Review Article

A Phytochemistry of the Genus *Premna*: A Review

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ABSTRACT

The genus *Premna* (Verbenaceae), consists of about 200 species that are native mainly to the tropical and subtropical Asia, Africa, Australia and the Pacific islands. The various *Premna* species are well known for their medicinal properties and have been used in Indian traditional system of medicine especially for diarrhea, stomach and hepatic disorders. Phytochemical work on this genus has resulted in the isolation of more than hundred secondary metabolites reported from the different species of this genus. The isolated compounds include iridoid and their glycosides, diterpenoids, sesquiterpenoids, triterpenoids, flavonoids, isoflavones, lignans, xanthones and other classes of compounds. The various biological activities including antioxidant, antibacterial, anti-inflammatory, cytotoxic and heapatoprotective have been displayed both at extract and pure compound level. The aim of this review is to summarize and to highlight the recent advances in the phytochemical and biological studies on the genus *Premna*. The chemical constituents isolated from the genus *Premna* over the past decades together with their biological activities have been compiled in this article.

Keywords: *Premna,* Verbenaceae, phytochemistry.

INTRODUCTION

The genus *Premna* belongs to family Verbenaceae which are generally trees and shrubs in habit and very rarely herbs and climbers. A phytochemical review of literatures indicates the genus *Premna* to be rich source of the iridoid glycosides, diterpenoids and flavonoids. Furthermore, other classes of secondary metabolites like sesquiterpenoids, triterpenoids, isoflavones, lignans and xanthones are known to be isolated from different species of *Premna* genus. The isolated secondary metabolites from this genus have been reported to display interesting biological activities including antioxidant, antibacterial, anti-inflammatory, cytotoxic and heapatoprotective. The essential oil obtained from *Premna* species has displayed antibacterial property. *Premna* genus is well known for its medicinal properties and has been used in Indian traditional system of medicine especially for diarrhea, stomach and hepatic disorders[1]. An increasing number of phytochemical studies are being carried out on plants belonging to this genus due to their various traditional uses. This review describes the secondary metabolites and their biological activities of *Premna*.

Botanical Classification

Kingdom	:	Plantae
Phylum	:	Tracheophyta
Class	:	Magnoliopsida
Subclass	:	Lamiidae
Superorder	:	Lamianae
Family	:	Verbenaceae
Genus	:	*Premna*

Distribution of the genus

Premna genus comprises of about more than 200 known species native mainly to the tropical and subtropical Asia, Africa, Australia and the Pacific islands[2].

Phytochemical investigation

An overview of the literature search indicated that only 25 *Premna* species have been investigated phytochemically as compared to about 200 plant species known from this genus. The species for which their chemical constituents have been investigated include *Premna latifolia, Premna serratifolia, Premna fulva, Premna integrifolia, Premna subscandens, Premna microphylla, Premna tomentosa, Premna japonica, Premna barbata, Premna oligotricha, Premna schimperi, Premna herbacea, Premna corymbosa, Premna odorata,*

Premna obtusifolia, Premna resinosa, Premna szemaoensis and *Premna flavescens*.

The chemical constituents obtained provide an understanding of the general biological and chemical information like probable pharmacological activity of the species, mechanisms of action as well as for the further exploitation of the plant resources in this genus. The isolated secondary metabolites includes iridoid and iridoid glycosides, diterpenoids, sesquiterpenoids, triterpenoids, steroids, flavonoids, alkaloids, xanthones and lignans. Interestingly maximum work is reported from leaves, root bark and stem bark. This calls for further and extensive research work to be done from other plant parts like fruits, seed and flower. The names of these secondary metabolites and the plant parts from which they are isolated are listed in Table 1.

BIOLOGICAL STUDIES

Antioxidant activity

Different plant parts of *Premna* are known to contain antioxidant compounds such as flavanoids and phenols[59]. The various solvent extracts of *Premna integrifolia* root (petroleum ether, ethyl acetate, chloroform and methanol) showed potent antioxidant activity with an IC_{50} values ranging from 12.40 to 22.30 µg /mL. Chloroform extract showed potent activity in nitric oxide, deoxyribose and lipid peroxidation methods. Ethyl acetate and petroleum ether extracts showed potent activity in nitric oxide and deoxyribose method, respectively. Total antioxidant capacity was highest for methanol extract in phosphomolybdenum method[60]. The methanolic extract of *Premna integrifolia* root was evaluated for antioxidant activity by using the anti radical, superoxide scavenging, erythrocyte membrane stability, anti lipid peroxidation, hydroxyl radical scavenging, nitric oxide scavenging and reducing power (ferric thiocynate method and β-carotene bleaching test) assays[61]. Investigation for antioxidant compounds from stem bark of *Premna integrifolia* lead to the isolation of two lignans (Premnadimer and 4β-hydroxyasarinin-1-O-β-glucopyranoside) along with four iridoid glycosides (10-O-trans-p-coumaroylcatalpol, 4''-hydroxy-Eglobularinin, Premnosidic acid and 10-O-trans-p-coumaroyl-6-O-α-rhamnopyranosyl catalpol) and they were evaluated for radical scavenging and ferric reducing antioxidant power (FRAP). Radical scavenging activity was found maximum in 4''-hydroxy-Eglobularinin and Premnadimer. In FRAP assay, Premnosidic acid and 10-*O*-trans-*p*-coumaroyl-6-*O*-*α*-rhamno pyranosyl catalpol showed maximum ferric reducing ability supported by high reducing power[58].

The methanolic extract of *P. serratifolia* also displayed free radical scavenging activity against superoxide radical, nitric oxide radical, hydroxyl radical, DPPH radical, ABTS radical and inhibition of lipid peroxidation[62].

The flavonoids in *Premna fulva* Craib and their anti-oxidative activities *in vitro* were studied by the model of lipid peroxidation induced by free radicals in mice liver. The flavonoids showed potent anti-oxidative activities[41].

Antibacterial activity

The alcoholic extract of the fresh root bark of *Premna integrifolia* was evaluated for antibacterial activity against *Staphylococcus aureus, Bacillus subtilis, Streptococcus pyogenes,* the substances was only active against gram-positive organisms[63]. A novel sesquiterpene, 7α-hydroxy-6,11-cyclofarnes-3(15)-en-2-one, isolated from the aerial parts of *Premna oligotricha* showed weak activity against Gram-positive bacteria *Bacillus pumilus*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Streptococcus faecalis*[55]. Similarly, a novel diterpene, (5R,8R,9S,10R)-12-oxo-ent-3,13(16)-clerodien-15-oic acid, obtained from the leaves of *P. schimperi* was active against the Gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis* in the concentration range 20-25 µg mL^{-1}. [64]

Anti-inflammatory activity

An alcoholic extract from the leaves of *Premna tomentosa* Willd at a dose of 100 mg/kg body weight exhibited significant anti-inflammatory activity in albino rats. The extract caused reduction in the weight of spleen, thymus and adrenals. It reduced cotton pellet granuloma by 32.21%. The serum biochemical parameters showed reduction in protein, acid phosphatase and transaminases. The anti inflammatory activity of *P. tomentosa* alcoholic extract was found to be comparable to phenylbutazone[65]. The ethanolic extract of *Premna corymbosa* leaves also exhibited significant antiinflammatory activity[66]. Premnazole isolated from the leaves of *P. integrifolia* displayed an anti-inflammatory activity comparable to that of phenylbutazone in reducing cotton pellet-induced granuloma formation in rats[54].

Cytotoxic activity

Extracts and purified compounds from *Premna* genus have been studied for their potential as cytotoxicity. The bioassay guided-isolation of hexane extract from stem bark of *Premna tomentosa* gave four icetexane diterpenes (I-IV)[39]. Cytotoxic activities of these Icetexanes I-IV were evaluated by determining their inhibitory effects on the human cancer cell lines (MCF-7, HT-29, Hep-G2, A-431, and A-549). Icetexane I and Icetexane III showed selective inhibitory activity against MCF-7 (15.96 µg/mL and 15.84 µg/mL) and HT-29 cell lines (16.21 µg/mL and 14.57 µg/mL), respectively[39]. Premnalatifolin A, a dimeric diterpene, isolated from the stem-bark of *Premna latifolia* was evaluated for its cytotoxicity against cancer cell lines (HT-29, A-431, MCF-7, Hep-G2, PC-3, A-549, B-16 F10, and ACHN), and found to display potent activity against HT-29 and MCF-7 cell lines with an IC_{50} values of 12.15 and 1.11 µg/mL respectively[28]. In another study three icetexane diterpenes (Latifolionol, Dihydrolatifolionol and Latiferanol), obtained from hexane extract of the stem-bark of *Premna latifolia,* were evaluated for their cytotoxicity against the cancer cell lines (HT-29, A-431, MCF-7, Hep-G2, PC-3, A-549, B-16 F10 and ACHN). Among these compounds, Latifolionol and Dihydrolatifolionol displayed potent cytotoxic activity against HT-29 and Hep-G2 cell lines with an IC_{50} values of 0.04 and 0.18 µg/mL, respectively[37]. The alcoholic extract of leaves of *Premna serratifolia* exhibited an IC_{50} value of 75µg/mL which indicates the significant *in-vitro* cytotoxic activity of the extract[67]. The cytotoxic activity for four extracts (Petroleum ether, Chloroform, ethyl acetate and methanol) of *Premna integrifolia* roots by MTT assay showed that the methanolic extract exhibited stronger cell growth inhibition in human cancer cells (A-549, HCT-116, HEPG2 and Hela) than other extracts, with an IC_{50} values ranging from 8 to 13 µg/mL. The ethyl acetate and petroleum ether extract also showed potent activity against the above mentioned cell lines[60]. The cytotoxicity of diterpenes isolated from *P. schimperi* and *P. oligotricha* were studied against 3 human (HeLa, Sk.N.SH, and ECV304) and 2 murine (L929 and RAW 264.7) carcinoma cell lines ranged 1.5-35 µg/mL which were comparable with those of azauridine and chlorambucil[68].

Antifeedant activity

The extracts and essential oil isolated from *Premna latifolia* Roxb. were tested against polyphagous crop pest *Spodoptera litura* for antifeedant activity. The maximum growth reduction of 56.83% was shown by the essential oil as compared to the extracts[69].

Heapatoprotective activity

Hepatoprotective activity of alcoholic extract from leaves of *Premna serratifolia* was studied by carbon tetrachloride induced hepato-toxicity in rats. The degree of protection in hepatoprotective activity was measured by using biochemical parameters such as serum glutamate oxalate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT), alcoholic phosphatase (ALP), bilirubin and total protein. The results suggested that the alcoholic extracts at the dose level of 250mg/kg has produced significant ($p<0.001$) hepatoprotection by decreasing the activity of serum enzymes, bilirubin and lipid peroxidation which is comparable to that of standard drug silymarin[67]. The methanolic extract of *P. tomentosa* leaves has also been reported to possess heapatotoxic properties[70].

Table 1: Compounds isolated from the *Premna* genus

S. No.	COMPOUND	SPECIES	PLANT PARTS	REF
	Iridoid and Iridoid Glycosides			
1	Premnacorymboside A	*P. integrifolia*	Flower	3
2	Premnacorymboside B	*P. integrifolia*	Leaves	3
3	10-O-trans-p-methoxycinnamoylcatalpol	*P.corymbosa*	Flower	4
4	Premnafolioside	*P.corymbosa*	Stem	5
5	Premcoryoside	*P.corymbosa*	Leaves	6
6	Premnosidic acid	*P.barbata*	Leaves	7
7	(2S,3S,4R,11E)-2-[(2R)-2-hydroxytetracosanoylamino]-11-octadecene-1,3,4-triol	*P. microphylla*	Leaves	8
8	1-O-(9Z,12Z,15Z-octadecatrienoyl)-3-O-[β-D-galactopyranosyl-(1→6)-O-β-9Dgalactopyranosyl-(1→6)-α-D-galactopyranosyl] glycerol	*P. microphylla*	Leaves	8
9	Premnaodorosides D	*P. subscandens*	Leaves	9
10	Premnaodorosides E	*P. subscandens*	Leaves	9
11	Premnaodorosides F	*P. subscandens*	Leaves	9
12	Premnaodorosides G	*P. subscandens*	Leaves	9

13	Premnethanosides A	*P. subscandens*	Leaves	10
14	Premnethanosides B	*P. subscandens*	Leaves	10
15	Premnaodorosides A	*P.odorata*	Leaves	11
16	Premnaodorosides B	*P.odorata*	Leaves	11
17	Premnaodorosides C	*P.odorata*	Leaves	11
18	Premnosides A	*P.odorata*	Leaves	12
19	Premnosides B	*P.odorata*	Leaves	12
20	Premnosides C	*P.odorata*	Leaves	12
21	Premnosides D	*P.odorata*	Leaves	12
22	2''-Caffeoyl-6-α-L-rhamnopyranosylcatalpol	*P.odorata*	Leaves	13
23	3''-Caffeoyl-6-α-L-rhamnopyranosylcatalpol	*P.odorata*	Leaves	13
24	6-0-α-L-(2”-0- feruloyl) rhamnopyranosylcatalpol	*P. japonica*	Stem	14
25	6-O-α-(3”- 0- feruloyl) rhamnopyranosylcatalpol	*P. japonica*	Stem	14
26	6-O-α -L-(4”-0- feruloyl) rhamnopyranosylcatalpol	*P. japonica*	Stem	14
27	6-O-α-L-(2''-O-p-methoxycinnamoyl) rhamnopyranosylcatalpol	*P. japonica*	Leaves	15
28	6-O-α-L-(3''-O-p- methoxycinnamoyl) rhamnopyranosylcatalpol	*P. japonica*	Leaves	15
29	6-O-α-L-(2''-O-p-methoxycinnamoyl-4-Oacetyl)rhamnopyranosylcatalpol	*P. japonica*	Leaves	15
30	6-O-α-L-(3''-O-p-methoxycinnamoyl-4''-O-acetyl)rhamnopyranosylcatalpol	*P. japonica*	Leaves	15
31	6-O-α-L-(2''-O-isoferuloyl, 4''-O-acetyl)rhamnopyranosylcatalpol	*P. japonica*	Leaves	16
32	6-O-α-L-(3''-O-isoferuloyl, 4''-O-acetyl)rhamnopyranosylcatalpol	*P. japonica*	Leaves	16
33	6-O-α-L-(2''-O-trans-p-coumaroyl)rhamnopyranosylcatalpol	*P. japonica*	Leaves	17
34	6-O-α-L-(4''- O-trans- and cis-p-coumaroyl)rhamnopyranosylcatapols	*P. japonica*	Leaves	17
35	6-O-α-L-(2''-O-caffeoyl) rhamnopyranosylcatapol	*P. japonica*	Leaves	17
36	6-O-α-L-(3''-O-caffeoyl) rhamnopyranosylcatalpol	*P. japonica*	Leaves	17
37	6-O-α-L-(2''-O-isoferuloyl rhamnopyranosylcatalpols	*P. japonica*	Leaves	18
38	6-O-α-L-(2''-O-isoferuloyl soferuloyl)rhamnopyranosylcatalpols	*P. japonica*	Leaves	18
39	Bisdesoxydihydromonotropein	*P. latifolia*	Leaves	19
40	Geniposidic acid	*P. latifolia*	Leaves	19
41	Premfulvaoside	*P. fulva*	Leaves & stem	20
	Diterpenoids			
1	Pimarane I	*P. obtusifolia*	Roots & twigs	21
2	Pimarane II	*P. obtusifolia*	Roots & twigs	21
3	Rosane	*P. obtusifolia*	Roots & twigs	21
4	Abietane I	*P. obtusifolia*	Roots & twigs	21
5	Abietane II	*P. obtusifolia*	Roots & twigs	21
6	Abietane III	*P. obtusifolia*	Roots & twigs	21
7	Abietane IV	*P. obtusifolia*	Roots & twigs	21
8	6α-Hydroxy-5,6-dihydrosalviasperanol	*P. obtusifolia*	Roots	22
9	1β,3α,8β-Trihydroxy-pimara-15-ene	*P. integrifolia*	Root bark	23
10	6α,11,12,16-Tetrahydroxy-7-oxo-abieta-8,11,13-triene	*P. integrifolia*	Root bark	23
11	2α,19-Dihydroxy-pimara-7,15-diene	*P. integrifolia*	Root bark	23
12	6-Hydroxysalvinolone	*P. obtusifolia*	Roots	24
13	Premnones A	*P. tomentosa*	Leaves	25
14	Premnones B	*P. tomentosa*	Leaves	25
15	Premnones C	*P. tomentosa*	Leaves	25
16	Ent-12-Oxolabda-8,13(16)-dien-15-oic acid	*P. oligotricha*	Aerial parts	26
17	Ent-8β,12α-epidioxy-12β-hydroxylabda-9(11),13-dien-15-oic acid γ- lactone	*P. oligotricha*	Aerial parts	26
18	Sirutekkone	*P. herbacea*		27
19	Premnalatifolin A	*P. latifolia*	Stem bark	28
20	11,12,16-Trihydroxyabieta-5,8,11,13-tetraen-7-one	*P. integrifolia*	Root bark	29
21	11,14-Dihydroxy-12,16-epoxyabieta-5,8,11,13-tetraene-7-one	*P. integrifolia*	Root bark	29
22	14α-Hydroxyisopimar-7,15-diene	*P. latifolia*	Root bark	30
23	7α-Hydroxysandaracopimar(8n14),15-diene	*P. latifolia*	Root bark	30

24	7α-Hydroxyisopimar-8,15-diene	*P. latifolia*	Root bark	30
25	8β-Hydroxysandaracopimar-15-ene	*P. latifolia*	Root bark	31
26	1β,8β-Dihydroxysandaracopimar-15-ene	*P. latifolia*	Root bark	31
27	1β,7α,8β-Trihydroxysandaracopimar-15-ene	*P. latifolia*	Root bark	31
28	7α,8β,11α-Trihydroxysandaracopimar-15-ene	*P. latifolia*	Root bark	31
29	1α,8β,11α-Triolsandaracopimar-15-en-	*P. latifolia*	Root bark	32
30	Premnolal	*P. latifolia*	Root bark	33
31	Nellionol	*P. latifolia*	Root bark	34
32	Anhydronellionol	*P. latifolia*	Root bark	34
33	5-dehydronellionol	*P. latifolia*	Root bark	34
34	Obtusinones D	*P. obtusifolia*	Roots	35
35	Obtusinones E	*P. obtusifolia*	Roots	35
36	8, 11, 13-icetexatriene-10-hydroxy, 11, 12, 16-tri acetoxyl	*P. tomentosa*	Roots	36
37	8, 11, 13- icetexatriene-7, 10, 11-dihydroxy-12, 13-dihydrofuran	*P. tomentosa*	Roots	36
38	Latifolionol	*P. latifolia*	Stem bark	37
39	Dihydrolatifolionol	*P. latifolia*	Stem bark	37
40	Latiferanol	*P. latifolia*	Stem bark	37
41	11,12-Dihydroxy-10,6,8,11,13-icetexapentan-1-one	*P. obtusifolia*	Roots	38
42	Icetexane I	*P. tomentosa*	Stem bark	39
43	Icetexane II	*P. tomentosa*	Stem bark	39
44	Icetexane III	*P. tomentosa*	Stem bark	39
45	Icetexane IV	*P. tomentosa*	Stem bark	39
	Flavonoids			
1	4'-hydroxy-8,3'-dimethoxy-6-acroleinylflavan-3,4-diol	*P. fulva*	Stem bark	40
2	Apigenin	*P. fulva*	Stem	41
3	Naringenin	*P. fulva*	Stem	41
4	Cglucoside 6, 8-di-C-β-Apigenin	*P. fulva*	Stem	41
5	5,4'-dihydroxy-3,7,3'-trimethyoxyflavone	*P. szemaoensis*	Leaves	42
6	5-hydroxy-3',4',6,7- tetramethyoxyflavone	*P. szemaoensis*	Leaves	42
7	5,4'-Dihydroxy-7-methoxyflavonol	*P. szemaoensis*	Leaves	42
8	5,3'- Dihydroxy-7,4'-dimethoxyflavonol	*P. szemaoensis*	Leaves	42
9	3',4',5-Trihydroxy-3,7-dimethoxyflavone	*P. szemaoensis*	Leaves	42
10	5,7-Dihydroxy-4'-methoxyflavone	*P. szemaoensis*	Leaves	42
11	5-Hydroxy-7,3',4'-trimethyoxyflavonol	*P. szemaoensis*	Leaves	42
12	5,3'-Dihydroxy-3,7,4',5'-tetramethoxyflavone	*P.Tomentosa*	Leaves	43
13	Kaempferol 3-O-α-L-rhamnopyranoside), kaempferol 3-O-β-D-glucopyranoside	*P. flavescens*	Aerial parts	44
14	Quercetin 3-O-α-L-rhamnopyranoside	*P. flavescens*	Aerial parts	44
15	3,5,5'-Trihydroxy-6,7,3',4'-tetramethoxyflavone	*P. oligotricha*	Aerial parts	45
16	3,5,7,5'-Tetrahydroxy-6,3',4'- trimethoxyflavone.	*P. oligotricha*	Aerial parts	45
17	6-C-β-D-glucopyranosyl-8-C-β-D-xylopyranosyl apigenin.	*P. integrifolia*	Roots	46
18	Premnoside A	*P. latifolia*	Leaves	47
19	Apigen-4'-o-methyl-7-O-arabinopyranosylrhamnopyranoside	*P. latifolia*	Leaves	48
20	5-Hydroxy-4'-methoxyflavone-7-O-trioside.	*P. latifolia*	Leaves	48
	Isoflavone			
1	6,3'-Dihydroxy-7-methoxy-4',5'-methylenedioxyisoflavone	*P. microphylla*	Roots	49
2	6,3'-Dihydroxy-7-methoxy-4',5'-methylenedioxyisoflavone 6-O-β-D-glucopyranoside	*P. microphylla*	Roots	49
3	6,3'-Dihydroxy-7-methoxy-4',5'-methylenedioxyisoflavone 6-O-α-L-rhamnopyranoside	*P. microphylla*	Roots	49
4	6-3'-Dihydroxy-7-methoxy- 4',5'-methylenedioxyisoflavone 6-O-β-D-xylopyranosyl (1-6)-β-D-glucopyranoside	*P. microphylla*	Roots	49
	Xanthones			
1	1-Hydroxy-2,3-methylenedioxy-6-methoxycarbonyl-7-acetylxanthone	*P. microphylla*	Roots	50
2	1,3-Dihydroxy-2-methoxy-6-methoxycarbonyl-7-acetylxanthone	*P. microphylla*	Roots	50
	Triterpenoids and sterols			
1	28-O-α-L-rhamnopyranosyl (1→2)-β-D-glucopyranoside tormentic acid ester	*P. microphylla*	Leaves	51
2	Arjunolic acid	*P. microphylla*	Leaves	51
3	Hyptatic acid A	*P. microphylla*	Leaves	51

4	Friedelin	*P. fulva*	Stem	52
5	β-Sitosterol	*P. fulva*	Stem	52
6	Ursolic acid	*P. fulva*	Stem	52
7	β-Daucosterol	*P. fulva*	Stem	52
8	Lupeol octacosanoate,	*P. fulva*	Stem	53
9	Lupeol nonacosanoate	*P. fulva*	Stem	53
10	Lupeol melissate.	*P. fulva*	Stem	53
11	Actinidicoside	*P. fulva*	Leaves & stem	20
	Alkaloids			
1	Premnazole	*P. integrifolia*	Leaves	54
	Sesquiterpene			
1	7α-Hydroxy-6,11-cyclofarnes-3(15)-en-2-one	*P. oligotricha*	Aerial parts	55
2	Premnaspirodiene	*P. latifolia*	Root bark	56
3	Premnaspiral	*P. latifolia*	Root bark	56
	Lignans			
1	(+)-1-Hydroxypinoresinol,	*P. resinosa*	Leaves	57
2	(+)-Lariciresinol,	*P. resinosa*	Leaves	57
3	(-)-Seco-isolariciresinol	*P. resinosa*	Leaves	57
4	Premnadimer	*P. integrifolia*	Stem bark	58
5	4β-Hydroxyasarinin-1-O-β-glucopyranoside	*P. integrifolia*	Stem bark	58

CONCLUSION

This article has reviewed the existing phytochemical and pharmacological knowledge available for *Premna* genus. This genus includes about 200 known species from which nearly 25 species have been investigated phytochemically (Table 1). With this article we can conclude that *Premna* species has proved to be useful in treating various disorder in human. This calls for further phytochemical, pharmacognostical and pharmacological work to be done on other known species of this genus.

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REFERENCES

1. Devi KP, Sreepriya M, Balakrishna K and Devaki T. Protective effect of *Premna tomentosa* (L. Verbenaceae) extract on membrane-bound phosphatases and inorganic cations transport in acetaminophen-induced hepatotoxicity rats. J. Ethnopharmacol. (2004);93:371-5.
2. Harley RM, Atkins S and Budantsev PD. The families and genera of vascular plants flowering plantdicotyledons. In : K. Kubitzki editor, Labiatae. Germany Springer –Verlag. 2004:267-8.
3. Hang NTB, Ky PT, Van MC, Cuong NX, Thao NP and Van KP. Study on the chemical constituents of *Premna integrifolia* L. Natural Product Communications. (2008);3(9):1449-1452.
4. Pham TK, Nguyen Thi BH and Phan VK. 10-O-trans-p-methoxycinnamoylcatalpol and verbascoside from *Premna corymbosa* Rottl. ex Willd. Tap Chi Duoc Hoc. (2008);48(4):36-39.
5. Yuasa K, Ide T, Otsuka H and Takeda Y. Premnafolioside, a new phenylethanoid, and other phenolic compounds from stems of *Premna corymbosa* var.obtusifolia. Journal of Natural Products. 1993;56(10):1695-9.
6. Otsuka H, Watanabe E, Yuasa K, Ogimi C, Takushi, A and Takeda Y. A verbascoside iridoid glucoside conjugate from *Premna corymbosa* var. obtusifolia. Phytochemistry. 1993;32(4):983-6.
7. Negi S, Shukla V, Rawat MS, Pant G and Nagatsu A. Premnosidic acid, a new iridoid glycoside from *Premna barbata*. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 2004;43B(8):1805-1806.
8. Zhan ZJ and Yue JM. New glyceroglycolipid and ceramide from *Premna microphylla*. Lipids. 2003;38(12):1299-1303.
9. Sudo H, Takushi A, Hirata E, Ide T, Otsuka H and Takeda Y. Premnaodorosides D-G: acyclic monoterpenediols iridoid glucoside diesters from leaves of *Premna subscandens*. Phytochemistry. 1999;52(8):1495-1499.

10. Sudo H, Takushi A, Ide T, Otsuka H, Hiratat E and Takeda Y. Premnethanosides A and B: phenylethanoids from leaves of *Premna subscandens*. Phytochemistry. 1997;46(6):1147-1150.
11. Otsuka H, Kashima N, Hayashi T, Kubo N, Yamasaki K and Padolina W. Premnaodorosides A, B, and C, iridoid glucoside diesters of an acyclic monoterpenediol from leaves of *Premna odorata*. Phytochemistry. 1992;31(9):3129-33.
12. Otsuka H, Kubo N, Yamasaki K and Padolina WG. Premnosides A-D: diacyl 6-O-α-L-rhamnopyranosylcatalpols from *Premna odorata* Phytochemistry. 1989;28(11):3063-7.
13. Otsuka H, Kubo N, Yamasaki K and Padolina WG. Two iridoid glycoside caffeoyl esters from *Premna odorata.* Phytochemistry. 1989;28(2):513-15.
14. Otsuka H, Kubo N, Sasaki Y, Yamasaki K, Takeda Y and Seki T. Iridoid diglycoside monoacyl esters from stems of *Premna japonica.* Phytochemistry. 1991;30(6):1917-20.
15. Otsuka H, Sasaki Y, Kubo N, Yamasaki K, Takeda Y and Seki T. Isolation and structure elucidation of mono and diacyl iridoid diglycosides from leaves of *Premna japonica*. Journal of Natural Products. 1991;54(2):547-53.
16. Otsuka H, Sasaki Y, Yamasaki K, Takeda Y and Seki T. Isolation and characterization of new diacyl 6-O-α-L-rhamnopyranosylcatalpols from the leaves of *Premna japonica*. Chemical & Pharmaceutical Bulletin. 1990;38(2):426-9.
17. Otsuka H, Sasaki Y, Yamasaki K, Takeda Y and Seki T. Iridoid diglycoside monoacyl esters from the leaves of *Premna japonica.* Journal of Natural Products. 1990;53(1):107-11.
18. Otsuka H, Sasaki Y, Yamasaki K, Takeda Y and Seki T. 6-O-α-L-(2''-O- and 3''-O-isoferuloyl) rhamno pyranosylcatalpols from *Premna japonica.* Phytochemistry. 1989;28(11):3069-71.
19. Rao CB, Vijayakumar EK and Vijayalakshmi KV. Iridoids from *Premna latifolia.* Planta medica. 1981;41(1):80-3.
20. Niu KY, Wang LY, Liu SZ and Zhao WM. New iridoid glycoside and triterpenoid glycoside from *Premna fulva.* Journal of Asian natural products research. 2013;15(1):1-8.
21. Salae AW, Rodjun A, Karalai C, Ponglimanont C, Chantrapromma S, Kanjana-Opas A, Tewtrakul S and Fun HK. Potential anti-inflammatory diterpenes from *Premna obtusifolia*. Tetrahedron. 2012;68(3):819-829.
22. Asik SIJ, Abdul R, Ibrahim S, Abdul W, Chantrapromma S and Fun HK. 6α-Hydroxy-5,6-dihydrosalviasperanol Acta Crystallographica, Section E: Structure Reports Online. 2010;E66(11):2899.
23. Yadav D, Tiwari N and Gupta MM. Diterpenoids from *Premna integrifolia*. Phytochemistry Letters. 2010;3(3):143-147.
24. Salae AW, Chantrapromma S, Fun HK and Karalai C. 6-Hydroxysalvinolone. Acta Crystallographica, Section E: Structure Reports Online. 2009;65(10):o2379-o2380.
25. Chin YW, Jones WP, Mi Q, Rachman I, Riswan S, Kardono LBS, Chai HB, Farnsworth NR, Cordell GA and Swanson SM. Cytotoxic clerodane diterpenoids from the leaves of *Premna tomentosa*. Phytochemistry. 2006;67(12):1243-1248.
26. Habtemariam S, Gray AI, Lavaud C, Massiot G, Skelton BW, Waterman PG and White AH. Two new diterpenes from the aerial parts of *Premna oligotricha*. Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry. 1991;4:893-6.
27. Sandhya G, Rajagopalan K and Chandrakumar N. Structure of sirutekkone, a diterpenoid from *Premna herbacea.* Phytochemistry. 1988;27(7):2249-50.
28. Suresh G, Babu KS, Rao MSA, Rao VRS, Yadav PA, Nayak VL and Ramakrishna S. Premnalatifolin A, a novel dimeric diterpene from Premna latifolia Roxb. Tetrahedron Letters. 2011;52(39):5016-5019.
29. Rao PVS, Aruna GD, Raju GVS, Trimurtulu G and Rao CB. Chemical examination of Premna species. Part XII. Phenolic diterpenoids from root bark of Premna integrifolia Linn. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1987;26B(2):191-2.

30. Rao CB, Suseela K and Raju GVS. Chemical examination of Premna species: part IX - pimaradienols from Premna latifolia var. mollissima Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1984;23B(2):177-9.
31. Rao CB, Raju GVS, Krishna PG and Chari VM. Chemical examination of Premna species. Part VII. Constituents of root bark of Premna latifolia var. cuneata. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1982;21B(4):294-8.
32. Rao CB, Suseela K and Vijayakumar EKS. A new hydroxysandaracopimar-15-ene from Premna latifolia Roxb. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1981;20B(2):175-6.
33. Rao CB and Rao TN. Premnolal, a new aromatic bisnorditerpene from Premna latifolia Roxb. Current Science. 1978;47(14):498-9.
34. Rao CB, Rao TN and Vijayakumar EKS. Some novel aromatic diterpenes from Premna latifolia roxb. Current Science. 1978;47(13):455-6.
35. Salae AW and Boonnak N. Obtusinones D and E, linear and angular fused dimeric icetexane diterpenoids from Premna obtusifolia roots. Tetrahedron Letters. 2013;54:1356-59.
36. Ayinampudi SR, Domala R, Merugu R, Bathula S and Rao JM. New icetexane diterpenes with intestinal α-glucosidase inhibitory and free-radical scavenging activity isolated from Premna tomentosa roots. Fitoterapia. 2012;83(1):88-92.
37. Suresh G, Babu KS, Rao VRS, Rao MSA, Nayak VL and Ramakrishna S. Novel cytotoxic icetexane diterpenes from Premna latifolia Roxb.Tetrahedron Letters. 2011;52(12):1273-1276.
38. Abdul RI, Chantrapromma S, Salae AW and Fun HK. 11,12-Dihydroxy-10,6,8,11,13-icetexapentan-1-one. Acta Crystallographica, Section E: Structure Reports Online. 2011;E67(2):o256-o257.
39. Hymavathi A, Suresh Babu K, Naidu VGM, RamaKrishna S, Diwan PV and Madhusudana Rao J. Bioactivity-guided isolation of cytotoxic constituents from stem-bark of Premna tomentosa. Bioorganic & Medicinal Chemistry Letters. 2009;19(19):5727-5731.
40. Chen G-y, Dai C-y, Wang T-s, Jiang C-w, Han C and Song X-p. A new flavonol from the stem-bark of Premna fulva. ARKIVOC (Gainesville, FL, United States). 2010;2:179-185.
41. Huang Q, Chen L, Lin C, Li G, Wei T and Wei W. Flavonoids in Premna fulva craib and their anti-oxidative activities in vitro. Shizhen Guoyi Guoyao. 2009;20(11):2706-2708.
42. Li Q, Shen Y and Li P. Flavonoids in the leaves of Premna szemaoensis Pei. Zhongguo Yaoxue Zazhi (Beijing, China). 2008;43(6):417-419.
43. Etti S, Shanmugam G, Ponnuswamy MN, Balakrishna K and Vasanth S. 5,3'-Dihydroxy-3,7,4',5'-tetramethoxyflavone Acta Crystallographica, Section E: Structure Reports Online. 2005;E61(4):o846-o848.
44. Trinh TT, Tran VS, Ripperger H and Adam G. Flavonol glycosides from Premna flavescens. Tap Chi Hoa Hoc. 1998;36(3):49-52.
45. Habtemariam S, Gray AI and Waterman PG. Zeitschrift fuer Naturforschung, B: Chemical Sciences. 1992;47(1):144-7.
46. Purushothaman KK and Vasanth S. Di-C-glycosyl flavone from Premna integrifolia. Indian Drugs. 1986;23(8):482.
47. Rao B, Krishna PG, Devi PA, Raju GVS and Chari VM. Chemical examination of Premna species. Part XI. Structure of Premnoside A from Premna latifolia Roxb. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1986;25B(1):100-1.
48. Rao CB and Raju GVS. New flavone glycosides from the leaves of Premna latifolia Roxb. Current Science. 1981;50(4):180-1.
49. Zhong C and Wang D. Four new isoflavones from Premna microphylla. Indian Journal of Heterocyclic Chemistry. 2002;12(2):143-148.
50. Wang DY and Xu Su-Ying. Two new xanthones from Premna microphylla. Natural Product Research. 2003;17(1):75-77.
51. Zhan Z-J, Tang L and Shan W-G. A new triterpene glycoside from Premna

microphylla. Chemistry of Natural Compounds. 2009;45(2):197-199.
52. Dai C-y, Chen G-y, Zhu G-y, Fang H-x and Jiang C-w. Study on chemical constituents from petroleum ether fraction of Premna fulva stem. Hainan Shifan Xueyuan Xuebao, Ziran Kexueban. 2006;19(1):50-51.
53. Wei S, Si S, Xu X, Pu Q, Pannell LK and Highet RJ. Studies on the chemical constituents of Premna fulva. Planta Medica. 1991;57(1):93-4.
54. Barik BR, Bhowmik T, Dey AK, Patra A, Chatterjee A, Joy S, Susan T, Alam M and Kundu AB. Premnazole, an isoxazole alkaloid of Premna integrifolia and Gmelina arborea with anti-inflammatory activity. Fitoterapia. 1992; 63(4):295-9.
55. Habtemariam S, Gray AI and Waterman PG. A new antibacterial sesquiterpene from Premna oligotricha. Journal of Natural Products. 1993;56(1):140-3.
56. Rao CB, Raju GVS and Krishna PG. Chemical examination of Premna species. Part VIII. Spirosesquiterpenes from Premna latifolia Roxb. and var. cuneata. Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry. 1982;21B(3):267-8.
57. Habtemariam S, Gray AI and Waterman PG. Lignans from the leaves of Premna recinosa (Verbenaceae). Biochemical Systematics and Ecology. 1995;23(1):109.
58. Yadav D, Masood N, Luqman S, Brindha P and Gupta MM. Antioxidant furofuran lignans from Premna integrifolia. Industrial Crops and Products. 2013;41:397-402.
59. Suriyavathana M, Usha V and Shanthanayaki M. Studies on phytochemical analysis and antioxidant activity of selected medicinal plants from Kolli Hills. Journal of Pharmacy research. 2010;3(2):260-62.
60. Sathish M, Ayyasamy S, Roopa VP, Suresh AJ, Suresh R and Balaji R. In vitro antioxidant and cytotoxicity studies on root of Premna integrifolia Linn. Acta Ciencia Indica, Chemistry. 2010;36(1):67-73.
61. Gokani RH, Lahiri SK, Santani DD and Shah MB. Evaluation of anti-inflammatory and antioxidant activity of Premna integrifolia root. Journal of complementary & integrative medicine. 2011;8.
62. Selvam TN, Venkatakrishnan V, Damodar KS and Elumalai Preetham. Antioxidant and tumor cell suppression potential of Premna serratifolia linn leaf. Toxicology international. 2012;19(1):31-4.
63. Kurup KK and Kurup PA. Antibiotic substances from the root bark of Premna integrifolia. Naturwissenschaften. 1964;51(20):484.
64. Habtemariam S, Gray AI, Halbert GW and Waterman PG. A novel antibacterial diterpene from Premna schimperi. Planta Medica. 1990;56(2):187-9.
65. Alam M, Joy S, Susan T and Ali SU. Anti-inflammatory activiy of Premna tomentosa willd. In albino rats. Ancient science of life. 1993;13(1-2):185-8.
66. Karthikeyan M and Deepa MK. Anti-inflammatory activity of Premna corymbosa (Burm.f.) Rottl. & Willd. leaves extracts in Wistar albino rats. Asian Pacific journal of tropical medicine. 2011;4(7):510-3.
67. Vadivu R, Jerad SA, Girinath K, Boopathi KP, Vimala R and Sathish KNM. Evaluation of hepatoprotective and in-vitro cytotoxic activity of leaves of Premna serratifolia Linn. Journal of Scientific Research (Rajshahi, Bangladesh). 2009;1(1):145-152.
68. Habtemariam S. Cytotoxicity of diterpenes from Premna schimperi and Premna oligotricha. Planta Medica. 1995;61(4):368-9.
69. Kumar A, Tamta ML, Negi N, Chandrasekhar K and Negi, DS. Phytochemical investigation and antifeedant activity of *Premna latifolia* leaves. Natural Product Research. 2011; 25(18):1680-1686.
70. Devi KP, Sreepriya M, Balakrishna K and Devaki T. Protective effect of *Premna tomentosa* extract (L. verbanacae) on acetaminophen-induced mitochondrial dysfunction in rats. Molecular and Cellular Biochemistry. 2005;272(1&2):171-177.