

Phytochemistry and Pharmacological Potentials of *Premna serratifolia* L.: Traditional Medicinal Plant Used by Local People in Kalimantan

Khalisha Q. Khairunnisa^{1,2*}, Raden M. Febriyanti^{1,2}, Muhaimin^{1,2}

¹Department of Pharmaceutical Biology, Faculty of Pharmacy, Universitas Padjadjaran

²Herbal Study Center, Universitas Padjadjaran

Submitted 14 December 2022; Revised 18 December 2022; Accepted 27 December 2022; Published 28 December 2022

*Corresponding author: khalisha19001@mail.unpad.ac.id

Abstract

Millions of people worldwide have been using herbal medicines for thousands of years, due to their great interest in traditional medicines. One of the plants in Indonesia which has medicinal properties but is not widely known by the public and used is Bebuas plant. Bebuas (*Premna serratifolia* Linn) has been observed growing in West Kalimantan. The people of West Kalimantan used bebuas leaves to reduce cholesterol levels, the young leaves used as a traditional medicine to expel wind in the body quickly, treat intestinal worms, and increase breast milk for nursing mothers, and the decoction of fresh leaves is used for colds and fever medicine. Several studies report bebuas (*Premna serratifolia* L.) had many pharmacological activities. Bebuas contains flavonoids, saponins, tannins and triterpenoids/steroids that have a role in pharmacological activity. The present review aims to summarize the current state of scientific evidence on the pharmacological potentials of *P. serratifolia*. The subject of literature published from 2012 to 2022 were obtained from international research databases including PubMed, Google Scholar, EBSCO, SCOPUS, and Cochrane, using the keywords *Premna serratifolia* L., traditional medicine, medicinal plants, and pharmacology. The pharmacological activities which are discussed further in the review including antioxidant, anti-arthritic, anticholesterol, anti-inflammatory, antimicrobial, antihelminthic, antidiabetic, and anticancer/cytotoxic. The study suggests that *Premna serratifolia* L. is a potent source for further development of phytomedicine.

Keywords: bebuas, *Premna serratifolia* L., pharmacological effect, traditional medicine

Potensi Fitokimia dan Farmakologi *Premna serratifolia* L.: Tumbuhan Obat Tradisional yang Dimanfaatkan Masyarakat Kalimantan

Abstrak

Jutaan orang di seluruh dunia telah menggunakan obat-obatan herbal selama ribuan tahun karena ketertarikan mereka yang besar terhadap obat-obatan tradisional. Salah satu tanaman di Indonesia yang memiliki khasiat obat namun belum banyak diketahui oleh masyarakat dan dimanfaatkan adalah tanaman Bebuas. Tanaman bebuas (*Premna serratifolia* Linn) diamati banyak tumbuh di Kalimantan Barat. Masyarakat Kalimantan Barat memanfaatkan daun bebuas untuk menurunkan kadar kolesterol, daun mudanya digunakan sebagai obat tradisional untuk cepat mengeluarkan angin dalam tubuh, mengobati cacingan, dan memperbanyak ASI bagi ibu menyusui, dan rebusan daun segarnya digunakan untuk obat flu dan demam. Beberapa penelitian melaporkan bebuas (*Premna serratifolia* L.) memiliki banyak aktivitas farmakologis. Bebuas mengandung flavonoid, saponin, tanin dan triterpenoid/steroid yang berperan dalam aktivitas farmakologis. Tinjauan ini bertujuan untuk meringkas bukti ilmiah terkini tentang potensi farmakologis *P. serratifolia*. Subjek literatur yang diterbitkan dari tahun 2012 hingga 2022 diperoleh dari database penelitian internasional antara lain PubMed, Google Scholar, EBSCO, SCOPUS, dan Cochrane, menggunakan kata kunci *Premna serratifolia* L., obat tradisional, tanaman obat, dan farmakologi. Aktivitas farmakologis yang dibahas lebih lanjut dalam ulasan meliputi antioksidan, antirematik, antikolesterol, antiinflamasi, antimikroba, antihelminik, antidiabetes, dan antikanker/sitotoksik. Studi ini menunjukkan bahwa *Premna serratifolia* L. adalah sumber yang kuat untuk pengembangan obat herbal lebih lanjut.

Kata Kunci: bebuas, *Premna serratifolia* L., efek farmakologis, obat tradisional

1. Introduction

Indonesia has the second largest biodiversity in the world as indicated by a high number of native medicinal plants, after the Amazon rainforests¹. Indonesia is an archipelago country with millions of hectares of tropical forests which consists of thousand species of plants and is home to 80% of the world's medicinal plants. More than 30 thousand traditional medicine formulas have been widely used in the community. Indonesia with over 217 million population is a potential market for traditional medicine. Based on this rich source of medicinal plants, several medicinal plant/plant species in Indonesia are used by the local community in Indonesia as traditional herbal medicines to treat disease.

Medicinal plants are one of the alternative treatments to improve health and well-being. Some research found that traditional medicine with medicinal plants is more harmless and have minimum side effect. Indonesia is a biodiversity country that has a lot of medicinal plants/plant species that are used by the local people in Indonesia itself. There are more than around 1300 species of medicinal plants in Indonesia. In some places or ethnicities, the medicinal plant have different types of functions or efficacy².

In Javanese Ethnic, they use traditional medicine/medicinal plants to make traditional herbal medicines called Jamu to treat or prevent some diseases. There are various types and efficacy of Jamu, including Jamu Beras Kencur which consist of *Tamarindi pulpa* extract, *Zingiberis rhizoma* extract, *Cinnamomi cortex*, *Kaempferiae rhizoma* extract, and *Oryza sativa* that has efficacy to reduce fatigue, refreshes the body, prevents hemorrhoids and the common cold, raises stamina and immunity to disease. Jamu Srongpas Ginseng which consists of *Retofracti fructus*, *Zingiberis zerumbeti* rhizoma, *Elephantopi radix*, *Eurycoma radix*, *Panax ginseng* radix extract has the efficacy to increase vitality, relieves backache, sore muscles, fatigue, and general debility, improves appetite, and nourishes the kidneys¹.

Meanwhile, in Sundanese ethnic, the second largest ethnic group in Indonesia

inhabit in West Java, the traditional medicinal plant also still has an important role to treat and prevent disease. The local people in Sundanese Ethnic commonly use onion with coconut oil as an antipyretic, betel nut for anti-diarrhea, *Andrographis paniculate* or sambiloto to treat fever, *Pleomele angustifolia* or suji to treat cough and lung disease, *Ricinus communis* L. or jarak to treat stomachache, etc³.

Similarly, the local community in Kalimantan used *Premna serratifolia* L. as traditional medicine. *Premna serratifolia* L. locally known as bebuas is a medicinal plant. The people of West Kalimantan used bebuas leaves to reduce cholesterol levels, the young leaves used as a traditional medicine to expel wind in the body quickly, treat intestinal worms, and increase breast milk for nursing mothers, and the decoction of fresh leaves is used for colds and fever medicine⁴. Bebuas is a tropical plant and belongs to the family of Verbenaceae. This species is originally from Southeast Asia, often cultivated in tropical and subtropical areas. *P. serratifolia* is widely distributed along the coasts and islands of tropical and subtropical Asia, Africa, Australia and the Pacific⁵. It is an important Ayurvedic medicinal herb and its synonym is *Premna integrifolia*. It is popularly known as bebuas, smule, buas-buas, rogo, singkil, somule in Indonesia, and "Agnimantha" in Ayurvedic system of medicine.

P. serratifolia is a scandent, erect shrub or small tree that can grow to a height of 9 m. It has yellowish lenticolate bark, large spiny branches, and a yellowish brown woody aromatic root. The leaves are simple, occasionally whorled, elliptic-ovate, membranous, and have 4-6 pairs of primary lateral nerves. The flowers are small. It mostly grows in sandy soil and scrubs jungles along seacoasts and mangrove forests⁶.

The entire plant has therapeutic benefits that have been used for centuries to treat illnesses including colds, get rid of bad breath, get rid of intestinal worm infections, and rejuvenate women's bodies after giving birth by adding a decoction of leaves, roots, bark, and stems to their bathwater⁷. In

addition, young bebuas leaves can stimulate the production of breast milk. Locals generally use bebuas leaves as fresh vegetables, or as an addition to food as flavor⁸.

The present review aims to summarize and consolidate the current state of scientific evidence available on research databases from 2012 until 2022 on the pharmacological potentials of *P. serratifolia*. It will identify areas of further development of this herb as a novel alternative therapeutic agent and provide a direction for future research in the development of new *P. serratifolia*-based drugs. The subject of literature published from 2012 to 2022 were obtained from international research databases including PubMed, Google Scholar, EBSCO, SCOPUS, and Cochrane, using the keywords *Premna serratifolia* L., traditional medicine, medicinal plants, and pharmacology.

2. Method

The subject of literature published from 2012 to 2022 were obtained from international research databases including PubMed, Google Scholar, EBSCO, SCOPUS, and Cochrane, using the keywords *Premna serratifolia* L., traditional medicine, medicinal plants, and pharmacology.

3. Result and Discussion

3.1. Phytochemical Constituent of *Premna serratifolia* L.

The genus *Premna* was previously classified within the family Verbenaceae, but has been transferred into the family Lamiaceae, subfamily Viticoideae. Currently, the genus *Premna* contains of 200 species⁹. The different parts of the *Premna* species contain different chemical constituents. But most of all contains alkaloids, terpenoids, flavonoids, iridoids, and glycosides¹⁰. The leaves of *Premna obtusifolia* contain premnazole, flavanoids, β -sitosterol, premnalin, and flavonesglycoside¹¹. The leaves of *Premna barbata* contain flavanoids, terpenoids, alkaloids and polysaccharides¹². The leaves and roots of *Premna esculenta* contain phenols, tannins, terpenoids, flavonoids¹³. The leaves of *Premna latifolia* contain iridoids, glycosides,

diterpenes and saponins¹⁴ and many more.

Premna serratifolia L. contains secondary metabolites of flavonoids, saponins, tannins, and triterpenoids/steroids¹⁵. Methanol extract of *P. serratifolia* ripe fruit contains saponins, polyphenols, flavonoids, and terpenoids-steroid compounds. The n-hexane fraction contains terpenoid-steroids. The ethyl acetate fraction of *P. serratifolia* fruit contained terpenoids, steroids, flavonoids, and polyphenols⁴. The methanol fraction contains saponins, flavonoids, polyphenols, and terpenoid-steroid compounds. While the ethanol extract of *P. serratifolia* leaves contains flavonoids, tannins, saponins, and polyphenols¹⁶. The stem bark contains alkaloids aphelandrine, iridoid glucoside-7-deoxyloganic acid, geniposidic acid, beta-sitosterol, and betulin. The leaves contain isoxazole alkaloid as premnazole, iridoid glucoside conjugate as premcoryside verbocose, premenolal and nellional along with premnaspirodiene, premnaspiral, caryophyllane 3-one, and pimaradienols¹⁷.

3.2. Pharmacological Activities of *Premna serratifolia* L.

The reported pharmacological activities of *P. serratifolia* are described and summarised in the Table 1.

3.3.1. Antioxidant

Antioxidants are compounds that can fight toxic hazards and reduce cell damage to the body caused by free radical oxidation. The antioxidant activity test used was the DPPH method (2,2-Diphenyl-1-Pikrylhydrazil). The DPPH method is a simple, fast, sensitive, and reproducible method for testing antioxidant activity, where DPPH is a free radical that is stable at room temperature and is often used to assess the antioxidant activity of several compounds or extracts of natural ingredients, so this method is suitable to be used to assess the activity of antioxidant from ethanol extract of *P. serratifolia* leaves. The principle of the DPPH test is to remove color for antioxidants that directly reach the DPPH radicals by monitoring the absorbance using a UV-Vis spectrophotometer²⁹.

The antioxidant activity of *P. serratifolia*

Table 1. Reported Pharmacological Activities of *Premna serratifolia* L.

No	Activity	Compound Content	Method	Plant Part	Result
1.	Antioxidant	Flavonoid	DPPH method ¹⁵	Leaves	Antioxidant activity at concentration of 30 ppm has IC ₅₀ values of 20.66 µg /ml.
2.	Anti-arthritis	Alkaloids, steroids, flavonoids, phenolic compounds and glycosides specifically iridoid glycosides	Freud's adjuvant induced arthritis model ¹⁸	Wood	The ethanol extract at the dose of 300 mg/kg body weight inhibited the rat paw edema by 68.32%
3.	Anticholesterol/ Antihyperlipidemic	n/a	In vitro ¹⁹	Leaves	The greatest absorbance of the extract with either chloroform, ethanol, and n-hexane as solvents was indicated by the addition of 2.5 ml of chloroform extract in 5 ml of standard solution with a concentration of 100 ppm, which was 2.998.
4.	Anti-inflammatory	Alkaloids, flavonoids, and steroids	Carrageenan induced oedema ²⁰	Leaves	The anti-inflammatory evaluation showed that for dose 20 mg/KgBW the percentage inhibition was 76.94% with ED ₅₀ = 4.06 mg/kgBW.
		Flavonoids and saponins	The HBRC membrane stabilization method ²¹	Flowers	Anti-inflammatory activity at the concentration of 300 mg/ml was 97.30±0.59 compared to the standard drug Indomethacin was 99.38±0.19.
5.	Antimicrobial	Flavonoid and phenolic (eugenol)	Paper disc diffusion method (DDM) ²²	Leaves	diameter of the clear zone against <i>S. aureus</i> and <i>S. typhi</i> is included in the weak category at concentration of 100% (4.6 mm for <i>S. aureus</i> and 4.7 mm for <i>S. typhi</i> bacteria)
6.	Antihelmintic	Alkaloid, phenolic, triterpenoid, steroid, flavonoid, tannin and saponin	determined by in vitro based on motility and mortality of worm ²³	Leaves	The mortality of <i>Ascaridia galli</i> worms at concentrations of 100 mg/ml, 200 mg/ml, and 400 mg/ml were ± 24.66 h, ± 7 h, and ± 2.8 h
7.	Antidiabetic	Flavonoid, saponin, tannin, and polyphenol.	In vitro α-glucosidase inhibition assay ²⁴	Leaves	The concentration of 2.5 % inhibited in vitro α-glucosidase with a percentage of 91.69 %.
		Phenolic	In vitro α-glucosidase inhibition assay ²⁵	Leaves	The inhibitory activities if infusion and decoction sample were 4.27 ±0.31 µg/ml and 0.046 µg/ml, better than positive standard (acarbose) with 824 ±0.06 µg/ml.

Table 1. Reported Pharmacological Activities of *Premna serratifolia* L.

No	Activity	Compound Content	Method	Plant Part	Result
8.	Anticancer/ cytotoxicity	n/a	Carbon tetra chloride induced liver cancer ⁵	Leaves	IC ₅₀ = 27.3 µg/ml
		n/a	MTT Assay ²⁶	Leaves	IC ₅₀ = 58.40 µg/ml
		n/a	SRB Assay ²⁷	Leaves	IC ₅₀ = 18.5 µg/ml
		n/a	Alamar blue ²⁸	Leaves, root- barks, and root- wood	IC ₅₀ = 31.7 µg/ml

leave is due to the presence of phenolic compounds, especially the high flavonoid group with total flavonoids of 4.67 mg/g and 0.47% w/w. The ethanol extract of bebuas leaves contains flavonoid compounds which are known to have antioxidant properties and ward off free radicals. Based on the results of the research conducted by Puspita et al, it can be concluded that the ethanol extract of *P. serratifolia* leave has a very high antioxidant activity with an IC₅₀ potential of 20.66 g/ml antioxidant activity¹⁵.

3.3.2. Anti-arthritis

Anti-arthritis activity was evaluated by Freund's adjuvant-induced arthritis model using *P. serratifolia* wood ethanol extract. Body weight loss during arthritis was corrected by treatment with the *P. serratifolia* wood ethanol extract and the standard drug, indomethacin. Biochemical parameters such as hemoglobin content, white blood cells, red blood cells, erythrocytes and sedimentation rate were also estimated. Ethanol extract at a dose of 300 mg/kg body weight inhibited rat paw edema by 68.32%, which is comparable to the 74.87% inhibition of rat paw edema by of the standard drug indomethacin after 21 days. Because of its good ability to inhibit rat paw edema, it can be concluded that the *P. serratifolia* wood ethanol extract possessed a significant antiarthritic activity against adjuvant-induced arthritis¹⁸.

3.3.3. Anticholesterol/Antihyperlipidemic

Cholesterol is mainly present in the blood as lipoprotein fractions such as low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Hyperlipidemia is an excess of fatty substances called lipids in the blood, mainly containing cholesterol and triglycerides. Because these protein-bound fatty substances migrate into the blood, it is also called hyperlipoproteinemia³⁰. This is the only way that these fatty substances can remain dissolved while in circulation³¹.

Anticholesterol activity was tested using an in vitro assay. In addition, the maximum absorption wavelength was measured to obtain the maximum cholesterol wavelength. *P. serratifolia* extract has anti-cholesterol properties. Absorption recovery of 100 ppm cholesterol standard solution was also detected when 0.5 ml of chloroform extract was added. The greatest absorbance of the extract with either chloroform, ethanol, and n-hexane as solvents was indicated by the addition of 2.5 ml of chloroform extract in 5 ml of standard solution with a concentration of 100 ppm, which was 2.998. While the lowest absorbance was indicated by the addition of 0.5 ml of chloroform extract in 5 ml of standard solution with a concentration of 100 ppm, which was 2.735. This decrease in absorbance shows that chloroform extract with the addition of 0.5 ml is the most effective as an anti-cholesterol¹⁹.

This preliminary study has proven that *P. serratifolia* extract has potential as an anti-

cholesterol. The increase in absorbance along with the addition of the extract volume in the standard cholesterol solution could be caused by the presence of tannin compounds. Tannins can affect the color of the supernatant solution that will be absorbed. The addition of the extract also makes the supernatant solution dark so that the absorbance obtained is high due to the large number of molecules that interact with light¹⁹.

3.3.4. Anti-inflammatory

Inflammation is a biological defense response in the vascularized tissues of multicellular organisms to a stimulus such as a foreign pathogen or internal tissue damage³². The anti-inflammatory activity evaluation was carried out on male albino rats (*Rattus norvegicus*). These rats were used as test animals because many human condition symptoms can be replicated on them and their genome is similar to human genome (90%)³³.

Each rat's paw was injected subplantarily with 0.1 ml carrageenan 1% solution. Ethanol extract at a dose of 250, 500, 1000 mg/KgBW was able to reduce the rat's paw swelling at first 60 minutes after induction. In contrast, the hexane extract that had a significant effect at first 60 minutes only observed with a dose of 1000 mg/KgBW. The animals treated with ethanol extract at dose 250, 500, and 1000 mg/KgBW showed 25.35%; 45.42%; and 68.35% inhibition of carrageenan induced acute inflammation. The animals treated with hexane extract dose 250, 500, and 1000 mg/KgBW showed 8.37%; 22.90%; and 43.83% inhibition. These showed that both hexane and ethanol extract have strong anti-inflammatory activity (percent inhibition is above 40%). However, the anti-inflammatory activity of the hexane extract was weaker than that of the ethanol extract. This can be seen from the percentage of inhibition above 40% was only achieved by hexane extract at a dose of 1000 mg/KgBW. Meanwhile, the ethanol extract was able to reach above 40% at a dose of 500 mg/KgBW²⁰.

The active anti-inflammatory compounds in hexane extract were thought to be steroids. This was consistent with the results of the

phytochemical screening which showed that the hexane extract was only positive for steroids. Meanwhile, the anti-inflammatory active compounds in ethanol extract could come from the phenolic or alkaloid groups⁹.

Methanol extract from *P. serratifolia* flowers induced hemolysis by stabilizing the red blood cell membrane with a hypotonic solution. Hypotension-induced inhibition of HRBC membrane lysis was taken as a measure of anti-inflammatory activity. The methanol extract exhibited significant anti-inflammatory activity at the concentration of 300 mg/ml, comparable to the standard drug indomethacin. At the 300 mg/ml dose, the inhibitory efficacy of the extract was 97.30 ± 0.59 , whereas that of the Indomethacin formulation was 99.38 ± 0.19 . It shows that the methanolic extract has anti-inflammatory activity which is comparable to the standard drug Indometachin²¹.

Lysosomal membranes and red blood cells have much in common, and red blood cells can extrapolate the stabilization of the lysosomal membrane. Methanolic flower extract also exhibits significant antioxidant activity. Phytochemical testing of flower extracts indicated the presence of flavonoids, alkaloids, tannins and saponins. Flavonoids are well documented as having powerful antioxidant and anti-inflammatory effects. The anti-inflammatory effect of methanol extract may be due to the presence of flavonoids and saponins²¹.

3.3.5. Antimicrobial

Antibacterial is one of the potentials that is good enough to be developed in the health sector to treat various diseases caused by bacteria such as food poisoning and typhoid fever³⁴. The disease is caused by bacteria that are pathogenic for humans, such as *Staphylococcus aureus* and *Salmonella typhi*. *S. aureus* is a gram-positive bacterium that is commonly found on human skin. These bacteria are classified as pathogenic bacteria that can cause poisoning in humans, especially through food and are classified in cases of intoxication, namely ingestion of staphylococcal enterotoxins. While the bacterium *S. typhi* is a

gram-negative bacterium that causes typhoid fever which is transmitted through food and drink contaminated by feces or feces from a person with or suffering from typhoid fever³⁵.

The antibacterial activity of *P. serratifolia* was tested using the sterile paper disc diffusion method. *P. serratifolia* as an antibacterial was controlled with amoxicillin as a positive control and tween oil as a negative control. The use of amoxicillin as a positive control because amoxicillin is an antibacterial with a broad spectrum of penicillin derivatives used to treat various bacterial infections²².

The results of the analysis of the antibacterial activity of *P. serratifolia* in inhibiting the growth of *S. aureus* and *S. typhi* bacteria show that each variation in the concentration (12,5%, 25%, 50%, and 100%) of *P. serratifolia* has different activities. This is because the higher the concentration of oil, the greater the inhibition zone formed³⁶. The data shows that the diameter of the clear zone of *P. serratifolia* against *S. aureus* and *S. typhi* is included in the weak category at a concentration of 100% (4.6 mm for *S. aureus* and 4.7 mm for *S. typhi*) in accordance with Afnidar's opinion³⁷ which states that the diameter of the clear zone of 1-15 mm gives a weak growth inhibition response.

Most of the secondary metabolites in essential oils are phenol derivatives. The activity of phenolic compounds such as eugenol in inhibiting bacterial growth is to work by poisoning the cytoplasm, damaging and penetrating the walls and precipitating bacterial cell proteins²².

3.3.6. Antihelmintic

Antihelmintic activity of bebuas extract was determined by in vitro based on the motility and mortality of worms. The motility and mortality of the worm were observed each hour. In vitro method showed extract of bebuas leaves 100 mg/ml, 200 mg/ml and 400 mg/ml had antihelmintic activity against *Ascaridia galli* worms. The extract that has the fastest effect in causing the death of worms was extract with a concentration of 400 mg/ml with an average time of death of worms for 2.8 h. Meanwhile, the time of death occurred

in the positive control group (Albendazole) was ± 7 h²³.

Alkaloid compounds work on the central nervous system which can stop nerve cells, causing the *Ascaridia galli* worm to experience paralysis which eventually die. In addition, alkaloid compounds can disrupt local homeostasis by reducing nitrate which is needed in protein synthesis and suppressing the delivery of sucrose to the small intestine. The alkaloid compounds contained have the ability to act as enzyme inhibitors where this ability can cause paralysis of the worms and even cause death in large doses. Tannins can bind to free proteins in the digestive tract of worms or glycoproteins in the cuticles of worms so that they interfere with physiological functions such as motility, nutrient absorption, and reproduction³⁸.

3.3.7. Antidiabetic

The extract was made in five concentration variations, from 0.125, 0.5, 1, 2, and 2.5% so that we can see the relationship between the addition of the concentration of *P. serratifolia* leaf extract and the inhibition achieved. The highest percentage of inhibition was at the concentration of *P. serratifolia* extract 2.5%, which was 91.69%. However, based on IC₅₀ of 0.2, the leaf extract of *P. serratifolia* was stated to be able to inhibit α -glucosidase at a concentration of 2% with a percentage of 91.03%. The percentage of inhibitory power was lower than the positive control Acarbose which was able to inhibit α -glucosidase by 93.84% at a concentration of 1%. *P. serratifolia* leaf extract can inhibit α -glucosidase 97% of the percentage of Acarbose inhibition. One of the secondary metabolites contained in the leaf extract of *P. serratifolia* is flavonoids. Flavonoids are very effective as α -glucosidase inhibitor. The flavonoid group that plays a role in inhibiting the α -glucosidase enzyme is 3', 4'-hydroxy in ring B which plays a role in interaction with the active site of the enzyme. While the 3-OH on the carbon ring functions to maintain proper binding to the flavonoid molecule²⁴.

Both infusion and decoction extracts showed α -glucosidase inhibitor activity, with

an IC_{50} that was lower than the positive control acarbose, according to Timotius' research. Infusion and decoction samples had 200 and 18×10^3 times more potent inhibitory effects than acarbose, respectively. These results imply that both extracts are more effective in inhibiting α -glucosidase than acarbose. It was shown that the ability of leaf decoction to inhibit α -glucosidase was 90 times stronger when compared to infusion²⁵.

3.3.8. Anticancer/Cytotoxicity

Malignant neoplasia is the term for cancer, which is also known as abnormal cell proliferation. When a person has cancer, their cells proliferate quickly and grow out of control, resulting in a malignant tumor. Cancer can attack any parts of the body, spread and rapidly invade other organs³⁹.

Anticancer activity of biosynthesized silver nanoparticles (AgNps) using the ethanolic leaf extract of *P. serratifolia* was evaluated against carbon tetra chloride (CCl_4) induced liver cancer in Swiss albino mice (Balb/c). By using SEM, FTIR, and XRD studies, the produced silver nanoparticles were identified. Particle size was determined using the Debye-Scherrer equation, and the average size of silver nanoparticles produced from *P. serratifolia* leaf extract was 22.97 nm. The characteristic pattern showed that the sample had cubic-shaped silver nanoparticles. The reduction by capping material of the plant extract is what causes the bioreduction of silver ions to silver nanoparticles, according to FTIR analysis. To assess the anticancer effectiveness of synthetic silver nanoparticles, mice were placed into 5 groups of 6 animals each.

Group I: Healthy control mice. Group II: To cause liver cancer in animals, 50% CCl_4 in olive oil was injected intraperitoneally twice weekly for a period of six weeks. Liver cancer-induced mice were divided into five groups: Group III received treatment with *P. serratifolia* leaf extract (500 mg/kg) for 15 days; Group IV received treatment with synthesized AgNps coated with *P. serratifolia* leaf extract (500 mg/Kg) for 15 days; and Group V received treatment with isoleucine (3 g/d) for 15 days. Blood serum and plasma samples from control

and cancer-induced animals were collected for biochemical examination after the experimental period. After developing liver cancer, the mice's body weight dropped.

Mice treated with *P. serratifolia* leaf extract and the amino acid isoleucine regained their body mass. Mice treated with AgNps-coated *P. serratifolia* leaf extract recovered body mass closer to control than mice treated with plant extract and amino acids. SGOT, SGPT, and total protein levels in experimental mice in each group were significantly increased in mice with CCl_4 -induced liver cancer compared to control groups. AgNps treatment from *P. serratifolia* powder extract significantly reduced SGOT, SGPT, and total protein levels and brought control closer than liver cancer mice treated with *P. serratifolia* leaf powder extract + isoleucine.

There was a significant decrease in plasma levels of thiobarbituric acid reactive substances (TBARS) in mice with CCl_4 -induced liver cancer compared with control groups. AgNps treatment of mice coated with *P. serratifolia* leaf extract limited plasma TBARS levels significantly closer to control than mice with liver cancer treated with *P. serratifolia* leaf extract + isoleucine. Silver nanoparticles from *P. serratifolia* leaf extract were effective in treating liver cancer in Swiss albino mice compared to *P. serratifolia* leaf extract containing isoleucine⁵.

The anticancer activity of the crude extracts of *P. serratifolia* was evaluated using the MTT assay to determine the cytotoxic effect of each extract against breast cancer cells, MCF-7. The results showed that both crude methanol and hexane extracts had high cytotoxic activity against MCF-7 cells with IC_{50} of 58.40 μ g/ml and 53.81 μ g/ml, respectively. Both ethyl acetate crude extracts and ethanol extracts showed weak activity with IC_{50} of 272 μ g/ml and 820 μ g/ml, respectively²⁶.

Using the SRB assay, the tumor cell suppression activity of the MCF7 (breast cancer), HepG2 (liver cancer), and A549 (lung cancer) cancer cell lines was evaluated. The IC_{50} values show that effectiveness is dose-dependent. Each cell line's GI50, TGI,

and LC₅₀ values were calculated, and they were compared with the standard drug Adriamycin²⁷. Two cancer cell lines, SHSY-5Y neuroblastoma and B16 melanoma cells, were tested for cytotoxic activity using methanol extracts of *P. serratifolia*'s leaves, root bark, and root wood. As previously mentioned by Habtemariam and Jackson, Alamar Blue™ fluorescence was used to measure cell viability. The active ingredient was recovered using a combination of Sephadex LH-20 column, Combiflash chromatography, and HPLC after fractionation of the RB extract demonstrating promising activity with a solvent that improves polarity.

Compound 11,12,16-trihydroxy-2-oxo-5-methyl-10-dimethyl-beet-1, isolated through extensive spectroscopic analysis including 1D and 2D NMR (COSY, HMQC, HMBC, NOESY) and MS analysis, was confirmed that it has been used to be 10.6,8,11,13-pentene appears to be a novel compound based on a novel diterpene backbone. The cytotoxic activity of the isolated compound was 21 and 23 times higher than the cytotoxic activity of the crude extract against SHSY-5Y and B16 cells, respectively²⁸.

4. Conclusions

According to the current review, *P. serratifolia* has antioxidant, anti-arthritic, anticholesterol, anti-inflammatory, antimicrobial, antihelminthic, antidiabetic, and anticancer/cytotoxic properties. According to the literature, methanol and ethanol are used as extractive solvents to study the majority of *P. serratifolia*'s pharmacological properties. This solvent typically contains large amounts of phytoconstituents like phenols, flavonoids, amino acids, vitamins, and carbs. These phytocompounds could be the cause of the activity in the extracts. Typically, leaves and roots were used to assess pharmacological activity. This article gives a readily available source for information on the pharmacological effects of different *P. serratifolia* plant sections. Further scientific investigation may be sparked by the identification of active ingredients, their biological effects, clinical safety, and the confirmation of *P. serratifolia*'s traditional

usage. The material presented here will be helpful for building up research methods for developing modern drugs formulations for treating and curing a variety of conditions, which can demonstrate its efficacy as a cutting-edge source for developing new drugs.

References

1. Elfahmi, Woerdenbag HJ, Kayser O. Jamu: Indonesian Traditional Herbal Medicine towards Rational Phytopharmacological Use. *J Herb Med.* 2014;4(2):51–73.
2. Astutik S, Pretzsch J, Kimengsi JN. Asian Medicinal Plants' Production and Utilization Potentials: A Review. *Sustainability (Switzerland).* 2019 Oct 1;11(19):1–33.
3. Roosita K, Kusharto CM, Sekiyama M, Fachrurazi Y, Ohtsuka R. Medicinal plants used by the villagers of a Sundanese community in West Java, Indonesia. *J Ethnopharmacol.* 2008 Jan 4;115(1):72–81.
4. Veronika V, Agus Wibowo M, Hadari Nawawi JH. Aktivitas Antioksidan dan Toksisitas Ekstrak Buah Buas-Buas (*Premna serratifolia* Linn). *JKK.* 2016;5(3):45–51.
5. Paul JAJ, Selvi BK, Karmegam N. Biosynthesis of Silver Nanoparticles from *Premna serratifolia* L. Leaf and Its Anticancer Activity in CCl₄-Induced Hepato-cancerous Swiss Albino Mice. *Applied Nanoscience (Switzerland).* 2015 Nov 1;5(8):937–44.
6. Yee KS, Sukwattanasinit T, Sotaphun U, Wetwitayaklung P, Wangwattana B, Narakornwit W. Optimization of Solvent Extraction of the Leaves of *Premna serratifolia* and Quantitation of *Premnaodoroside A* by Validated TLC-densitometric Method. *Pharmacognosy Journal.* 2021 Dec 1;13(6):1656–63.
7. Yuniarti R, Nasution HM, Rani Z, Fahmi. Utilization Of Buas Buas Leaf (*Premna Pubescens* Blume) Ethanol Extract As Liquid Soap With Anti-Bacteria Activity. *International Journal of Science, Technology & Management [Internet].* 2022;3(3):733–43. Available from: <http://ijstm.inarah.co.id733>
8. Isnindar, Wahyuono S, Widyarini S,

- Yuswanto. Determination of Antioxidant Activities of Buas-Buas Leaves (*Premna serratifolia* L.) Using DPPH (2,2-diphenyl-1-picrylhydrazyl) Method. *Traditional Medicine Journal*. 2016;21(3):111–5.
9. Dianita R, Jantan I. Ethnomedicinal Uses, Phytochemistry and Pharmacological Aspects of the Genus *Premna*: A review. *Pharm Biol*. 2017;55(1):1715–39.
 10. Kabra A, Kabra R, Baghel US. *Premna* Species: A Review. *Journal of Biological and Chemical Chronicles*. 2015;1(1):55–9.
 11. Kumari H, Shrikanth P, Chaithra, Pushpan R, Nishteswar K. A Comparative Experimental Evaluation of Anti-inflammatory Activity of *Premna obtusifolia* Linn and *Premna latifolia* Roxb Leaves in Charles Foster Rats. *Anc Sci Life*. 2012;31(2):58–61.
 12. Tamta M, Kumar A, Shukla N, Negi D. Effects of Crude Extracts of *Premna barbata* Wall. and *Clerodendrum viscosum* Vent. (Verbenaceae) on Different Pathogenic Bacteria. *Asian J Tradit Med*. 2012;7(1):1–7.
 13. Mahmud ZA, Bachar SC, Qais N. Antihyperlipidemic Activity of Leaf and Root Extracts of *Premna esculenta* (Roxb.) in Poloxamer-407 Induced Hyperlipidemic Mice and Rats. *Orient Pharm Exp Med*. 2011 Dec;11(4):263–70.
 14. Mahire NB, Tote M v, Jain AP, Undale VR, Bhosle A v. Anti-inflammatory Effect of *Premna latifolia* Leaves. *Pharmacologyonline* 3. 2009;929–37.
 15. Puspita W, Sari DY, Rahman IR. Uji Aktivitas Antioksidan Ekstrak Etanol Daun Buas-buas (*Premna serratifolia* L.) Asal Kabupaten Melawi Provinsi Kalimantan Barat dengan Metode DPPH. *Jurnal Insan Farmasi Indonesia*. 2020;3(2):405–12.
 16. Hadiarti D, Haryadi W, Matsjeh S, Swasono RT. Understanding Phytochemical Roles on α -glucosidase Inhibitory Activity Based on Metabolomic Approach of *Premna serratifolia* Leaves from West Borneo, Indonesia. *Rasayan Journal of Chemistry*. 2021 Apr 1;14(2):1216–22.
 17. Rani S, Suriyaprakash TNK, Prabu SL. Monograph on *Premna serratifolia* Linn. In: Eddouks M, editor. *Phytotherapy in the Management of Diabetes and Hypertension*. Bentham Science Publisher Ltd.; 2016. p. 204–12.
 18. Rajendran R, Krishnakumar E. Anti-Arthritic Activity of *Premna serratifolia* Linn., Wood against Adjuvant Induced Arthritis. *Avicenna Journal of Medical Biotechnology* . 2010;2(2):101–6.
 19. Hadiarti D. Uji Aktivitas Ekstrak Buas-Buas (*Premna serratifolia* Linn.) Sebagai Anti Kolesterol secara In Vitro. *Ar-Razi Jurnal Ilmiah*. 2017;5(1):22–9.
 20. Muhaimin M, Irvash Shalihin M, Latief M. Anti-Inflammatory Activity of an Indole Alkaloid Isolated from Bebuas (*Premna serratifolia*). *The Journal of Pure and Applied Chemistry Research [Internet]*. 2021 Aug 31;10(2):84–103. Available from: <https://jpacr.ub.ac.id/index.php/jpacr/article/view/584>
 21. Rajagopal PL, Aneeshia S, Sreejith KR, Kiron SS, Premaletha K. Antioxidant and Anti-inflammatory Studies on the Flowers of *Premna serratifolia* Linn. *International Journal of Advances in Pharmacy, Biology, and Chemistry [Internet]*. 2014;3(3):679–82. Available from: www.ijapbc.com
 22. Nursin, Nurliana L, Imran, Musta R. Uji Aktivitas Antibakteri *Staphylococcus aureus* dan *Salmonella typhi* dari Hasil Mikroenkapsulasi Minyak Atsiri Rogo (*Premna Serratifolia* Linn). *Hydrogen: Jurnal Kependidikan Kimia*. 2019;7(2):73–81.
 23. Meilina NI, Kahtan MI, Widiyantoro A. Aktivitas Anthelmintik Ekstrak Etanol Daun Buas-buas (*Premna serratifolia* L.) terhadap Cacing *Ascaridia galli* secara In Vitro. *Jurnal Kesehatan Khatulistiwa*. 2019;5(2):780–9.
 24. Hadiarti D. In Vitro α -Glucosidase Inhibitory Activity of Ethanol Extract of Buas-buas (*Premna serratifolia* Linn). *Traditional Medicine Journal*. 2017;22(2):80–3.
 25. Timotius KH, Simamora A, Santoso AW. Chemical Characteristics and In Vitro Antidiabetic and Antioxidant Activities of *Premna serratifolia* L. Leaf Infusion and Decoction. *Pharmacognosy Journal*. 2018

- Nov 1;10(6):1114–8.
26. Salih GA, Ahmad-Raus R, Shaban MN, Abdullah N. Extraction and Purification of Cytotoxic Compounds from *Premna serratifolia* L. (Bebuas) for Human Breast Cancer Treatment. *International Food Research Journal* 24(Suppl). 2017 Dec;281–6.
27. Selvam TN, Venkatakrisnan V, Kumar D, Elumalai P. Antioxidant and Tumor Cell Suppression Potential of *Premna serratifolia* Linn Leaf. *Toxicol Int*. 2012 Jan;19(1):31–4.
28. Habtemariam S, Varghese GK. A Novel Diterpene Skeleton: Identification of a Highly Aromatic, Cytotoxic and Antioxidant 5-methyl-10-demethyl-abietane-type Diterpene from *Premna serratifolia*. *Phytotherapy Research*. 2015;29(1):80–5.
29. Baliyan S, Mukherjee R, Priyadarshini A, Vibhuti A, Gupta A, Pandey RP, et al. Determination of Antioxidants by DPPH Radical Scavenging Activity and Quantitative Phytochemical Analysis of *Ficus religiosa*. *Molecules*. 2022 Feb 1;27(4):1–19.
30. Shattat GF. A Review Article on Hyperlipidemia: Types, Treatments and New Drug Targets. *Biomedical and Pharmacology Journal*. 2014 Dec 1;7(2):399–409.
31. Chandran TAD, Vairammal V. A Comparative Study on the Effects of Ethanolic and Aqueous Extracts of *Premna serratifolia* leaves in Hyperlipidemic Male Albino Rats. *Research Teaching Learning Letters (ReTeLL)*. 2015;15:1–8.
32. Figurová D, Tokárová K, Greifová H, Knížatová N, Kolesárová A, Lukáč N. Inflammation, Its Regulation and Antiphlogistic Effect of the Cyanogenic Glycoside Amygdalin. *Molecules*. 2021 Oct 1;26(19):5972–95.
33. Vandamme TF. Use of Rodents as Models of Human Diseases. *J Pharm Bioallied Sci*. 2014;6(1):2–9.
34. Wahyuni S, Mukarlina, Yanti AH. Aktivitas Antifungi Ekstrak Metanol Daun Buas-Buas (*Premna serratifolia*) Terhadap Jamur *Diplodia* sp. Pada Jeruk Siam (*Citrus nobilis* var. *microcarpa*). *Protobiont*. 2014;3(2):274–9.
35. Nurliana L, Musta R. Studi Kinetika Antibakteri dari Hasil Pirolisis Cangkang Biji Jambu Mete terhadap *Staphylococcus aureus*. *Indo J Chem Res*. 2019;6(2):74–80.
36. Ahmad A, Shaheen A, Owais M, Gaurav SS. Antimicrobial Activity of *Syzygium Aromaticum* Oil and Its Potential in the Treatment of Urogenital Infections. *Formatex: Microbial Pathogens and Strategies for Combating Them Sciences, Technology, and Education*. 2013;
37. Afnidar. Fitokimia dan Uji Aktivitas Antibakteri Ekstrak Kalus Tumbuhan Sernai (*Wedelia biflora* (L)DC.). *Jesbio*. 2014;3(4):9–16.
38. Jain P, Singh S, Singh SK, Verma SK, Kharya MD, Solanki S. Antihelmintic Potential of Herbal Drug. *International J Res Dev Pharm Life Sci*. 2013;2(3):412–27. Available from: <https://www.researchgate.net/publication/324495926>
39. World Health Organization. World Cancer Report 2014. Stewart BW, Wild CP, editors. Geneva: WHO Press; 2014. 1–630 p.