how they are processed (Sasidharan et al., 2011). It is very important to set up good quality control systems, such as fingerprint chromatographic profiling and measuring marker compounds like quercetin and borneol. Standardized extracts make ensuring that the pharmacological benefits and safety are the same every time, make it easier for regulators to approve them, and build trust with patients. Also, rules should be set for planting and harvesting to make sure that the process stays sustainable and can be done the same way every time. Even though a lot of progress has been achieved, there are still a lot of gaps in research. The fact that there are no clinical trials right now to test effectiveness, safety, and dose in people shows a big gap that has to be looked at more in future studies. It is important for these trials to include pharmacokinetic and biomarker evaluations so that clinical results can be linked to quantities of bioactive substances. Studying the mechanisms that explain molecular targets, signal transduction pathways, and how phytochemicals work together can help us understand how drugs work and make it easier to create new drugs. It is important to focus on research of reproductive toxicity and herb-drug interactions in order to make sure that the safety evaluation is complete. In the end, biotechnological methods like plant tissue culture, metabolomics, and molecular docking studies could speed up the search for and creation of novel drugs made from *B. balsamifera*.

8. Conclusion

Blumea balsamifera is a well-known medicinal plant that has been used in traditional medicine in Asia and the Pacific for a long time. The different pharmacologically active compounds, such as flavonoids, terpenoids, and essential oils, make it more effective at treating illnesses. These include anti-inflammatory, antibacterial, antioxidant, and hepatoprotective properties. The paper focuses on notable ethnopharmacological uses that have been backed up by preclinical pharmacological studies. The phytochemical profile is complicated and rich, with many bioactive chemicals that have been found and described. Pharmacological studies give us a lot of proof that traditional uses work, but we need more controlled clinical trials to prove that they work in people. Toxicological studies often show that the plant is safe when used properly, but higher doses and longer use may require caution. Pharmacokinetic results show that the main ingredients are absorbed and bioavailable only a little, metabolized a lot, and excreted quickly. However, more studies on humans are needed to get a better picture of how pharmacokinetics works. Combining modern pharmacological tools with traditional medicine knowledge can help *B. balsamifera* reach its full potential. Standardized extracts, advanced delivery methods, and thorough clinical testing are all important parts of making herbal medicines that are based on evidence. Future studies need to focus on combining traditional knowledge with clinical use, especially when it comes to safety, pharmacokinetics, dosage optimization, and formulation development. To reach this goal, professionals

from different fields, such as ethnobotany, pharmacognosy, toxicology, and medicine, must work together.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Burkill, I. H. (1966). A dictionary of the economic products of the Malay Peninsula. Ministry of Agriculture and Cooperatives.

[2] Chomchalow, N. (2000). Herbal medicine and health: Traditional uses of herbs for health and well-being. ASEAN Review of Biodiversity and Environmental Conservation, 1–10.

[3] Chowdhury, A. R., Mandal, S. C., & Das, A. (2010). Phytochemical screening and antibacterial activity of essential oil of *Blumea balsamifera*. Asian Pacific Journal of Tropical Medicine, 3(10), 777–780.

[4] de Padua, L. S., Bunyapraphatsara, N., & Lemmens, R. H. M. J. (1999). Plant Resources of South-East Asia: Medicinal and poisonous plants 1 (Vol. 12). PROSEA Foundation.

[5] DOH (Department of Health). (1997). Traditional medicine in the Philippines. Bureau of Health Promotion, Manila.

[6] Duke, J. A. (2002). Handbook of medicinal herbs (2nd ed.). CRC Press.

[7] Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives, 109(Suppl 1), 69–75.

[8] Heinrich, M., Ankli, A., Frei, B., Weimann, C., & Sticher, O. (2018). Medicinal plants in Southeast Asia: Ethnopharmacological relevance and potential phytochemical and pharmacological interest. Journal of Ethnopharmacology, 189, 40–51.

[9] Kennedy, D. A. (2011). Herb–drug interactions: New evidence brings new concerns. Canadian Pharmacists Journal/Revue des Pharmaciens du Canada, 144(6), 268–269.

[10] Perry, L. M. (1980). Medicinal plants of East and Southeast Asia: Attributed properties and uses. MIT Press.

[11] Rahman, M. A., Sahabuddin, M., & Saha, S. (2020). Essential oil composition and antibacterial activity of *Blumea balsamifera* leaves from Bangladesh. BMC Complementary Medicine and Therapies, 20(1), 1–8.

[12] Thongkhao, S., Anuchapreeda, S., & Limtrakul, P. (2010). Chemical composition and antibacterial activity of essential oil from *Blumea balsamifera* DC. Chiang Mai Journal of Science, 37(3), 488–495.

[13] Wiart, C. (2006). Medicinal plants of Asia and the Pacific. CRC Press.

[14] Wongpanich, V., Saenphet, K., & Chaichan, A. (2007). Study of the effects of *Blumea balsamifera* leaf extracts on postpartum uterine involution. Journal of Health Research, 21(1), 21–26.

[15] Wu, C. C., Chen, H. M., & Lin, C. T. (2018). Antioxidant and anti-inflammatory properties of *Blumea balsamifera* essential oils. International Journal of Molecular Sciences, 19(11), 3706.

[16] Yang, X., Kong, F., & Ji, J. (2013). Chemical composition and antioxidant activity of essential oils from *Blumea balsamifera* leaves. Journal of Essential Oil Bearing Plants, 16(4), 546–552.

[17] Yenjai, C., Suksamrarn, A., & Tip-Pyang, S. (2004). Toxicological evaluation of *Blumea balsamifera* essential oil. Thai Journal of Pharmaceutical Sciences, 28(1–2), 29–37.

[18] Zhao, Z., Liang, Z., & Guo, P. (2005). Macroscopic identification of Chinese medicinal materials: Traditional experiences and modern understanding. Journal of Ethnopharmacology, 96(1–2), 1–20.

[19] Guevara, B., Guevara, L., Lantican, N. G., & Santos, G. G. (2005). Philippine medicinal plants in common use: Their properties and applications. National Research Council of the Philippines.

[20] Kongkathip, B., Kongkathip, N., Phonnak, R., & Sunthornsuk, L. (2009). Ethnobotanical uses and pharmacological activities of *Blumea balsamifera*. Thai Journal of Phytopharmacology, 16(2), 59–70.

[21] Perry, L. M., & Metzger, J. (1980). Medicinal plants of East and Southeast Asia: Attributed properties and uses. MIT Press.

[22] Philippine Department of Health. (1997). Traditional medicine in the Philippines. Bureau of Research and Laboratories, DOH.

[23] Quisumbing, E. (1978). Medicinal plants of the Philippines. Katha Publishing.

[24] Wiart, C. (2006). Medicinal plants of Asia and the Pacific. CRC Press.

[25] Xu, Y., Zhang, J., Fu, C., & Chen, Y. (2019). Traditional uses, phytochemistry, pharmacology and toxicology of *Blumea balsamifera* (L.) DC.: A comprehensive review. Journal of Ethnopharmacology, 239, 111875. https://doi.org/10.1016/j.jep.2019.111875

[26] Zhang, L., Wang, Y., Zhang, W., & He, X. (2020). Ethnopharmacological review of *Blumea balsamifera* (L.) DC.: Bioactive compounds, traditional uses, and therapeutic potential. Frontiers in Pharmacology, 11, 1236.

[27] Zhao, Y., Zhou, Y., Zhang, M., & Liu, Y. (2016). Chemical constituents and bioactivities of *Blumea balsamifera* essential oil: A review. Natural Product Research, 30(24), 2835–2844. https://doi.org/10.1080/14786419.2015.1135140.

[28] Chen, Y., Zhang, J., Li, Y., & Huang, Y. (2013). Seasonal variation of essential oil content and composition of *Blumea balsamifera* (L.) DC. Industrial Crops and Products, 44, 405–411. https://doi.org/10.1016/j.indcrop.2012.11.034.

[29] Jiang, Y., Zhang, L., Zhang, W., & Liu, J. (2020). Advances in nanoformulations of essential oils from *Blumea balsamifera* for improved therapeutic delivery. Journal of Drug Delivery Science and Technology, 57, 101707. https://doi.org/10.1016/j.jddst.2020.101707.

[30] Rawat V. Formulation, optimization and characterization of ellagic acid phyto-vesicular system for bioavailability enhancement. Indian Drugs. 2023 Jul 1.

[31] Xu, Y., Zhang, J., Fu, C., & Chen, Y. (2019). Traditional uses, phytochemistry, pharmacology and toxicology of *Blumea balsamifera* (L.) DC.: A comprehensive review. Journal of Ethnopharmacology, 239, 111875. https://doi.org/10.1016/j.jep.2019.111875.

[32] Zhang, L., Wang, Y., Zhang, W., & He, X. (2020). Ethnopharmacological review of *Blumea balsamifera* (L.) DC: Bioactive compounds, traditional uses, and therapeutic potential. Frontiers in Pharmacology, 11, 1236

[33] Zhao, Y., Zhou, Y., Zhang, M., & Liu, Y. (2016). Chemical constituents and bioactivities of *Blumea balsamifera* essential oil: A review. Natural Product Research, 30(24), 2835–2844. https://doi.org/10.1080/14786419.2015.1135140.

[34] Chen, Y., Zhang, J., Li, Y., & Huang, Y. (2013). Seasonal variation of essential oil content and composition of *Blumea balsamifera* (L.) DC. Industrial Crops and Products, 44, 405–411. https://doi.org/10.1016/j.indcrop.2012.11.034.

[35] Jiang, Y., Zhang, L., Zhang, W., & Liu, J. (2020). Advances in nanoformulations of essential oils from *Blumea balsamifera* for improved therapeutic delivery. Journal of Drug Delivery Science and Technology, 57, 101707. https://doi.org/10.1016/j.jddst.2020.101707.

[36] Wiart, C. (2006). Medicinal plants of Asia and the Pacific. CRC Press.

[37] Xu, Y., Zhang, J., Fu, C., & Chen, Y. (2019). Traditional uses, phytochemistry, pharmacology and toxicology of *Blumea balsamifera* (L.) DC.: A comprehensive review. Journal of Ethnopharmacology, 239, 111875. https://doi.org/10.1016/j.jep.2019.111875.

[38] Zhang, L., Wang, Y., Zhang, W., & He, X. (2020). Ethnopharmacological review of *Blumea balsamifera* (L.) DC.: Bioactive compounds, traditional uses, and therapeutic potential. Frontiers in Pharmacology, 11, 1236.

[39] Zhao, Y., Zhou, Y., Zhang, M., & Liu, Y. (2016). Chemical constituents and bioactivities of *Blumea balsamifera* essential oil: A review. Natural Product Research, 30(24), 2835–2844. https://doi.org/10.1080/14786419.2015.1135140.

[40] Abubakar, A. R., Hadi, N. R., Yusuf, A. A., & Ismail, A. R. (2022). Assessment of the acute and chronic toxicity studies of ethanol extract of *Blumea balsamifera* leaves on murine models. Tropical Journal of Natural Product Research, 6(2), 218–223.

[41] Philippine Food and Drug Administration (FDA). (2020). Product Information Leaflet – *Blumea balsamifera* (Sambong) Leaf. https://verification.fda.gov.ph/files/HMRP-27_PIL_01.pdf.

[42] Piaraksa, P., Prajuabpansri, P., & Boonmars, T. (2018). Evaluation of genotoxicity of *Blumea balsamifera* extracts by Ames test and micronucleus assay. Asian Pacific Journal of Tropical Biomedicine, 8(4), 185–190.

[43] Tan, T. S., Chuah, L. H., & Sim, K. S. (2022). Antiproliferative and antioxidant activities of methanol extract of *Blumea balsamifera* against A549 lung cancer cells. Tropical Journal of Natural Product Research, 6(9), 1517–1522. https://doi.org/10.26538/tjnpr/v6i9.12.

[44] Wang, L. F., Wang, Y. Y., & Liu, H. M. (2014). Volatile oil from *Blumea balsamifera* improves skin conditions in human volunteers. Molecules, 19(11), 18479–18495. https://doi.org/10.3390/molecules191118479.

[45] Widowati, W., Rizal, R., & Nugroho, W. A. (2023). *Blumea balsamifera* leaf extract maintains testosterone levels in hypercholesterolemic rats through antioxidant mechanism and upregulation of StAR gene expression. Biomedical and Pharmacology Journal, 16(3), 1367–1374. https://doi.org/10.13005/bpj/2851.

[46] Yuniarto, A., Kurniawan, A., & Nugroho, A. E. (2017). Subacute oral toxicity of *Blumea balsamifera* leaf extract in Wistar rats. Pharmacognosy Journal, 9(5), 644–648. https://doi.org/10.5530/pj.2017.5.100

[47] Zhao, Y., Zhang, L., & Shen, X. (2022). Enzyme-modulating effects of phytochemicals from *Blumea balsamifera* on cytochrome P450s. Molecules, 27(2), 515. https://doi.org/10.3390/molecules27020515.

[48] Chen, J., Liu, Y., & Zhang, H. (2022). Metabolism and pharmacokinetics of terpenoids from *Blumea balsamifera*: Insights from LC-MS/MS analysis. Journal of Ethnopharmacology, 285, 114832. https://doi.org/10.1016/j.jep.2021.114832.

[49] Kim, S., & Lee, J. H. (2021). Tissue distribution and plasma protein binding of flavonoids in rodents: Implications for *Blumea balsamifera* efficacy. Phytomedicine, 86, 153567. https://doi.org/10.1016/j.phymed.2021.153567

[50] Lee, M. S., Park, Y. J., & Kim, D. H. (2021). Enhancing the bioavailability of *Blumea balsamifera* flavonoids: Nanoformulation and pharmacokinetic perspectives. Frontiers in Pharmacology, 12, 645835.

[51] Patel, R., & Sharma, P. (2021). Nanoemulsion-based delivery systems for hydrophobic phytochemicals from *Blumea balsamifera*: A review. Pharmaceutical Nanotechnology, 9(4), 297–308.

[52] Singh, S., & Kumar, R. (2020). Modulatory effects of *Blumea balsamifera* constituents on cytochrome P450 enzymes: Implications for herb-drug interactions. Drug Metabolism and Disposition, 48(5), 391–400. https://doi.org/10.1124/dmd.120.000123.

[53] Wang, T., Li, X., & Ma, C. (2020). Blood-brain barrier permeability and pharmacokinetics of borneol and camphor from *Blumea balsamifera* in rats. European Journal of Drug Metabolism and Pharmacokinetics, 45(3), 441–448. https://doi.org/10.1007/s13318-019-00589-3.

[54] Zhao, L., Chen, J., & Wang, Y. (2019). Absorption and metabolism of quercetin in rodents following oral administration of *Blumea balsamifera* extract. Journal of Natural Medicines, 73(4), 789–797. https://doi.org/10.1007/s11418-019-01309-8.

[55] Bakkali, F., Averbeck, S., Averbeck, D., & Idaomar, M. (2008). Biological effects of essential oils – A review. Food and Chemical Toxicology, 46(2), 446–475. https://doi.org/10.1016/j.fct.2007.09.106.

[56] Chen, X., Wang, Y., Zheng, J., et al. (2019). Phytochemical and pharmacological review of *Blumea balsamifera* (L.) DC. Phytochemistry Letters, 29, 24-34. https://doi.org/10.1016/j.phytol.2018.11.009.

[57] Dang, T. N., Phan, D. M., Nguyen, T. H., et al. (2018). Antioxidant and anti-inflammatory activities of *Blumea balsamifera* leaf extract and its active compounds. Journal of Ethnopharmacology, 215, 137–144. https://doi.org/10.1016/j.jep.2018.01.017.

[58] Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives, 109(Suppl 1), 69-75. https://doi.org/10.1289/ehp.01109s169.

[59] Harborne, J. B., & Williams, C. A. (2000). Advances in flavonoid research since 1992. Phytochemistry, 55(6), 481–504. https://doi.org/10.1016/S0031-9422(00)00235-1.

[60] Lao, P. T., Lim, M. C., & Chua, L. S. (2016). Ethnomedicinal uses of plants by the indigenous peoples of Southeast Asia. Journal of Ethnobiology and Ethnomedicine, 12, 23. https://doi.org/10.1186/s13002-016-0087-8.

[61] Liu, Y., Lin, Y., Zhou, X., et al. (2019). Protective effects of *Blumea balsamifera* extract on oxidative stress-induced liver injury in mice. Journal of Ethnopharmacology, 234, 191–199. https://doi.org/10.1016/j.jep.2019.02.030.

[62] Manach, C., Williamson, G., Morand, C., et al. (2005). Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. The American Journal of Clinical Nutrition, 81(1), 230S–242S. https://doi.org/10.1093/ajcn/81.1.230S.

[63] Nguyen, V. H., Nguyen, D. M., & Tran, T. D. (2017). Chemical composition and antioxidant activity of *Blumea balsamifera* leaf extracts. Industrial Crops and Products, 109, 199-206. https://doi.org/10.1016/j.indcrop.