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Biological Activities of Extracts of *Gmelina asiatica* L. - A review

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Abstract

Gmelina asiatica L. is a shrub that belongs to the *Lamiaceae* family. In various traditional medicines, this plant species is employed to cure several disorders like rheumatism, gonorrhea, catarrh of the bladder, edema, and malaria. Furthermore, phytochemicals including cleomeolide; cleomiscosin D; kaempferide-3-glucuronide; nitidine; ovalifolin; and stigmasta-5, 24(28)-diene-3-O-rhamnoside were detected from different parts of *G. asiatica.* This paper aims to evaluate, summarize, and document the published biological activities related to investigations of *G. asiatica*. SpringerLink, Semantic Scholar, Scopus, ScienceDirect, Taylor & Francis Online, Wiley Online Library, Sage journals, Mary Ann Liebert, Inc. Publishers, PubMed, and Web of Science databases were used to identify the relevant published articles from 1900 to August 2021. Up to now, only *in vivo* and *in vitro* scientific evidence are present for various bioactivities. In addition, anti-anxiety, antibacterial, anticancer, antidandruff, antidiabetic, antifungal, anti-inflammatory, antioxidant, antipyretic, hepatoprotective, and nephroprotective activities were detected for various parts of this plant. This article will be advantageous to carry out support further biological activity investigations of this plant in the future.

Keywords: *Gmelina asiatica*, Phytochemical, Bioactivity

Introductıon

Gmelina asiatica L. [synonyms: *Bignonia discolor* A.Rich.; *B. moluccana* DC.; *Premna parvifolia* Roth; *Gmelina parvifolia* Roxb.; *G. asiatica* f. *lobata* Moldenke; *G. paniculata* H.R.Fletcher; *G. asiatica* f. *parvifolia* (Roxb.) Moldenke; *Gmelina lobata* Gaertn.; and *Gmelina attenuata* H.R.Fletcher] is a wild and medicinal shrub that grows up to 8 m high and goes into the *Lamiaceae* family. It is called நிலக்குமிழ் (Nilakkumil) in Tamil / Siddha Medicine; Gambhaari, Vikarini, and Gopabhadra in Ayurveda; and Asian bush beech in English. Further, this plant species is native to Sri Lanka, India, Bangladesh, Vietnam, Cambodia, Thailand, Laos, and Myanmar and was introduced into Malaysia, Indonesia, and the Philippines (Kew science, 2021; Global Biodiversity Information Facility, 2021). At the moment, traditionally, root, aerial parts (Merlin and Parthasarathy 2011), leaf (Bakkiyaraj and Pandiyaraj, 2011), young shoot, bark, and fruit (Silvia and Satyanaraya 2014) of this plant species have been applied in powder form, to cure various disorders including

rheumatism, gonorrhea, catarrh of the bladder (Shibu et al. 2012; Merlin and Parthasarathy 2010, 2011; Merlin et al. 2009; Sudhakar et al. 2006), edema, malaria (Sudhakar et al. 2006), diabetes, microbial activity (Bakkiyaraj and Pandiyaraj, 2011), jaundice, hepatic diseases and fever (Silvia and Satyanaraya 2014; Khare, 2007; Vivekanandarajah, 2015, 2016a, 2016b, 2017, 2017a, 2018a, 2018b, 2021a, 2021b, 2021c, 2021d, 2021e; Rajamanoharan, 2021). Phytochemicals like cleomeolide; cleomiscosin D; kaempferide-3-glucuronide; nitidine; ovalifolin; and stigmasta-5, 24(28)-diene-3-O-rhamnoside were identified from different parts of *G. asiatica* (Satyanarayana et al. 2007; Kumar et al. 1988; Songsak and Lockwood 2002; Sudhakar et al. 2006).

This paper aims to analyze, summarize, and document the published biological activities related to investigations of *G. asiatica*. This paper will be helpful for academics who are willing to carry out further biological activities studies employing *G. asiatica.*

Materıals and Methods

Major electronic research article databases (SpringerLink, Semantic Scholar, Scopus, ScienceDirect, Taylor & Francis Online, Wiley Online Library, Sage journals, Mary Ann Liebert, Inc. Publishers, PubMed, and Web of Science) were applied to identify the relevant published articles from 1900 to July 2021. *"Bignonia discolor*", *"Bignonia moluccana", "Premna parvifolia", "Gmelina parvifolia", "Gmelina asiatica", "Gmelina paniculate", "Gmelina lobata",* and "*Gmelina attenuate*" were applied as search terms. Furthermore, only biological activities related to reported studies were considered in this work.

Reported biological activities of *G. asiatica*

Table 1 describes the information of the level of scientific evidence, part used, extract/fraction/compound, assay/model, dose/concentration, and reference of reported bioactivity studies. Up to now, *in vivo* and *in vitro* scientific evidence is present for various bioactivities, whereas *in vitro* studies lead in position amongst these studies. Further, antianxiety, antibacterial, anticancer, antidandruff, antidiabetic, antifungal, antiinflammatory, antioxidant, antipyretic, hepatoprotective, and nephroprotective activities of *G. asiatica* were observed. *In vitro* evidence is available for antibacterial, antidandruff, antifungal, antioxidant, and nephroprotective activities. Also, *in vivo* evidence is available for antianxiety, anticancer, antidiabetic, antiinflammatory, antipyretic, and hepatoprotective activities. The investigation of the antibacterial property was observed in a greater number of studies, and both *in vivo* and *in vitro* scientific evidence are available for anticancer and antiinflammatory activities. Among the various parts (aerial, leaf, root, and stem) used, the leaf was employed in a higher number of studies. Aqueous, chloroform, ethanol, ethyl acetate, methanol, and petroleum ether extracts showed several biological activities whereas, ethanol extract was used in more investigations. Bioactive compounds such as E-11-Hexadecanoic acid; hexadecanoic acid; Linoleic acid; (E)-9-Octadecanoic acid; heptadecanoic acid; 1,2-benzene dicarboxylic acid; benzene, (1-butylhexadecyl), cholesterol trimethylsilyl ether, and nitidine were recognized from *G. asiatica* (Florence and Jeeva 2016; Sudhakar et al. 2006). So far, traditional medicinal uses include diabetes, edema, and

rheumatism have scientific evidence (Merlin et al. 2009; Sudhakar et al. 2006; Bakkiyaraj and Pandiyaraj 2011). The noteworthy studies with the uppermost levels of scientific evidence exist, the lowest concentration/dose used, and the bioactive compounds identified are detailed underneath.

Reported *in vivo* biological activities

Antianxiety activity

The antianxiety activity was investigated using an *in vivo* raised plus-maze paradigm. In this study, a dosage of 400 mg/kg methanol leaf extract was used. The authors did not specify the standard drug or dose utilized in this study. The plant extract enhanced the time spent and the number of entries in the open arm in the light compartment, according to the findings. Furthermore, this plant extract possessed a significant anti-anxiety effects (Kamboj, 2015).

Anticancer activity

Chloroform was employed to prepare the plant extract, and the extract was orally administered at a dose of 200 mg/kg to animals. After 14 days of treatment, the measurements on changes in body weight, lifespan, and variations in cancer cell count were measured. In this study, the 5-fluorouracil was served as a standard drug at a dose of 20 mg/kg. The results explored that the extract significantly lowered the cancer cell count, increased the lifespan, and lowered the tumor weight in the treated animals (Merlin and Parthasarathy 2010).

Antidiabetic activity

A research was conducted on the root ethanol extract to observe how blood glucose levels changed. Alloxan-induced diabetic rats were given a dosage of 100 mg/kg orally. After the therapy, blood glucose levels were monitored at 0, 1, 2, 4, 6, 8, and 16 hours. When compared to the conventional medicine Tolbutamide at a dose of 40 mg/kg, there was a possible dose-dependent drop in blood glucose levels (Kasiviswanath et al. 2005).

Antiinflammatory activity

The goal of this investigation was to determine whether ethanol aerial extract has a substantial anti-inflammatory effect. This research used carrageenan-induced rat paw edema, histamine-induced edema, dextran-induced edema, and cotton pellet-induced granuloma models. The extract was given orally at a dose of 250 mg/kg, and the results were compared to the standard drug, Indomethacin, at a dose of 10 mg/kg. After administering the extract, the paw volume was measured plethysmographically at 1, 2, 3, and 4-hour intervals. The percentage of edema inhibition was then determined. The findings revealed that the extract has potent anti-inflammatory properties (Merlin et al. 2009).

Antipyretic activity

Ikram et al. (1987) investigated the potential antipyretic activity of 150 mg/kg chloroform and hexane fractions of 90% ethanol root extract. In this study, the yeast-induced pyrexia model was used to see the significant effect of plant extract. Aspirin was used as a standard drug, and the dose administered was not mentioned by the

authors. Further, up to 24 hours period, the pyrexic condition was maintained. The results exhibited that the root extract explored the significant antipyretic activity against the tested models (Ikram et al. 1987).

Hepatoprotective activity

In a study conducted by Merlin and Parthasarathy (2010), hepatoprotective activity was analyzed using ethanol extract of the aerials of *G. asiatica*. The carbon tetrachloride-induced hepatic damage model in rats employed in this study. The ethanol extract at the dose of 400 mg/kg was orally administrated for five days. The standard drug, Silymarin, was used at a dose of 50 mg/kg. It evidenced that the extract showed potent hepatoprotective activity against the tested model (Merlin and Parthasarathy 2011).

Reported *in vitro* biological activities

Antibacterial activity

The broad-spectrum bacterial growth inhibition of ethanol root extract (25 mg/ml) was evaluated by Sudhakar et al. (2006). Bacterial strains *(Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Bacillus subtilis, Bacillus pumilus, Staphylococcus aureus,* and *Streptococcus faecalis)* were used to study the effects, and substantial growth inhibition was observed. Ampicillin (40 µg/ml) was used as a positive control in this study (Sudhakar et al. 2006).

Antidandruff activity

The stem was used to prepare an extract using the supercritical fluid extraction method. The extract (250 µg/ml) was applied in *Malassezia furfur* assay. Climbazole was used as a positive control at 0.97 µg/ml concentration. The findings of this study exhibited that the extract exposed the antidandruff activity (Chandrika et al. 2015).

Antifungal activity

The goal of this study was to reveal the aerial components' antifungal activity. The extract was made using a soxhlet extraction using chloroform as the solvent. Against *Aspergillus niger* and *Candida albicans*, a disc diffusion approach was used. To compare the impact on fungal growth inhibition, a positive control (Griseofulvin) was used at a concentration of 20 g/ml. Regardless, the authors did not specify the concentration of extract used in the study (Merlin et al. 2009).

Antioxidant activity

Kiruba et al. (2014) investigated the antioxidant property of aqueous leaf extract in thiobarbituric acid reactive substance inhibitory assay. The results revealed that the IC_{50} of 13.29 µg/ml of the extract showed antioxidant activity. Butyl hydroxyl was used as a positive control, and the concentration of the positive control used did not mention by the authors (Kiruba et al. 2014).

Table 1. Reported biological activities of *G. asiatica*

Level of scientific evidence	Bioactivity	Part used	Extract / fraction	Assay / model	Dose / concentration	Reference
In vivo	Antianxiety	Leaf	Methanol	Elevated plus-maze	200 mg/kg	Kamboj, 2015
In vivo	Anticancer	Aerial	Chloroform	Dalton's Ascitic Lymphoma	200 mg/kg	Merlin and Parthasarathy 2010
In vivo	Antidiabetic	Root	Ethanol (95%)	Alloxan-induced diabetic	100 mg/kg	Kasiviswanath et al. 2005
In vivo	Antiinflammatory	Root	NS	Carrageenan-induced rat paw edema, Cotton pellet granuloma	NS	Syed et al. 1997
In vivo	Antiinflammatory	Aerial	Ethanol	Carrageenan-induced rat paw edema, Histamine-induced edema, Dextran-induced edema, Cotton pellet-induced granuloma	250 mg/kg	Merlin et al. 2009
In vivo	Antipyretic	Root	Chloroform fraction [Ethanol (90%) extract], Hexane fraction [Ethanol (90%) extract]	Yeast-induced pyrexia	150 mg/kg	Ikram et al. 1987
In vivo	Hepatoprotective	Aerial	Ethanol	Carbon tetrachloride-induced hepatic damage	400 mg/kg	Merlin and Parthasarathy 2011
In vitro	Antibacterial	Leaf, Root, Stem	Acetone, Aqueous, Benzene, Chloroform, Ethanol, Ether	*Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, Micrococcus luteus, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumoniae*	NS	Shibu et al. 2012

Level of scientific evidence	Bioactivity	Part used	Extract / fraction	Assay / model	Dose / concentration	Reference
In vitro	Antibacterial	Leaf	Methanol	NS	NS	Madhu et al. 2001
In vitro	Antibacterial	Leaf	Methanol	*Bacillus subtilis*	NS	Parekh et al. 2005
In vitro	Antibacterial	Leaf	Aqueous	*Pseudomonas pseudoalcaligenes*	NS	Parekh et al. 2005
In vitro	Antibacterial	Root	Ethanol	*Escherichia coli*	0.075 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Root	Ethanol	*Proteus vulgaris*	0.125 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Root	Ethanol	*Pseudomonas aeruginosa*	0.200 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Root	Ethanol	*Bacillus subtilis, Bacillus pumilus*	0.250 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Root	Ethanol	*Staphylococcus aureus*	0.325 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Root	Ethanol	*Enterococcus faecalis*	0.450 mg/ml (MIC)	Sudhakar et al. 2006
In vitro	Antibacterial	Leaf	Aqueous	*Pseudomonas aeruginosa*	NS	Bakkiyaraj and Pandiyaraj 2011
In vitro	Antibacterial	Leaf	Methanol	*Bacillus subtilis*	NS	Bakkiyaraj and Pandiyaraj 2011
In vitro	Antibacterial	Leaf	Methanol	*Bacillus cereus, Klebsiella pneumoniae*	NS	Parekh, 2006
In vitro	Antibacterial	Fruit	Ethanol	*Pseudomonas aeruginosa, Staphylococcus aureus*	2500 µg	Jeevan Ram et al. 2004
In vitro	Antibacterial	Aerial	Chloroform	*Cutibacterium acnes*	20 mg/ml	Mahendra et al. 2015

Level of scientific evidence	Bioactivity	Part used	Extract / fraction	Assay / model	Dose / concentration	Reference
In vitro	Antibacterial	Aerial	Petroleum ether, Ethyl acetate	*Cutibacterium acnes*	50 mg/ml	Mahendra et al. 2015
In vitro	Antibacterial	Aerial	Chloroform, Petroleum ether, Ethyl acetate	*Corynebacterium diphtheriae*	20 mg/ml	Mahendra et al. 2015
In vitro	Antibacterial	Aerial	Chloroform	*Bacillus subtilis, Staphylococcus aureus, Micrococcus luteus, Escherichia coli, Salmonella typhi, Pseudomonas aeruginosa*	NS	Madhu et al. 2001
In vitro	Anticancer	Root	Ethyl acetate	Estrogen receptor-positive (MCF-7) human breast cancer cell	32.9 µg/ml (IC_{50})	Balijepalli et al. 2010
In vitro	Anticancer	Root	Ethyl acetate	Estrogen receptor-negative (MDA-MB-231) human breast cancer cell	19.9 µg/ml (IC_{50})	Balijepalli et al. 2010
In vitro	Anticancer	Aerial	Petroleum ether, Chloroform, Ethyl acetate, Ethanol	Human breast cancer MCF-7cell	200 µg/ml	Merlin and Parthasarathy 2011
In vitro	Antidandruff	Stem	Supercritical fluid extract	*Malassezia furfur*	250 µg/ml	Chandrika et al. 2015
In vitro	Antifungal	Leaf	Methanol	NS	NS	Madhu et al. 2001
In vitro	Antifungal	Aerial	Chloroform	*Candida albicans, Aspergillus niger*	NS	Merlin et al. 2009

Level of scientific evidence	Bioactivity	Part used	Extract / fraction	Assay / model	Dose / concentration	Reference
In vitro	Antiinflammatory	Leaf	Aqueous	Protein denaturation inhibitory	241.5 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antiinflammatory	Leaf	Aqueous	Human red blood cell membrane stabilization	270.3 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antiinflammatory	Leaf	Aqueous	Protease inhibitory	73.73 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Aerial	Chloroform	DPPH free radical scavenging	600 mg/ml	Merlin and Parthasarathy 2011
In vitro	Antioxidant	Aerial	Ethanol	DPPH free radical scavenging	500 mg/ml	Merlin and Parthasarathy 2011
In vitro	Antioxidant	Stem	Methanol	DPPH free radical scavenging	18.38 µg/ml (IC_{50})	Silvia and Satyanaraya 2014
In vitro	Antioxidant	Stem	Methanol	Nitric oxide radical scavenging	78.18 µg/ml (IC_{50})	Silvia and Satyanaraya 2014
In vitro	Antioxidant	Stem	Methanol	Ferric reducing ability of plasma	84.15 µg/ml	Silvia and Satyanara 2014
In vitro	Antioxidant	Leaf, Root, Stem	Methanol, Ethyl acetate, Aqueous, Chloroform, Ethanol	Ferric thiocyanate method, Thiobarbituric acid method	NS	Girija and Ravindhran 2011
In vitro	Antioxidant	Leaf	Aqueous	DPPH free radical scavenging	206 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Leaf	Aqueous	Superoxide radical scavenging	199.2 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Leaf	Aqueous	Hydrogen peroxide scavenging	67.8 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Leaf	Aqueous	Lipid peroxidation inhibitory	135.5 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Leaf	Aqueous	Nitric oxide radical scavenging	14.97 µg/ml (IC_{50})	Kiruba et al. 2014

Level of scientific evidence	Bioactivity	Part used	Extract / fraction	Assay / model	Dose / concentration	Reference
In vitro	Antioxidant	Leaf	Aqueous	Reducing power	48.5 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Leaf	Aqueous	Thiobarbituric acid reactive substance inhibitory	13.29 µg/ml (IC_{50})	Kiruba et al. 2014
In vitro	Antioxidant	Stem	Methanol	DPPH free radical scavenging	18.38 µg/ml (IC_{50})	Silvia and Satyanaraya 2014
In vitro	Antioxidant	Stem	Methanol	Nitric oxide radical scavenging	78.18 µg/ml (IC_{50})	Silvia and Satyanaraya 2014
In vitro	Antioxidant	Stem	Methanol	Ferric reducing	84.15 µg/ml (IC_{50})	Silvia and Satyanaraya 2014
In vitro	Nephroprotective	Leaf	Aqueous	Kidney cell	500 mg/ml	Kiruba et al. 2014

Abbreviations: NS: Not Stated; DPPH: 2,2-diphenyl-1-picrylhydrazyl; MIC: Minimum Inhibitory Concentration; IC_{50}: Half maximal inhibitory concentration

Nephroprotective activity

The potential nephroprotective activity of aqueous leaf extract was studied by Kiruba et al. (2014). The authors used the epifluorescence staining method using kidney cells. The extract at a concentration of 500 mg/ml exhibited nephroprotective activity. In this evaluation, Vitamin E was used as a positive control, and concentration of the positive control was not mentioned Kiruba et al. 2014).

Toxicity Studies

Merlin and Parthasarathy (2011) stated that oral administration of chloroform and ethanol extracts of aerial parts produced neither mortality nor adverse effects. It found that the extracts were safe up to a dose of 2000 mg/kg (Merlin and Parthasarathy 2011).

Conclusion

This review exhibits that *G. asiatica* there is only a few scientific evidences currently available for its traditional medicinal uses. This was evidenced by different studies associated with a range of bioactive properties. To make sure the different potentials of various extracts of this plant species, it is vital to propose different scales of clinical studies. Isolation and identification of bioactive compounds will lead to a better understanding of the pharmacological uses of this *G. asiatica* and will support further studies in the future. This paper examined, briefed, and documented the published biological activities associated with investigations of *G. asiatica*.

Conflict of interest

The authors declare that there are no conflicts of interest.

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