International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Review Article

Phytochemical and ethno-pharmacological profile of *Desmodium gangeticum* (L.) DC.: A review

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Abstract

Desmodium gangeticum (L.) DC. is a well explored traditional Indian medicinal plant used to treat neurological imbalances. Recent pharmacological studies established its multi-directional therapeutic significance as anti-leishmanial, anti-inflammatory, cardio-protective drug. Moreover, it has detoxifying, blood purification property which might be attributed to its immunomodulatory activity. Phytochemical research revealed the plant is rich in alkaloids, pterocarpans, phospholipids, sterols and flavanoids. The review emphasizes primarily on folkloric uses, pharmacological activities of the extracts, biological activities of isolated compounds, toxicity and safety profile of *Desmodium gangeticum* to provide a comprehensive data for researchers to hit upon new chemical entity responsible for its claimed traditional uses and further clinical trials.

Keywords: Medicinal plant, Alkaloids, Antileishmanial, Folkloric use

1. Introduction

Desmodium gangeticum (*D. gangeticum*) (L.) DC. (Family: Fabaceae) commonly known as Shalaparni is an important species of the genus Desmodium. Due to broad spectrum therapeutic potentiality, it is extensively practiced as traditional medicine in India and other parts of sub-continent over a long period of time[1]. *D. gangeticum* is a sub-tropical perennial herb grows in dry hill areas, mainly in the basement of Westernghat region and Himalayan territory. It is sweet in taste and mild warming in action[2]. Vedic literatures describe its potentiality as regulator of nervous (Vata), venous (Pitta) and arterial (Kapha) systems essential to restore health[3]. Traditionally, the roots are used as expectorant and in snake bite and scorpion sting[4]. It is an ingredient of Ayurvedic preparations like 'Dashmoolarishta' and 'Dashmoolakwaath' recommended for post-natal care to avoid secondary complications[5]. Moreover, pharmacological studies reveal the potentiality of *D. gangeticum* extract and its active principles viz. desmodin, hordenine and gangetin as anti-amnesic, immunomodulator, anti-diabetic, antioxidant, cardio-protective, hepatoprotective, anti-inflammatory drug[6]. An attempt has been taken to compile the upto date information regarding phytochemical and ethnopharmacological aspects of *D.*

gangeticum.

2. Taxonomy and botanical description

The genus Desmodium is derived from Greek word 'Desmos' means 'bond' or 'chain' like due to the resemblance of the jointed seed pods to links of a chain. It is distributed mainly in tropical and subtropical regions of the world. Among 20-25 different species, *D. gangeticum* shows highest bio-diversity in India (Figure 1).

The taxonomical classification of *D. gangeticum* is as follows[7].

Kingdom : Plantae

Division : Magnoliophyta

Phylum : Spermatophyta

Class : Magnoliopsida

Order : Fabales

Family : Fabaceae

Genus : Desmodium

Species : gangeticum (Linn.)

D. gangeticum is a perennial erect or ascending shrub, grows upto 2 to 4 feet. The stem is angular, woody with numerous prostrate branches. Leaves are small (3–14 x 2–7 cm), ovate-oblong or rounded in shape, covered with numerous gray colour numerous trichomes; Flowers are small (4-7 cm), purple or white in color. Calyx are 4–5cm long, pubescent. Seeds are small, pale yellow, kidney-shaped. The lateral roots appear yellow with smooth texture. Its flowering–fruiting season is during the months of March to December[8].

Figure 1: Aerial parts of *Desmodium gangeticum* (L.)

3. Traditional uses and Ethno-pharmacology

In Indian sub-continent, the shrub traditionally being used as antipyretic, diuretic, astringent (used in irritable bowel syndrome, diarrhoea and dysentery), anticatarrhal, diuretic, anthelmintic, laxative and nervine tonic where as in China *D. gangeticum* is used as folkloric medicine primarily to treat fever, neutralize toxins, inhibit pain, invigorate blood circulation, suppress cough and alleviate dyspnea[9].

The roots of *D. gangeticum* (Local name: Kaganila akatono) chewed by the tribal people of Bulamogi community, Uganda to cure premature ejaculation[10].

Pawara tribals of Satpuda Hills of Nandurbar district, Maharashtra, India combine the root powder of *D. gangeticum* (Local name: Salvan) with honey and applied frequently to treat mouth ulcer[11].

Kharwas, Polekero, Kevat, Dhobhi communities of Chandauli district, Uttar Pradesh, India apply topically the leaf

paste along with *Aloe-vera* as anti-dandruff and to prevent hair falling[12].

Assamese people of Assam province in India, topically apply the paste of leaves of to cure the eczema infection along with other dermal disorders[13].

10 gm of dried crushed roots and Pseudarthria is mixed together and boiled in 200 ml of water for 3 minute and 2 ml of water decoction is prescribed thrice daily after meal by tribal people of Waynad of Kerala, India, to treat type 2 diabetes mellitus[14].

Root powder is boiled with milk and half cup of it is prescribed for seven or more days by tribal people of Jalgaon District, Maharastra, India, to promote flatulence[15].

Whole plant is prescribed traditionally by Tribals of Jhalod Taluka of Dhahod district, Gujrat, India against several gynecological disorders and to prepare "Salampak" tonic[16].

Villagers of Sivagangai district, Tamilnadu, India, drink leaf decoction (locally known as Pulladi) twice a day for 2 - 3 days to cure diarrhea and dysentery. Leaf paste is applied on anus once a day for two weeks to cure piles[17].

Chenchu tribal communities, Rudrakod of Nallamalai hill ranges of Andhra Pradesh, India, orally administer one spoonful root extract (locally known as Gitanaramu) twice a day, to cure whooping cough. Moreover, the leaves powder with a pinch of salt and applied on boils and blisters[18].

Bheel and Bhilala tribes, Jhabua District Madhya Pradesh, India apply topically fresh leaves juice to treat scabies and ringworm[19].

Chinese tribes administer root extract (9–15 gm/day) orally to treat diarrhea and given to children as sedative agent. Root and leaf pastes are applied externally to get relief from toothache and headache respectively [9].

Water decoction of root and aerial parts of *D. gangeticum* is used as antipyretic, anti-inflammatory and anti-nociceptive phyto-medicine by various Indian tribes throughout India[20].

Paliyar and Muthuvar Tribes, Theni District of Tamil Nadu, India, prescribe shade dried roots decoction (locally called Muvilai kurunthu) against asthma and other bronchial complications[21].

Tribes like Gond, Kols, Mushar, Baiga & Nutts in Vindhya region of Uttar Pradesh, India, administered orally root paste and powder to treat typhoid fever, cerebrospinal meningitis and also as an antidote of snake venom[22].

Different Indian tribes drink dried leaves powder decoction as health tonic[23].

4. Phytochemistry

Preliminary phytochemical screening reveals *D. gangeticum* is rich in flavonoids, alkaloids, steroids, terpenoids, phenylpropanoids, pterocarpans, coumarins and volatile oil[24]. Among the isolated compounds flavonoids, alkaloids and pterocarpans are considered as major bio-active constituents. Alkaloids like 5-methoxy N, N-dimethyl tryptamine, N_b-methyl-H_4–Harman, β-carbolinium cation, indole-3-alkyl-amines have been isolated from aerial parts of the plant[25]. Pterocarpans such as gangetin, gangetinin, desmodin, and desmocarpin were reported to be present in roots[26]. Recently a new pterocarpan, gangetial, had been isolated from the chloroform extract of the roots of *D. gangeticum*[27]. Flavones like 4′,5,7-Trihydroxy-8-prenylflavone, 4′-O-α-L-rhamnopyranosyl-(1→6)-β-d-glucopyranoside, 8-C-prenyl-5,7,5-trimethoxy-3,4-methylenedioxyflavone, rutin and quercetin-7-O-β-d-glucopyranoside were also reported from the aerial parts. Phytosterols viz. β-sitosterol, α-amyrone, lupeol and its acetate, stigmastrol had been isolated from aerial parts. Moreover, aminoglucosyl glycerolipid was reported for the first time from seed[28]. Further, minor phytoconstituents viz. trans-5-hexadecenoic acid, salicylic acid, 5-O-methylgenistein-7-O-β-d-glucopyranoside, 3,4- dihydroxy benzoic acid, kaempferol-7-O-β-d-glucopyranoside, and uridine triacetate were also reported[12]. The isolated compounds of different classes are summarized in Table 1 and the structures are displayed in Figure 2.

Figure 2: Isolated compounds from *D. gangeticum*

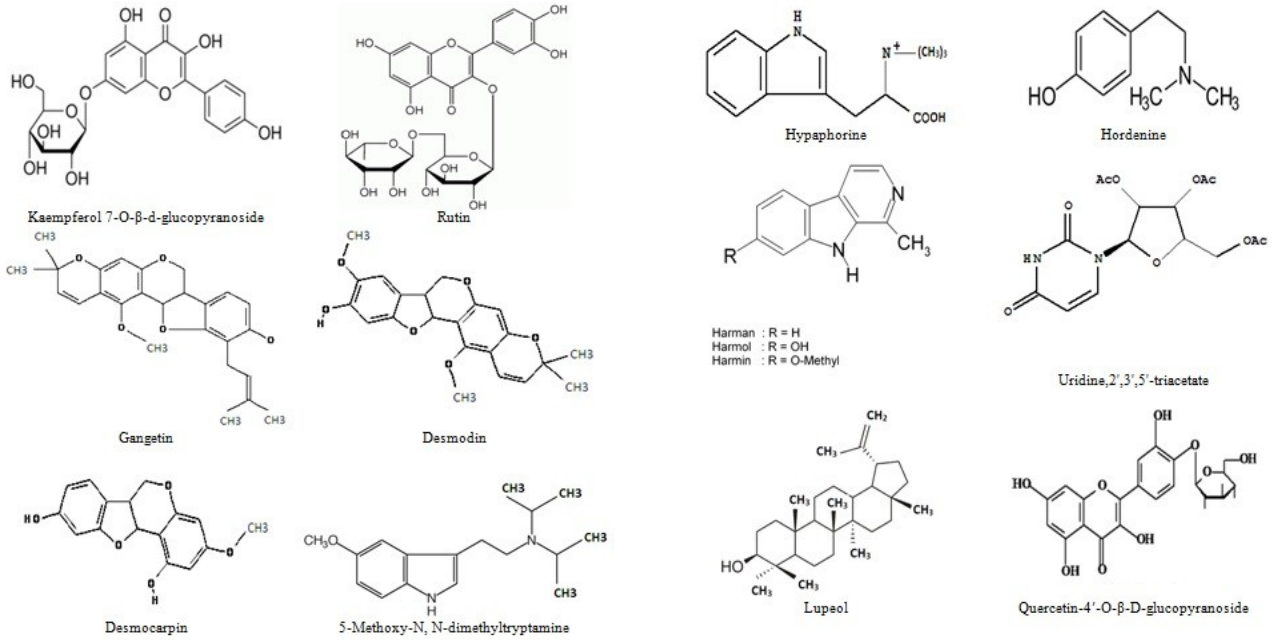

Table 1: Phytoconstituents of *D. gangeticum*

Chemical nature of phytoconstituents	Example	Parts of plant
Flavonoids		
Flavones	4/,5,7-Trihydroxy-8-prenylflavone 4/-O-α-L-rhamnopyranosyl-(1→6)-β-d glucopyranoside	Stem
	8-C-prenyl-5,7,5- trimethoxy-3,4_- methylene di oxy flavone	Whole plant
Flavonols	Kaempferol 7-O-β-d-glucopyranoside, Rutin, Quercetin-4′-O-β-D glucopyranoside	Aerial parts
Isoflavones	5-O-Methylgenistein7-O-β-d-glucopyranoside	Whole palnt
Pterocarpans	Gangetin, Gangetinin, Desmodin, Desmocarpin	Aerial parts
Alkaloids		
Indole-3-alkylamines	5-Methoxy-N, N-dimethyltryptamine, N-methylserotonin Bufotenine N-oxide, Hypaphorine, 6-Methoxy-2-methyl-β-Carbolinum, Nb-methyltetrahydro Harman, hordenine	Whole palnt, stem
Amide alkaloids	Uridine triacetate,	Whole plant
Phenylethylamine alkaloids	N-methyltyramine, β-Phenylethylamine, 3,4- Dihydroxy phenethyltrimethyl ammonium hydroxide	Leaf, stem
Terpenoids	β- Amyrone	Whole plant
Steroids	24-Ethylcholesta-5,22-dien-3β-ol, 24-Methylcholesta-5-en-3β –ol, β –Sitosterol, lupeol and its acetate, stigmastrol	Aerial part, root
Phenolic acid	3,4-Dihydroxybenzoic acid, Vanillic acid	Aerial parts
Phenylpropanoids	Chlorogenic acid	Aerial parts
Volatile Oils	1-Tritriacontanol, 1-Heptadecanol, Aliphatic β-lactone, Trans-5-hexadecenoic acid	Roots and whole plant
Others	Phosphatidyl ethanolamine, Phosphatidyl serine, Phosphatidyl choline	Seed

5. Pharmacological activity

5.1 Antioxidant activity

Chloroform root extract of *D. gangeticum* (2-1000 µg/ml) were tested *in-vitro* to establish the antioxidant potential against ischemia reperfusion injury model in isolated rat heart. The IC_{50} values in DPPH, superoxide, hydroxide and nitric oxide scavenging activity and lipid per oxidation models were found to be 36.0, 55.3, 43.7, 39.4 and 297 µg/ml respectively. These findings revealed the cardioprotective activity of the extract against ischemia reperfusion injury mediated through several reactive oxygen species. Further, GC/MS analysis revealed presence of Oleic acid (RT: 20.90), N, hexadecanoic acid (RT: 17.70), 1,2 Benzenedicarboxylic acid bis(2 methylpropyl)ester (RT:15.94), 9 Dodecenoic acid methyl ester (RT: 19.80), 9,9 Dimethoxybicyclo [3,3,1]nona 2,4 dione (RT: 21.18), 1,2 Bis(trimethysilyl) benzene (RT: 26.46), and Didodecyl phthalate (RT: 27.55) as major compounds which might be associated with the therapeutic potential of the plant[29].

The antioxidant activity of flavonoids and alkaloidal fractions of methanolic extract of *D. gangeticum* were evaluated *in-vitro*. The results showed flavanoids fraction possessed potent antioxidant activity compared to alkaloid fraction [30].

Further, two novel compounds viz. caffeic acids and chlorogenic acid were isolated from flavanoid fraction and their antioxidant activity was tested *in-vitro* under arthritic conditions. The results supported strong antioxidant activity, which might be associated with the anti-arthritic activity of the plant as most of the anti-arthritic drugs act by reducing the oxidant damage at sites of inflammation[31].

In-vivo free radical scavenging potential of aqueous extract of *D. gangeticum* root was accessed by inducing oxidative stress in ischemic reperfused rat heart model. The observations supported antioxidant capacity of *D. gangeticum* as compared to standard drug verapamil against revascularization injury[32].

Hydro-alcoholic extract of *D. gangeticum* strongly scavenged DPPH radical (IC_{50} 2.01 mg/ml) and NO (IC_{50} 14.79 mg/ml) in dose dependent manner. was found to have activity. The total antioxidant capacity of the extract was found to be 149.91 % as compared to standard ascorbic acid 87.8 %. The extract also inhibited the ferrylbipyridyl (chromogen) formation in a dose dependent fashion (IC_{50} 0.115 mg/ml)[33].

5.2 Anti-inflammatory and anti-nociceptive activity

Aqueous decoction (5, 10 and 20 mg/kg) of roots and aerial parts of *D. gangeticum* showed anti-inflammatory and anti-nociceptive activity *in-vivo* in dose-dependent manner. The inhibition of swelling caused by carrageenan was equivalent to 14.58–51.02 % protection and in cotton pellet granuloma the protection was observed up to 14.43–38.67 %. Moreover, a significant increase in analgesio-meter-induced force and acetic acid induced writhing were observed equivalent to 6.56-67.66 % & 22.18–73.83 % protection respectively[34].

Juice of whole plant of *D. gangeticum* posses anti-rheumatic and anti-osteo arthritic activity via anti-inflammatory activity. The activity might be associated with several phytoconstituents like polyphenolics, pterocarpinoid (gangetin)[35].

Gangetin, a pterocarpens, isolated from n-hexane extract of root of *D. gangeticum* showed significant anti-inflammatory activity in both exudative and proliferative phases of inflammation in rat model at dose of 50 and 100 mg/kg body weight[36].

5.3 Anti-leishmanial and immunomodulatory activities

Glyco-lipids viz. Aminoglucosyl glycerolipid and glycosphingolipid, isolated from the roots of *D. gangeticum* showed potent antileishmanial and immunomodulatory activities *in-vitro* by enhancing nitric oxide (NO) production and provided resistance against infection established in peritoneal macrophages by the protozoan parasite *Leishmania donovani*[37].

Moreover, ethanolic extract and n-hexane, n-butanol, aqueous fractions of the ethanolic extract of *D. gangeticum* were evaluated chemoprophylactically and chemotherapeutically against experimental visceral leishmania in hamsters at a dose of 250 mg/kg for seven days. Results revealed highest prophylactic efficacy (41.2±5.3% inhibition) in n-butanol fraction and moderate efficacy (66.7±6.1% inhibition) in ethanol extract[38].

5.4 Cardio-protective activity

Methanolic extract of *D. gangeticum* roots preserve mitochondrial respiratory enzymes and thereby protecting rat heart against oxidative stress induced by reperfusion injury at a dose of 50, 100 mg/kg body weight[39].

Further, chloroform root extract (100 mg/kg) mediates cardio protection in ischemic reperfusion injury model in isolated frog heart through negative ionotropic and chronotropic. The effect was mediated by stimulating the G coupled receptors similar to the action of acetylcholine. Both the studies were compared with verapamil (0.2 mg/kg body weight, i.p.), standard cardioprotective drug[40].

Pre-treatment of the aqueous extract of *D. gangeticum* (3 ml/100 g) for thirty days showed reduced cholesterol level and free radical scavenging potential *in-vitro* against isoproterenol induced myocardial infracted rats. These findings were associated with cardio-protective activity of the plant[41].

Ethyl acetate extract of *D. gangeticum* root (100 mg/kg) showed potent cardio-protection against ischemia reperfusion-induced oxidative stress models. The extract reduced TBARS in myocardium along with enhanced the recovery of antioxidant enzymes from the assault of ischemia reperfusion injury. The effects of the extract might be related to the inhibition of lipid peroxidation[42].

Methanol extract of *D. gangeticum* root (80 µg/ml) showed myocardial protection in rat ischemia reperfusion injury model by stimulating muscarinic receptors. The activity might be due to the reduction of calcium overload and free radical release and improved recovery of antioxidant enzyme towards myocardium[43].

5.5 Anti ulcer activity

Oral administration of ethanolic extract of *D. gangeticum* (200mg/kg) showed potent anti-ulcerogenic property *in-vivo* in Sprague Dawley rats and guinea pigs. A significant protection against cold resistant (68.37%), alcohol (88.87%), aspirin (38.2%), pyloric ligation (40.63%) and HST (63.15%) induced ulcer models was observed. Further, reduction in acid secretion (41.61%) and increase in mucin secretion (56.17%) were also recorded. Results indicate cytoprotective effect along with anti-secretory activity of *D. gangeticum* may be responsible for its anti-ulcer property[44].

Oral administration of root ethanolic extract of *D. gangeticum* significantly decreased the ulcer index and lesion number in a dose dependent manner against ethanol induced acute gastric ulcer in mice. The highest dose (150 mg/kg) of the extract provoked a marked increase in protein and glutathione levels, when compare to control. Furthermore, gastric juice, free acidity and total acid output were inhibited in a dose-dependent manner at $p<0.05$ level[45].

5.6 CNS activity

Aqueous extract of *D. gangeticum* showed potent anti-writhing activity in the acetic acid-induced abdominal writhing assay. It also exhibited moderate CNS depressant activity *in-vivo*. The effects of extract on locomotion were compared with standard CNS drugs[46].

5.7 Antiamnesic (nootropic) activity

Aqueous extract of *D. gangeticum* (50, 100 and 200 mg/kg) showed potent anti-amnesic effects in mice against scopolamine (0.4 mg/kg, i.p.) induced interoceptive behavioral models. The study was compared with Piracetam (200 mg/kg, i.p.), standard nootropic agent[47].

Pretreatment with aqueous extract of *D. gangeticum* (100, 200 mg/kg, p.o.) for seven successive days, reversed scopolamine induced amnesia in mice. Study revealed that the plant increased mice brain acetylcholine content and decreased acetyl cholinesterase activity in a similar fashion to the standard cerebro-protective drug piracetam. Hence, aqueous extract of *D. gangeticum* can be used to delay the onset and reduce the severity of the symptoms of dementia and Alzheimer's disease[48].

5.8 Antidiabetic activity

Methanolic extract of aerial parts of *D. gangeticum* (100 and 250 mg/kg) for 3 weeks showed a significant antidiabetic activity in rats by stimulating insulin secretion from MIN6 and pseudoislets cells of pancreatic islet.

It plays a major role to maintain the lipid profile of the rats by reducing cholesterol and triglycerides level and increase in high density lipoproteins (HDL) significantly ($p < 0.05$). This supports the traditional use of *D. gangeticum* as anti-diabetic drug[49].

5.9 Hepatoprotective activity

Hepatoprotective activity of the chloroform extract of roots of *D. gangeticum* was evaluated *in-vivo* against CCl_4 induced liver damage in rat models. The study revealed extract caused an increase in serum levels of total proteins and decrease levels of bilirubin, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) in pretreated groups[50].

5.10 Renal protective activity

Oral administration of ethanolic extract of whole plant of *D. gangeticum* (100, 200, 400 mg/kg) for 30 days showed marked renal protective activity *in-vitro* against streptozotocin induced diabetic rats. The study was compared with glibenclamide (600 µg/kg), standard anti-diabetic drug[51].

5.11 Wound healing activity

Topical application (10% w/w ointment of aqueous extract of *D. gangeticum*) showed marked wound healing potential *in-vivo* in Wistar rat models. Results indicated a decrease in wound closure time and increment in wound contraction. Moreover, a significant increase in proline content was also observed. All the studies were compared with standard povidone iodine ointment[52].

6. Safety profile

Toxicity of *D. gangeticum* extract was accessed in mice at different doses (50–2000 mg) and parameters like hyperactivity, grooming, convulsions, sedation, hypothermia and mortality were observed. No mortality was observed following oral administration of highest dose (2000 mg/kg) of extract. However, doses more than 1000 mg/kg produced profuse watery stools, ptosis (dropping of upper eyelids) and lethargy in animals. Further, studies conducted on gangetin showed no acute toxicity up to 7 g/kg orally which made it quite safe. Further, as traditional medicine no reports of toxicity of *D. gangeticum* have been documented[53].

7. Discussion

For ages, *D. gangeticum* has been used for the treatment of various ailments in traditional and folklore medicine throughout India, China and other African countries. *D. gangeticum* is one of the main ingredients of several Ayurvedic formulations like Dashamularishta, Cyavanaprasam and Agasthyarasayanam, routinely prescribed to treat colic pain, fever, respiratory diseases[54]. The decoction of Dasamula and Laghu pancamula, polyherbal formulations are used in pain, hysteria, rheumatism, asthma, cardiac and renal problems[55]. Isolated phytoconstituents like Gangetin, Desmodin, 5-Methoxy-N,N-dimethyltryptamine are considered as predominant bioactive constituents due to their diverse therapeutic potentiality[56]. Although the constituents responsible for the pharmacological properties of the plant seem to have been determined, the molecular mechanisms of most of these principles are still unknown. The bioassay guided isolation, identification of the bioactive components is essential and in depth research is also crucial to reveal the structure-activity relationship of these active compounds. Based on these facts, the authors made an upto date information highlighting the current ethno-pharmacological and phytochemical status of the plant.

Acknowledgement

The authors acknowledge the financial support of NGSM Institute of Pharmaceutical Sciences and Nitte University, Mangalore, India for the research work (Grant no. NU/PhD/Pharm/Res-10/2011).

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