



REVIEW ARTICLE

Ethnomedical uses, Phytochemistry, Pharmacological and therapeutic properties of *Desmodium gangeticum* (L.) DC.- A scoping review

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Abstract

A surge in laboratory research into the pharmacological properties of bioactive compounds, as well as their potential to cure a wide range of ailments, has resulted in an influx of new herbal medications and extracts onto the international market in recent years. *Desmodium gangeticum* (L.), one of the essential herbs of Indian traditional system of medicines is part of many essential formulations viz. "Dashamoola" and is used to treat various diseases. It is a perennial herb, locally known as "Shalparni" (Hindi) in India and also reported in many other tropical countries. This review presents the traditional uses, phytochemistry, pharmacology, and clinical effectiveness of *D. gangeticum*. Literature was systematically searched through various databases, journals and gray literature through electronic and manual search. Collected data was further critically reviewed and summarized in this paper. It contains many bio-active phytochemicals viz. gangeticoside, leonuriside A, tortoside A, dehydrosoyasaponin, gangetin, gangetinin, desmocarpin, desmodin etc. among them, some have drug likeliness properties. Critical literature analysis revealed that it possessed many pharmacological activities viz. anti-inflammatory, antinociceptive, anti-oxidant, cardioprotective, antidiabetic and hepatoprotective anti-bacterial, and anti-amnesic activities. Despite a large number of traditional therapeutic uses, *D. gangeticum* was evaluated for limited therapeutic efficacy through clinical trials and evidence suggested it may have therapeutic benefits on bronchitis, gout, hypertension. The biochemical and physiological mechanisms involved in the different biological effects exhibited by it need to be investigated. The herb should be investigated further, focusing on pharmacodynamic, pharmacokinetic and safety profiles. Well-designed Randomized Controlled trials (RCTs) should be conducted to support its therapeutic use.

Keywords

Animal experiment study, Clinical study, *Desmodium gangeticum*, Ethno-medicine, Phytochemistry, 'Shalparni'

Introduction

Since the earliest days of civilization, plants had been employed for health promotion and disease treatment in many regions and communities worldwide. For many people in the developing world, plant based traditional medicine is crucial for their healthcare. Plants are the source of around a quarter of all prescribed medications globally (1). Drug development and pharmacology rely heavily on ethnobotanicals, which can be employed in

various ways, from raw materials for drug production to modeling biologically active chemicals (2). Ethnomedicinal knowledge and natural sources have developed the basis of biomedicine and contribute largely to the commercial drug preparations manufactured today.

Experiments on medicinal plants and their possible properties have drawn attention of many scientists. Contemporary research in drug development from herbal plants includes a multidimensional approach combining pharmacognostical, phytochemical, pharmacological biotechnology and molecular sciences (3). Many therapeutic agents employed presently for various targets have been discovered through their known ethnomedicinal use (4). Therefore, it is essential to screen medicinal to provide novel and significant leads against various pharmacological targets.

Desmodium gangeticum (L.) DC. (Fabaceae), commonly known as 'Salpan' or 'Shalaparni,' is distributed widely in several regions in Asia, Africa and Australia (5, 6). *D. gangeticum* is an erect undershrub, up to 1.2 m tall; the stem is angled, hairy when young, glabrescent on aging. It can be characterized among *Desmodium* species by lax flowers scattered on peduncles and joints of pods longer than broad (Fig. 1) (7).

It is one of the essential herbs of ethnomedicine that have been used extensively either as a single drug or



A. *D. gangeticum* leaves.



B. *D. gangeticum* fruits.



C. *D. gangeticum* flowers.



D. *D. gangeticum* roots.

Fig. 1. Morphological characteristic of *D. gangeticum* in its natural habitat.

in combination with other drugs in the traditional system of medicines in India (8). In Ayurveda (Indian traditional system of medicine), it has been reported for various therapeutic uses such as in oedema, fever, cough, worm infestation, dyspnoea, diarrhoea, vomiting, pain and inflammation (9). It is one of the ingredients of 'Dashamoola' an essential herbal formulation of Ayurveda which is widely prescribed for many health ailments (10). Its roots have been used ethnomedicinally as an expectorant for lower respiratory tract infections and as an antitoxin in snakebite and scorpion sting (11, 12).

In the last few decades, *D. gangeticum* was screened to explore its biochemistry, pharmacological activities and clinical uses through scientific experiments. Findings of such researches supported its traditional uses and established it as potential herbal therapeutics. Many secondary metabolites and bioactive compounds have been reported in plants having various pharmacological activities (13, 14). Attempts have been made to review the researches carried out previously, but gathered data were not comprehensive (15). Thus, the purpose of this review is to provide comprehensive information on the ethnomedicinal uses, phytochemical profile, pharmacological activities and clinical trials on *D. gangeticum*, to investigate their therapeutic potential, identify gaps in our current knowledge and assess future research prospects.

Materials and Methods

Scientific published literature on *D. gangeticum* was strategically searched through various platforms to collect optimum available literature. Electronic databases such as PubMed, Google scholar, AYUSH Research portal, AYUSHDHARA, J-GATE, Research Gate portals, INFLIBNET, and preprint were searched from inception to June 2021 through a search strategy developed using key search terms. Keywords and terms used in search strategy included 'Shalaparni,' 'Desmodium gangeticum,' 'preclinical study,' 'Ethno medicine,' 'phytochemical,' 'pharmacological,' 'experimental' Boolean operator (AND, OR, NOT) was also used to limit or broaden the search wherever required. Ayurveda text books, unpublished dissertations and research were also searched manually.

Published or unpublished researches on ethnomedicine, phytochemistry, animal experiments, and clinical research carried out on *D. gangeticum* were included. Information was rigorously retrieved, critically analyzed and systematically summarized.

Results

Of 344 citations retrieved through systematic search from different databases, 46 were retrieved in PubMed, 14 in AYUSH Research Portal, 17 in DHARA and Google Scholar yielded 267 citations. Six studies were retrieved through manual search. However, only 49 studies were found relevant and hence were selected for review. Total 301 articles viz. duplicates (111), nonrelevant (166) and review (24) articles were excluded. Among 49 included studies, 13 were categorized in ethnobotanical uses, 16 in phytochemistry, 16 in pharmacological experiments and 4 in clinical trials (Fig. 2).

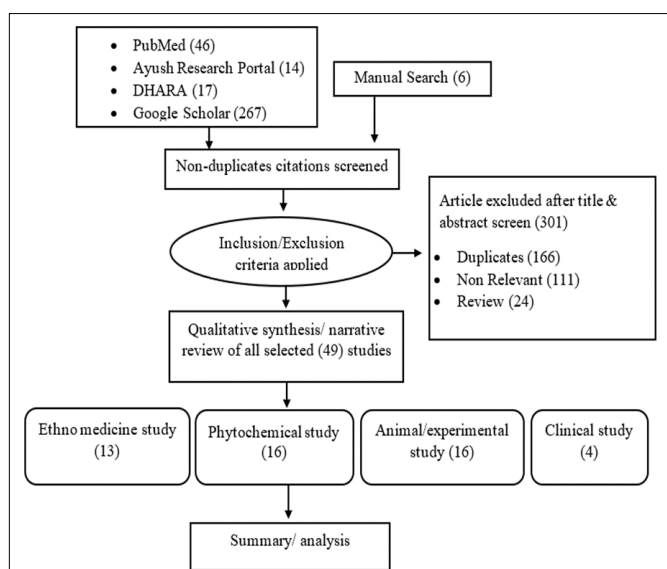


Fig. 2. Study flow chart.

Ethnomedicinal/traditional uses

D. gangeticum is traditionally used as therapeutics in many different geographical regions. In India, root decoction of *Shalaparni* is used as a snake bite remedy (16). Root paste also traditionally taken orally as an antidote for

snake and scorpion bites in the Dudhi block of District Sonbhadra, Uttar Pradesh, India (17). Its root decoction is utilized in rheumatism with a dose of one spoon in Eastern Ghats of Andhra Pradesh, India (18). Aqueous leaf extract is poisonous towards *E. coli*. In Odisha, India (19). The plant's stem and leaf are used as a diuretic, antitoxic, vomiting and diarrhea as a decoction in the Chandra Prabha Wildlife Sanctuary, Chandauli District, Uttar Pradesh (20). It is utilized in fever, vomiting, *Vata-Dosha* in Raipur District (21). In tribal areas of Adilabad District, Telangana Region, plant roots, bark and leaves are used to treat fever and kidney disorders (22). Inhabitant of eastern Ghats, Andhra Pradesh, India, its root decoction is traditionally utilized with half cup dose once daily for 2-3 months to alleviate respiratory disease (23). Paste of its stem bark is externally applied in goiter daily once for 3-4 days by tribes of Chhattisgarh state (24). Tonic "*Salampak*" prepared from *D gangeticum* is employed in gynecological diseases by tribals of Jhalod taluka of Dahod district, Gujarat, India (25). Root is used in premature ejaculation in Bulamogi district, Uganda (26). The root is also used for cough and cold in Deolapar forest range, Maharashtra (27). *D. gangeticum* is being utilized in Stomach ache and menstrual ache ethnomedically by the Khasia community people in Moulibazar district of Bangladesh (28).

Phytochemical properties

All parts of the *D. gangeticum* have been extensively screened for chemical investigations because of their high medicinal values. Various reports have been published regarding the phytochemical content of *D. gangeticum*. Phytochemical screening of various extracts indicated the presence of carbohydrates, amino acids, glycosides, proteins, alkaloids, saponins, phytosterol, flavonoids, steroids, terpenoids, phenolic compounds, reducing sugar, anthraquinone and fixed oils (29-36).

Eighteen compounds were recognized from the root, wherein 7 are acids (58.90%), 3 are phenolic compounds (4.1%) and plant sterols (5.12%). Other compounds reported were 9,12- Octadecadienoic acid, n-Hexadecanoic acid, octadecanoic acid and γ -sitosterol. Alkaloids, esters, ethers, alcohols and hydrocarbons are also recognized from it through GC-MS, HPTLC method (37). Minor substances in the GSMS study found were 4 dodecanol, 10 undecenal, 1, 2 benzenedicarboxylic acid bis (2 methylpropyl) ester, 1, 14 Tetradecanediol and 2 methyl pentanal, as well as N hexadecanoic acid, Oleic acid, 9 Dodecanoic acid methyl ester. The trace elements reported through an atomic absorption spectrophotometer were iron, magnesium, sodium, potassium, calcium and nickel confirmed (38).

The 2.01% total flavonoid content was reported in an aqueous extract of aerial parts, including Rutin, Quercetin, Genistein and Daidzein (39). gangeticoside (megastigmane glycoside), a new compound from the aerial part, along with three known compounds- leonuriside A, methyl benzoate 2- O-D-glucopyranoside and tortoside A was reported (40).

The aqueous extract of plants root and aerial parts

contains 0.608 mg/g of quercetin (56). Lauric acid, Lupeol, mixture of sitosterole and stigmasterol gallic acid, salicylic acid, caffeic acid, protocatechuic acid, quercetin, chlorogenic acid, rutin and kaempferol were found in the root and aerial parts through HPTLC and MS/MS analysis (41). Twelve alkaloids from different parts of *DG* comprising various groups viz. carboxylated, decarboxylated tryptamines, fl-phenethylamines were isolated from the roots, indole-3-alkylamines and 8-carbolines from stem and leaves (42). Kaempferol 7-O- β -D-glucopyranoside, rutin, quercetin 7-O- β -D glucopyranoside was reported in aerial parts (43, 44). Antileishmanial compound aminoglucosyl-glycerolipid were also reported (45).

Pharmacological/ Experimental study

Plant was reported for many pharmacological activities (Table 1). Details of pharmacological activities has been described below.

Anti-inflammatory activity

The anti-inflammatory activity of several extracts of aerial parts of *D. gangeticum* (aqueous, ethanolic, petroleum, acetone, benzene and chloroform extracts) was evaluated through carrageenan-induced paw edema method on albino rats. It reported an aqueous extract of *D. gangeticum*, at concentration of 100 mg/kg, b.w., p.o. exerted 48.33% inhibition of paw edema, followed by ethanolic extract 39.27% inhibition, petroleum extract 38.49% inhibition, acetone 36.94% inhibition, benzene 33.12% inhibition and chloroform 33.04 % inhibition. Standard reference NSAID demonstrated significant paw edema inhibition of 54.88 % at a 100 mg/kg dose. The aqueous extract of *D. gangeticum* demonstrated significant anti-inflammatory efficacy in a dose-dependent manner among all extracts (46). In another carrageenan-induced rat paw oedema study carried out on male Wistar rats, different doses of ethanolic extract

Table 1. Various pharmacological activities (*In-vivo* and *In-vitro*) of *Desmodium gangeticum* (L.) DC.

Activity	Extract		Animal Model	Author
Anti-inflammatory	Aqueous, Ethanolic, Petroleum, Acetone, Benzene, Chloroform of aerial Parts	<i>In-vivo</i>	Carrageenan-induced paw edema model on albino rats	Amit Kumar <i>et al.</i> (46)
	Ethanolic extract of leaves	<i>In-vivo</i>	Carrageenan-induced paw edema model on albino rats	Sagar MK <i>et al.</i> (47)
	Aqueous extract of aerial parts	<i>In-vivo</i>	Carrageenan-induced paw edema model on albino rats	Kurian GA <i>et al.</i> (48)
	Aqueous extract of root	<i>In-vivo</i>	Carrageenan-induced paw edema model on albino rats	Nagarkar B <i>et al.</i> (49)
Cardio tonic	Aqueous extract of root	<i>In-vitro</i>	Ischemic reperfusion injury in an isolated rat heart	Kurian GA <i>et al.</i> (50)
Anti - ischemic reperfusion injury	Methanol extract of root	<i>In-vitro</i>	Ischemic reperfusion injury in an isolated rat heart and frog heart.	Kurian GA <i>et al.</i> (51)
Anti-nociceptive	Ethanolic extract of leaves	<i>In-vivo</i>	Thermal model (Eddy's hot-plate and Tail flick test) and chemical model (acetic acid induced writhing, Formalin induced nociceptive pain) in wistar albino rat	Sagar MK <i>et al.</i> (47)
Antioxidant	Aqueous extract of root	<i>In-vivo</i> and <i>In-vitro</i>	DPPH, superoxide scavenging activity, hydroxide scavenging activity, nitric oxide scavenging activity and lipid peroxidation	Kurian GA <i>et al.</i> (52)
Anti- Asthamatic	Chloroform, Ethanolic, Hydro - Alcoholic of Root	<i>In-vivo</i>	Ovalbumin-induced Wister rats	Vedpal <i>et al.</i> (53)
Anti-bacterial	Ethanol, Methanol, Aqueous, Chloroform of whole plant	<i>In-vitro</i>	Antibacterial assay (agar well diffusion method) for <i>Klebsiella pneumoniae</i> , <i>E. coli</i> , <i>Streptococci</i> , <i>Pseudomonas aeruginosa</i> , <i>S. mutants</i> and <i>S. typhi</i>	Karthikeyan K <i>et al.</i> (54)
Anti-amnesic	Aqueous extract of aerial part and root of <i>D. gangeticum</i>	<i>In-vivo</i>	Exteroceptive behavioral models (elevated plus maze and passive avoidance paradigm), Interoceptive behavioral models (Scopolamine produced and ageing-linked amnesia) in young and aged mice	Joshi H <i>et al.</i> (55)
Antidiabetic	Aqueous extract of aerial part	<i>In-vivo</i>	Streptozotocin-induced diabetes in rats	Govindarajan R <i>et al.</i> (56)
Antiulcer	Aqueous extract of aerial parts of plant.	<i>In-vitro</i>	DPP-IV inhibitory assay	Bisht R <i>et al.</i> (57)
	Ethanolic extract of whole plant	<i>In-vivo</i>	Four gastric ulcer models (Cold restraint stress induced, <i>aspirin</i> induced and ethanol induced and pyloric ligation induced gastric ulcer) in Sprague Dawley rats. Histamine induced duodenal ulcer in guinea pig.	Dharmani P <i>et al.</i> (58)
	Ethanolic extract of root	<i>In-vivo</i>	Ethanol-induced gastric ulcer model in mice, Pylorus ligated gastric ulcer in mice	Mahesh A <i>et al.</i> (59)

Renal Protective	Ethanollic extract (whole plant)	<i>In-vivo</i>	Streptozotocin-induced diabetes in rats	Yasmeen N <i>et al.</i> (60)
Hepato-protective	Ethanollic extract of leaves	<i>In-vivo</i>	Paracetamol induced hepatotoxicity in Wistar albino rats	V Usha <i>et al.</i> (61)
Antitussive	Aqueous extract of whole plant	<i>In-vivo</i>	SO ₂ generated cough reflexes in mice	Kumar V <i>et al.</i> (62)
Antihistaminic	Aqueous extract of whole plant	<i>In-vitro</i>	Histamine-induced contraction of isolated guinea pig ileum	Kumar V <i>et al.</i> (62)
Antidiarrheal	Aqueous extract of whole plant	<i>In-vivo</i>	Castor oil-induced diarrhea in wistar albino rats	Patel B <i>et al.</i> (43)

reduces paw oedema by 13.75 % (50 mg/kg), 23.75 % (100 mg/kg), and 27.5 % (200 mg/kg) after a 3-hr post-dosing interval. After 6 hrs of treatment, paw oedema was significantly reduced up to 15.68 %, 24.5 %, 45.09 % and continued for 24 hrs, up to 27.39 %, 35.61 % and 43.83 % at 50, 100 and 200 mg/kg doses respectively. Standard reference NSAID showed a 51.95 % reduction after 6 hrs and 46.57 % after 24 hrs. It confirms the dose-dependent effect of the extract (47). Furthermore, the plant's aqueous extract was tested for COX-1 (cyclooxygenase), COX-2 and LOX (lipoxygenase) inhibitory activities to determine a valid mechanism for anti-inflammatory effect. The results of the study indicated that plant extract reduces paw swelling significantly ($p < 0.0001$) when compared to the standard medicine Ibuprofen (100 mg/kg b.w.). The % inhibitory activity of *D. gangeticum* AqE against COX-2 (IC₅₀=39.5 g/ml) was significantly higher than that of COX-1 (IC₅₀=49.5 g/ml). The plant also showed moderate inhibition of LOX interest (IC₅₀=57.0 g/ml) (48). Another study on anti-inflammatory activity on albino rats revealed that standard control diclofenac sodium (10 mg/kg) reduced oedema volumes by 30.07 % and 44.95 % and oral administration of *D. gangeticum* water decoction reduced oedema volumes by 9.80 % and 26.74 % at the 3rd and 6th hrs respectively (49).

Cardiotonic effect

The aqueous root extract of *D. gangeticum* was effective for treating ischemic reperfusion injury at a dose of 50 mg/kg weight in rat hearts. The level of creatinine phosphokinase in the coronary perforate was lower. Significant improvement in Sarcoplasmic ATPase and mitochondrial enzymes were observed in *D. gangeticum* treated rat hearts. A structural improvement in the myocardium was also observed in *D. gangeticum* treated rats. The study revealed aqueous root extract improved cardiac function after ischemia reperfusion injury by mitochondrial and sarcoplasmic ATPase preservation in the myocardium. Gas chromatography-mass spectrometry and atomic absorption study of *Shalaparni* root extract the showed presence of bio-constituents that can activate the release of calcium in cardiac tissue (50).

The mechanism of action of methanol extract of *D. gangeticum* root was investigated for the anti-ischemic reperfusion property in an isolated frog heart and rat heart. The findings revealed that methanolic extract exerted dose-dependent negative inotropic and chronotropic effects on isolated frog hearts, mimicking acetylcholine-like action. Root extract exhibited a cardio-protective

effect in the isolated rat heart model for ischemia reperfusion injury and action was similar to acetylcholine (G protein agonist). Thus, root extract showed cardioprotection through negative inotropic and chronotropic effects by activating the G-coupled receptors analogous to the action of acetylcholine (51).

Antinociceptive activity

The antinociceptive activity of the ethanolic extract of *D. gangeticum* leaves was evaluated in rats by thermal (Eddy's hot-plate and Tail flick test) and chemical (Acetic acid and Formalin) induced nociceptive actions. Oral administration of ethanolic extract of *DG* (50, 100, 200 mg/kg), positive control morphine (5 mg/kg i.p.) and aspirin (300 mg/kg o.p.) reduced acetic acid-induced writhing by 25.92 %, 55.12 %, 68.13 %, 85.61 % and 72.19 % ($P < 0.05$) respectively. In Eddy's hot-plate test, the largest dose of the plant extract increased the latency stage by 37.65% and in the tail-flick test, it increased the latency stage by 28.26% ($P < 0.05$). In formalin-elicited sensitive pain, a 200 mg/kg dose of extract suppresses 29.67% ($P < 0.05$) of neurogenic pain (47).

Antioxidant activity

The antioxidant and experimentally induced ischaemic reperfusion effects of aqueous extract of *D. gangeticum* root were evaluated in an isolated rat heart. Oral administration of extract (50 and 100 mg/kg once daily for thirty days) increased enzymatic activity of superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) and reduced the lipidperoxidations. The results indicated that the liquid extract of the root has a significant radical scavenging effect (52).

Anti-Asthmatic activity

Chloroform, ethanolic and hydro-alcoholic root extracts were evaluated for the anti-asthmatic activity in ovalbumin-induced Wistar rats. WBC count was significantly lower in extract-treated rats than sensitized control (ovalbumin treated) rats in the study. There was also a significant decrease in Malonyldialdehyde (MDA) levels in the experimental rats compared to ovalbumin-treated rats (53).

Antibacterial activity

The antibacterial activity of ethanol, methanol, aqueous and chloroform extract of *D. gangeticum* was evaluated against bacterial pathogens such as *Klebsiella pneumoniae*, *E. coli*, *Streptococci*, *Pseudomonas aeruginosa*, *S. mutants* and *S. typhi*. Amoxicillin, Ciprofloxacin, Kanamycin, Penicillin and Tetracyclin were used in the antibiotic sensi-

tivity test. The methanolic extract showed the maximum zone of inhibition (24 ± 2.3 mm) against *S. mutants*, whereas the aqueous extract showed the minimum zone of inhibition (7 ± 0.08) against *P. aeruginosa*. Antibiotic sensitivity was also found against all microorganisms with tetracyclin, kanamycin, and ciprofloxacin. The methanolic extract of *D. gangeticum* had the maximum antibacterial potential among all extracts. The methanolic extract of *D. gangeticum* can serve as a potential antibacterial source for various infections (54).

Anti-amnesic activity

An anti-amnesic effect of *D. gangeticum* aqueous extract was assessed at concentrations of 50, 100 and 200 mg/kg was administered orally to young and aged mice for one week. Elevated plus-maze and the fear-aggravated passive avoidance task were used to test learning and remembrance. Scopolamine (intraperitoneal) produced and ageing-linked amnesia were served as the interoceptive paradigm. Intraperitoneal piracetam (200 mg/kg) was administered as standard memory enhancer medicine. Animals treated priorly with aqueous extracts enhanced cognitive function remarkably in both models, scopolamine induced and ageing-linked amnesia. In addition, test drug lowered acetylcholinesterase effect in brain. *D. gangeticum* appears to be a promising cognitive function enhancer agent (55).

Antidiabetic activity

An antidiabetic activity was evaluated wherein diabetic rats were given aerial parts of *D. gangeticum* extract for three weeks. Blood glucose levels were significantly decreased after 30 min in *D. gangeticum*-treated rats compared to the control. It was suggested that *D. gangeticum* might act by direct stimulation of b-cells to secrete insulin (56).

In another antidiabetic study, *D. gangeticum* aqueous extract exhibited good alpha glucosidase and DPP-IV (Dipeptidyl peptidase IV) inhibitory activity, with IC₅₀ values of 950 g/ml and 255.5 g/ml respectively (57).

Antiulcer study

An antiulcer activity has been evaluated through four gastric ulcer models such as cold restraint stress induced, aspirin induced and ethanol induced and pyloric ligation induced in Sprague Dawley rats; and histamine produced duodenal ulcer paradigm in guinea pigs. Oral administration of plant extract at 200 mg/kg dose remarkably decreased the occurrence of ulceration among all paradigms. Plant extract provided 68.37 % protection against cold restraint stress, 38.2 % protection against aspirin, 40.63 % against pyloric ligation and 63.15 % protection against histamine induced ulcer models, whereas active comparator omeprazole provided protection of 83.86%, 56.35%, 70.31% and 84.21% in respective models. Plant extract reduced gastric juice secretion by 41.61 %, whereas omeprazole reduced it by 43.13%. Plant extract administration increased 56.17 % in mucin secretion, whereas 12.45 % rise was observed in omeprazole treated group (58).

In another study where in root extract orally administered remarkably protected the gastric ulcer by reducing size and lesion number in a concentration-depending way at the doses of 50 mg/kg, 100 mg/kg and 150 mg/kg against an ethanol-induced gastric ulcer model in mice. Prior treatment of plant extract also decreased ulcer index in chronic state in Pylorus ligated mice model. At higher concentration (150 mg/kg), the plant extract increased protein and glutathione levels significantly. Moreover, concentration-dependent significant reduction was observed in gastric secretion, free acidity and total acid output in extract-treated animals suggesting potential of gastroprotection of plant extract through regeneration of gastric mucosal injury (59).

Renal protective study

Renal protective activity of *D. gangeticum* was observed along with antidiabetic activity in Streptozotocin-induced diabetic rats. The administration of *D. gangeticum* ethanolic extract (100, 200 and 400 mg/kg body weight) for 30 days lowered levels of renal markers (Blood Urea Nitrogen (BUN), Serum Creatinine and Urea) in dose depending manner, indicating its renal protective potential (60).

Hepatoprotective Activity

The hepatoprotective activity of *D. gangeticum* against paracetamol in toxicated rats was tested using Wistar albino rats. It reduced the serum ALT (Alanine aminotransferase), ALP (alkaline phosphatase), AST (Aspartate aminotransferase), LDH (lactate dehydrogenase), GGT (gamma-glutamyl transferase), total protein and bilirubin levels. It showed that *D. gangeticum* significantly attenuated hepatotoxicity (61).

Antitussive activity

D. gangeticum provided 52.51 % protection against SO₂ generated cough reflexes in mice in antitussive efficacy against SO₂ induced cough reflexes (62).

Anti-histaminic activity

The *in vitro* anti-histaminic activity was investigated against histamine-induced contraction of isolated guinea pig ileum. At the dose of histamine (100 ng/ml bath fluid), *D. gangeticum* produced 41.33% inhibition of histamine-induced contraction of guinea pig ileum (62). In another study on the same model, *D. gangeticum* produced 41.86% inhibition of histamine-induced contraction of guinea pig ileum (43).

Antidiarrheal activity

Antidiarrheal activity against castor oil-induced diarrhea was conducted in Wistar albino rats. A concoction of *D. gangeticum* showed significant antidiarrheal activity against castor oil-induced diarrhea in rats compared to the castor-oil control group (43).

In vitro Mast cell stabilization study

In vitro Mast cell stabilization study, the aqueous and methanolic extract of *D. gangeticum* exerted the mast cell stabilization effect in a dose-dependent manner against control (compound 40/80) in the isolated mesentery of albino rats (43, 62).

Clinical study

Bronchitis

A randomized, open-labeled, single-centric clinical trial was conducted for evaluating efficacy of *D. gangeticum* on bronchitis. Arm of patients was treated with 50 ml decoction of *D. gangeticum* and another with 50 ml decoction of *Pseudarthria viscida* for 2 weeks. Participants were randomly divided into *D. gangeticum* and *P. viscida* groups. *D. gangeticum* exhibited better effectiveness compared to *P. viscida* on bronchitis symptoms. However, the difference was not statistically significant. The small sample size, open-labeled study and Ayurvedic drug control were limitations. Thus, *D. gangeticum* needs to be further evaluated in a sufficient sample size with a standard control from a conventional system of medicine to assess the effect on bronchitis (62).

Gout

The effectiveness of *D. gangeticum* on *Vatarakta* (gout) was investigated through a randomized, double-blind, single-centric clinical trial. In the trial, total 76 participants were randomized equally in two arms, receiving either 50 ml decoction of *D. gangeticum* or *Flemingia strobilifera* for one month. At the end of the trial, symptomatic improvement was observed in both groups (63). In another randomized, double-blind, single-centric clinical trial, comparing the effect of *D. gangeticum* and *Desmodium laxiflorum* on gout (*Vatarakta*), was conducted (64). Total 66 patients were randomized, wherein 33 were treated with *D. gangeticum* decoction and 33 with *D. laxiflorum* decoction for one month. The outcome was clinical improvement in the symptoms. At the end of the trial, clinical improvement was observed in both groups. The small sample size and Ayurvedic drug control were limitations of both trials. Thus, further study on *D. gangeticum* is needed with a sufficient sample size and having appropriate control to assess its effect on gout.

Hypertension

The effect of the drug on hypertension was also assessed by randomized control trial. Patients were randomly divided into two groups (30 each group). One group of patients were treated with active control Telmisartan-20 mg or 40 mg per day, and another group of patients with *Shalaparni Ksheerapaka* (*D. gangeticum* processed with milk), 150 ml twice a day for 45 days. The active control Telmisartan reduced blood pressure better compared to it. However, *D. gangeticum* improved the hypertension symptoms and the cholesterol level. The sample size was small which compelled further clinical evaluation (65).

Discussion

D. gangeticum is believed to be native to India and also found in tropical Africa and Australia. Other than that, it has also been famously used as medicinal herbs, mainly as an ingredient of *Dashamoola* formulation in Ayurveda, the Indian traditional system of medicines since ancient times. Its documented therapeutic uses recorded in Ayurvedic texts are oedema, fever, cough, worm infestation, dysp-

noea, diarrhoea, vomiting, pain and inflammation. Other than that, it is also used therapeutically in various ways by many ethnic groups for snake bites, diuretic, antitoxic, goiter, gynecological diseases, premature ejaculation, cold, abdominal pain and menstrual ache. Many of these claims have been evaluated experimentally via *in vitro* and *in vivo* techniques of biological evaluation and confirmed its bio-activities.

Due to high medicinal values, its root, stem and leaves have been evaluated extensively through phytochemical investigations and revealed many bio-active phytochemical contents, viz. Gangeticoside, Leonurisode A, Methyl benzoate 2-O- β -D-glucopyranoside, Tortoside A, Dehydrosoyasaponin, gangetin, gangetinin, desmocarpin, desmodin etc. Further, phytochemical and *in-silico* study assessing ADME properties of selected pterocarpan of *D. gangeticum* viz. gangetin, gangetinin, desmocarpin and desmodin revealed drug-likeness of molecules (66). It may lead to further exploration of these molecules for effective drug development. There is still a lot of confusion about the pharmacological effects of plants that are influenced by their known or unknown compounds. Thus, structure-guided isolation and identification of the bioactive components are needed to understand these active compounds' structure-activity relationship.

Experiment on animal models suggested *D. gangeticum* can be confirmed to possess anti-inflammatory, antinociceptive, anti-amnesic, antidiabetic, anti-ulcer, anti-bacterial, antidiarrheal and antioxidant, antitussive, anti-histaminic, hepatoprotective, renal protective and cardioprotective activities. However, the biochemical mechanisms of *D. gangeticum* on the human body remain largely unexplored. Various bio-activities of *D. gangeticum* may be attributed to multiple compounds rather than a single molecule. *D. gangeticum* containing multi-components may produce multi-target activities that are difficult to detect by the present pharmacological one-target, one-drug approach. A new approach is required to understand multi-component effects of traditional medicine's effects. Network pharmacology, a novel approach in systems biology, may satisfy the need for herbal medicines and effectively explore the mechanism of the biochemical pathway for multi-components herbs (67, 68).

Presently, natural source is its only source. As *D. gangeticum* is a high-demand herb of Ayurveda, its root is being collected from natural source. It may lead to its scarcity and adulteration in the market for commercial purposes. Ayurvedic Pharmacopoeia of India also recommended the whole plant alternate to the root (69). An effort has also been made to find alternate sources for the root. Aerial parts and other closely related *Desmodium* species were evaluated for alternate sources through insufficient preliminary investigations (70, 71). However, further experiments were highly warranted to confirm the alternate source. Adulteration is a considerable concern for traditional medicines due to the lack of an effective quality control system that provides genuine and high-quality herbs for therapeutic use. The scientific and reliable quality assurance system complying with the characteristics of traditional medicine is yet to be entirely con-

structured.

Considering traditional Ayurvedic uses and preliminary animal experiments, few clinical trials were conducted to evaluate the therapeutic effect of *D. gangeticum* on various diseases, viz. hypertension, bronchitis and gout, and showed a trend towards benefits. However, its findings are uncertain as all trials had a small sample size and concern of bias. Well-designed randomized clinical trials are warranted to prove the therapeutic benefits of the species.

Conclusion

Desmodium gangeticum has been used in Ayurvedic medicine for centuries. The thorough literature review revealed that it is an essential source of medicinally important compounds such as gangetin, gangetinin, desmocarpin and desmodin. The plant has also been widely studied for its various pharmacological activities like anti-inflammatory, antinociceptive, antioxidant, cardioprotective, antidiabetic, hepatoprotective, antibacterial and anti-amnesic activities. It was also evaluated clinically in bronchitis, gout, hypertension for possible therapeutic benefits through clinical trials. Despite the positive results of the review, there are some limitations observed in the present literature on the use of the plant as a multi-purpose therapeutic agent. The biochemical and physiological mechanisms involved in the different biological effects exhibited by *D. gangeticum* need to be investigated. Further research is required focusing pharmacodynamic, pharmacokinetic and safety profiles to validate its efficacy reported through preliminary animal experimentations. Moreover, well-designed RCTs should be conducted to support its therapeutic use.

Authors contributions

DV participated in data search, wrote the original draft and serve as a corresponding author. HV contributed to conception and designing of article and reviewed the original draft. KP and BP interpreted the data, reviewed and edited the original draft critically. PS, AV and SP contributed in data search and writing the original draft. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

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