Timotius KH , J Food Sci Nutr 2021, 7: 122
DOI: 10.24966/FSN-1076/100122

HSOA Journal of Food Science and Nutrition

Review Article

# Health Benefits of Edible Leave of *Premna serratifolia L.*

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## Abstract

Leave of Premna serratifolia is consumed as an edible food ingredient, particularly in Poso. Sulawesi. But, its function and benefits are still unclear. The goal of this review is to assess the current progress of research on Premna serratifolia. This review focuses on the bioactive compounds, in vitro and in vivo activities of Premna serratifolia. Relevant literature was searched with respect to the keywords "Premna serratifolia", "Premna integrifolia", "Premna obtusifolia". The most frequent used solvents are water, methanol, and ethanol. Information on bioactive compounds is mainly from the methanol and ethanol extracts. The most interesting bioactive compounds are oleanolic acid, diosmin, and terpenoids. Various extracts exhibit in vitro and in vivo activities, such as antioxidant, enzyme inhibition, anti-inflammation and immunomodulation. DNA protection, antibacterial activity. Premna serratifolia leave has potential in treating cancer, ageing and age association Parkinson Disease, Rheumatoid arthritis, skin melanogenesis, Leishmaniasis, hepatoprotection, diabetes, atherosclerosis, and obesity. Premna serratifolia is a good candidate for new vegetable and herbal drinks.

**Keywords:** Arogo; Poso; Premna integrifolia; Sulawesi

## Introduction

Premna Serratifolia (PS), a member of Lamiaceae, is widely distributed in tropical and subtropical countries [1]. But in Middle Sulawesi, Indonesia, particularly in Tentena, Poso. PS is known as arogo (local name) that its leave is a cooking ingredient [2]. Arogo leave is traditionally added in high-fat cook. P. serratifolia has several synonyms, namely P. corymbosa, P. integrifolia and P. obtusifolia [3,4].

Various parts of PS have health benefits. It has anti-parasitic activity against Leishmania donovani [5], anti-arthritic [6], antioxidant, and antitumor activity [7]. It is also an important nutraceutical food against ageing and Parkinson disease [8]. Leave of PS is able to inhibit several key enzymes associated with particular diseases [2] and to melanogenesis [9].

This review aimed to evaluate the available information on the bioactive compounds in the leave extract of PS, in vitro and in vivo activity of the extracts and their bioactive compounds, and the preparation of PS. For this review, the author searched relevant articles from various searching engines (PubMed, Science Direct, and Google Scholar).

## Bioactive compounds in the Leave Extract

Phytochemical studies on the leave of PS are minimal, particularly the aqueous extract. As listed in tables 1 and 2, various polar extractions used water, methanol and ethanol. Phytochemical studies of PS need further exploration. The conventional and unconventional extractions, fractionations, and purifications of bioactive constituents of PS remains to be investigated.

| Compound | Extract/group | Reported activity |
|---|---|---|
| Campneoside I | Ethanol/ phenylpropanoids | Antibacteria [10] |
| Diosmin | Ethanol/Flavone | Hemorrhoidal disease [11], Diabetes [12] Hyperlipidemic [13,14] Neurodegenerative [15] Venous disease [16] Anticancer and anti-inflammation [17] Protected against cerebral I/R injury [18] |
| Forsythoside A and B | Ethanol/polyphenolic | Anti-inflammation [19] Prevent BVDV infection [20] |
| Lavandulifolioside | Ethanol/ phenylethanoid | Antifungal [21] Decrease of blood pressure [22] |
| Isoacteoside | Ethanol/ phenylethanoid | Antioxidant [23], Anti-inflammation [24] Treating skin photo-damage [25] Xanthine oxidase inhibition [26] |
| Iridoid glycosides, alkaloids, phenolics and flavonoids | Ethanol wood | Rheumatoid arthritis [6] |
| 10-O-trans-p-Coumaroylcatalpol (OCC) | herbal formulation/ iridoid | Extend the life span of Caenorhaditis elegans, and decrease the aggregation of Parkinson's disease associated protein [8] |
| 4-Hydroxy-E-globularinin (4-HEG) | herbal formulation/ iridoid | prevent age-related disorders, supersede the ageing process [27] |

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**Citation:** Timotius KH (2021) Health Benefits of Edible Leave of *Premna serratifolia L.* J Food Sci Nutr 7: 122..

**Received:** September 29, 2021; **Accepted:** October 13, 2021; **Published:** October 22, 2021

| | | |
|---|---|---|
| Nobilin D | Ethanol/bibenzyl derivatives | Antioxidant, anti-inflammation [28,29] |
| Oleanolic acid (PS-01A) | hexane fraction of methanol extract/ Terpenoid | Anticancer [30], anti-metastasis activity. [31], Neuroprotective effect [32] Anti SARS-CoV-2 (COVID-19) [33,34] normalise the levels of gut mucosal dysfunction markers, reshape the gut microbiota [35], treatment of human Multiple schlerosis [36], Suppress liver carcinogenesis [37] Improves obesity-related inflammation and insulin resistance [38] Antidiabetic [39], α-glucosidase inhibitor [40], protect skin aging [41] Peripheral anti-nociceptive and anti-inflammation effect [42] Antihypertensive [43] Anti-inflammation [44] |
| Scroside E | Ethanol/Ethanol | Collagenase inhibition [45] |
| Spinosin | Ethanol/flavone C-glycoside | Anxiolytic [46], Attenuates Alzheimer's Disease [47-49] |
| Stigmasterol | hexane fraction of methanol extract /Sterol | Anticancer [30], antibacterial [50] Acetylcholinesterase and α-glucosidase [51], xanthine oxidase [52] and α-amylase antihyperalgesic and anti-inflammation [53], antidiabetic [54] |
| Terpenoid, PS-02A (unknown terpenoid) | hexane fraction of methanol extract/ terpenoid | Anticancer [30] |
| 1β,3α,8β-trihydroxy-pimara-15-ene | root bark/terpenoid, diterpenoid | [55] |
| 6α,11,12,16-tetrahydroxy-7-oxo-abieta-8,11,13-triene | root bark/terpenoid, diterpenoid | [55] |
| and 2α,19-dihydroxy-pimara-7,15-diene | root bark/terpenoid, diterpenoid | [55] |
| 11,12,16-trihydroxy-2-oxo-5-methyl-10-demethyl-abieta-1[10],6,8,11,13-pentene | Methanol/diterpene leave, root bark (RB), | Anticancer [3] |

**Table 1:** List of bioactive compounds from the leave of Premna serratifolia.

| Extract | Activity |
|---|---|
| Water | Enzymes inhibitions and antioxidant properties [2] |
| Ethanol | Enzymes inhibitions and antioxidant properties [2] |
| Methanol | Antioxidant and antitumor [7] |
| Methanol | Anticancer [3] |
| Hexane soluble fraction obtained from methanol extract | Anticancer [30] |
| Ethyl acetate, herbal formulation, phenolic content | Postnatal care, antioxidant activity [56] |

**Table 2**: Activity of extract.

Many bioactive compounds in PS extracts, such as forsythoside A and B, lavandulifolioside, diosmin, nobilin D, campneoside I, isoactoside. scoriside E [2], terpenoid, oleanolic acid, stigmasterol have important activities that are associated with various diseases.

## Activities of leave extract (*in vitro* and *in vivo*)

**Antioxidant:** Various in vitro model systems revealed the antioxidant activities of leave extracts of PS (Table 3). The antioxidant capacity is comparable with ascorbic acid, but still weaker than BHT or tocopherol.

| Extract | DPPH IC50 | TPC | TFC | Ref. |
|---|---|---|---|---|
| Water (infusion) | 6.82±0.01ug-GAE/mL | 347.81±0.21μg-GAE/mL | | [57] |
| Water (decoction) | 7.28±0.12ug-GAE/mL | 539.26±7.44μg-GAE/mL | | [57] |
| Water | 66.83±1.14μg/mL | 0.27±0.00mgGAE/gdw | 12,11±0.20mgRE/gdw | [2] |
| Ethanol | 50.63±0.93μg/mL | 2.12±0.06mgGAE/gdw | 9.43±0.04mgRE/gdw | [2] |
| methanol | 101.20μg/mL | | | [7] |
| 10-O-trans-p-coumaroylcatalpol | 0.37μM/mL | | | [58] |
| 4-hydroxy-E-globularinin | 0.29μM/mL | | | [58] |
| Ascorbic acid | 53.24±0.82μg/mL | | | [57] |
| BHT | 21.36±0.80μg/mL | | | [57] |
| α-Tocopherol | 1.71±0.01μg/mL | | | [57] |
| Phenol enriched extract | | 63.10±1.26GAE-mg/g | 75.33±0.23ruti-nmg/g | [56] |

**Table 3:** Antioxidant, TPC and TFC of leave extract of PS.

**Inhibitory activities against enzymes:** Several bioactive compounds have the potential to inhibit several key enzymes, such as Acetylcholinesterase and α-glucosidase inhibition, xanthine oxidase inhibition, α-amylase and α-glucosidase secretory phospholipase A2 collagenase inhibitory activity (Table 1). Simamora et al., have reported proteinase, lipase. Water and ethanol extract of PS can inhibit several key enzymes in health and diseases, namely α-glucosidase, α-amylase, xanthine oxidase, and protease [2]. Further researches are needed for the inflammatory and neurological enzymes, tyrosinase and lipase.

**Anti-inflammatory and immunomodulatory effects:** No information is available about the anti-inflammatory potential of the PS leave. Reports are available from the PS root that has an anti-inflammatory and immunomodulatory properties. PS root extract inhibit COX-2 and 5-LOX. It is necessary to investigate whether leave extract of PS has anti-inflammatory and immunological effects [59].

**DNA protection:** Ethanol extract of the PS leave has DNA-protecting effect [2]. This effect is associated with PS health benefit in life span or antiaging. One of the related bioactive compounds is Acacetin 7-O-α-l-rhamnopyranosyl (1-2) β-D-xylopyranoside (ARX) which may have antiaging effects. This bioactive compound can contribute in the therapy of ageing and age-related diseases [60].

**Antibacterial activity:** PS extract is considered to possess broad-spectrum antimicrobial activities. Several diterpenoids,

such as 1β,3α,8β-trihydroxy-pimara-15-ene, 6α,11,12,16-tetrahydroxy-7-oxo-abieta-8,11,13-triene and 2α,19-dihydroxy-pimara-7,15-diene have antibacterial activity [61]. Further antibacterial experiments are needed.

### Therapeutic potential of *Premna serratifolia*

**Anticancer:** Aqueous [1], methanol extract [7] and hexane fraction of methanol extract of PS [30], exhibit anticancer activity. Several isolated bioactive compounds have anticancer activity, such as oleanolic acid, PS-02A (unkwon terpenoid), and stigmasterol [30], diosmin [1].

**Aging and age associated Parkinson's disease:** PS leave contains two iridoids, 10-O-trans-p-Coumaroylcatalpol (OCC) and 4-Hydroxy-E-globularinin (4-HEG), ARX. OCC can promote life span of *Caenorhaditis elegans*. OCC can ameliorate a-syn aggregation and reduce oxidative stress. Therefore, OCC is considered as an good nutraceutical ingredient against aging and age associated Parkinson's Disease [8].

4-Hydroxy-E-globularinin (4-HEG) is also able to enhance the liife span of *C. elegans*. Its longevity-promoting activity is related to the reduced Reactive Oxygen Species (ROS) levels and fat accumulation [27].

Acacetin 7-O-α-l-rhamnopyranosyl (1-2) β-D-xylopyranoside (ARX) has antiaging effects in *C. elegans* [60].

**Rheumatoid arthritis:** PS wood is potential for the treatment of rheumatoid arthritis. So far, no information available on the use of PS leave for rheumatoid arthritis. Ethanol extract of PS wood shows anti-arthritic activity. Since many phytoconstituents of PS wood are similar to PS leave, such as iridoid glycosides, alkaloids, phenolic compounds and flavonoids [6], therefore it is wise to investigate whether PS leave also has rheumathoid arthritis activity.

**Skin melanogenesis:** Potential of PS leave on skin melanogenesis need to be investigated as what have been done for PS wood. PS wood contains lignoids, such as premnan A, premnan B, that can enhance melanogenesis [9]. It contains lignans, such as taungtangyiols A and B and several furofuran lignans that inhibit the deposition of melanin without notable cytotoxicity. The furofuran and dioxymethylene moieties of the lignans play a vital role in inhibiting melanogenesis [62].

**Leishmaniasis:** PS is active against *Leishmania donovani* with IC (50) values between 5 and 10microg/ml [5]. These observations serve as a basis to indicate novel routes for the development and design of effective anti-Leishmania drugs [63].

**Hepatoprotective effect:** Ethanol and ethyl acetate extracts of PS leaves have hepatoprotective effects. Ethanol extract of PS is able to protect the liver on aflatoxin B1-induced toxicity in mice. It can restore the lipid peroxidation and glutathione content, along with activities of antioxidant enzymes. It can ameliorate oxidative stress in aflatoxin-intoxicated mice. It protects mice liver against aflatoxin toxicity by inhibiting oxidative stress and apoptosis. This protective capacity may be due to the enriched flavonoids in the extract [64].

**Antidiabetic effect:** PS is proved to have antidiabetic activity. PS effect on blood glucose in induced type 1 and type 2 diabetic rats [65]. Ethanol ectract of PS has hypoglycaemic activities [66]. There is a need to reinvestigate and confirm the antidiabetic capacity of PS.

**Anti-atherosclerosis effect:** The anti-atherosclerosis effects of PS root bark is reported. The Hydroalcoholic Extract (HAE) of root bark of PS shows an anti-atherosclerotic activity. The anti-atherosclerotic activity of HAE of PS is due to its modulatory activity on the metabolic pathway of lipid [67]. HAE of PS has antioxidant potential. The HAE of PS is proved to have a protective role on antioxidant defence in high fat diet induced atherosclerosis model. As a whole PS increases the GSH content and in turn alters the redox cycle [68].

**Anti-obesity effect:** Chloroform: methanol extract of PS possesses anti-obesity activity. Animals treated with the extract showed dose-dependent activity [69].

### Preparation

Leave of PS can be prepared as herbal tea (infusion or cognation), cooking component, or herbal formulation. As a source of antioxidants, it is necessary to evaluate its potential as an ingredient of antioxidant drinks. It is never reported that PS leave is consumed as edible raw vegetable. It is possible to make PS leave paste or patch for topical or external use. PS is often used in herbal formulation [4,56,61].

The current development of theranostic nanomedicine is trying to add herbal extracts as biogenic nanomaterials. The biogenic nanomaterials and metals such as silver, gold, iron, titanium, copper, zinc, etc., can be successfully mixed for various biomedical applications [70].

## Conclusion and Future Perspective

In conclusion, *Premna serratifolia* leaves are a potential candidate for the development of nutraceutical and drug preparations. PS leave contain bioactive compounds that have health benefits, particularly in the field of chronic diseases. In vitro and in vivo activities of the leave extract confirm their functional role. PS leave can be prepared and consumed daily with the simple method. Even though further investigations are required to find the best knowledge for the functional of PS leaves.

## Funding

The author received no funding for this work.

## Competing Interests

The author declares that there is no competing interests.

## Author's Contribution

Kris Herawan Timotius analysed the data and information, prepared tables, reviewed the draft of the paper, and approved the final draft.

## Data Availability

The manuscript is a literature review and did not generate any data.

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