Ethnopharmacology, phytochemistry, and pharmacology of *Polygonum glabrum* Willd

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Abstract

The current paper reviewed the ethnomedicinal uses, phytochemistry, and pharmacology of *Polygonum glabrum* Willd. belonging to family *Polygonaceae*. All the available information on the traditional uses, phytochemistry, and pharmacology of *P. glabrum* was gathered through a library and electronic searches in Google Scholar, PubMed, Science Direct, and SciFinder for the period, 1886-2016. The plant *P. glabrum* was usually known as *Rasna* found almost in all parts of India ascending to an altitude of 1900 m from the sea level. *P. glabrum* is an important medicinal plant in the Indian system of medicine (Ayurveda). This plant is used by ethnic groups for the treatment of pain, jaundice, piles, pneumonia, burn, wound, etc. Major phytochemical compounds reported from the leaves and aerial parts of *P. glabrum* belong to sesquiterpenoids, flavonoids, and sterol which have a wide range of biological activities. Pharmacological activities reported for the plant *P. glabrum* are anti-inflammatory, analgesic, antifungal, antibacterial, antidepressant, hepatoprotective, antioxidant, antimalarial, nephroprotective, anti-HIV, antidiabetic, and antiproliferative activity. Present available information revealed that more than 27 compounds isolated from the different plant parts of *P. glabrum*. Most of the compounds isolated from the leaves and aerial part of *P. glabrum* belong to flavonoids category which has a wide range of biological activities. Clinical study of isolated compounds may be performed to get prospective candidates for the treatment of cancer, liver disorders, malaria, and cardiovascular, neurological, and renal diseases.

Key words: Antimalarial activity, flavonoids, nephroprotective, *Polygonum glabrum*, Rasna

INTRODUCTION

*Polygonum glabrum* Willd. (*Polygonaceae*) is usually known as *Rasna* in Indian system of medicine (Ayurveda). The genus Polygonum includes 150 species, in which 79 are known to occur in India.[1] The genus Polygonum is a rich source of flavonoids.[2] It is commonly distributed along riverbanks, marshy areas, and stream side, ascending to an altitude of 1900 m from sea level. *P. glabrum* is a glabrous perennial annual herb. Roots are arising from proximal nodes, and rhizomes are present. Erect and branched stem, 70-100 cm tall without noticeable ribs, glabrous or pubescent distally, and sometimes glandular-punctate. Light brown leaves, cylindrical 12-30 mm, truncate margins, chartaceous and inflated base, eciliate and glabrous surface, 8-10 mm petiole, scabrous leaf blade without dark triangular or lunate blotch adaxially, lanceolate or oblong-lanceolate, tapered base, glabrous margin, acute to acuminate apex, and glabrous or scabrous faces along with mid-veins. Terminal inflorescences, spicate, usually with numerous dense spikes aggregated and panicle like; funnel-shaped bracts, not ciliate, usually each 3 or 4 flowered. Pedicel large longer than bracts, articulate at apex. Perianth white or pinkish, elliptic tepals 3-4 mm, slender veins, furcate at the apex, not curved downward. Achenes included in persistent perianth, dark brown to brownish black, shiny, smooth, ovoid, biconvex, 2.5-3 mm.[3]

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Phytochemistry

Phytochemical compounds isolated from the different parts of *P. glabrum* are mentioned in Table 1.

Pharmacology

**Analgesic activity**

Analgesic effect of aqueous extract of leaves of *P. glabrum* was performed in albino rats and mice of either sex by the tail-flick latent period, formalin-induced paw licking in rat, and hot plate reaction time and acetic acid-induced writhing test in mice. Aspirin (25 mg·kg\(^{-1}\), i.p.), pentazocine (10 mg·kg\(^{-1}\), i.p.), and indomethacin (5 mg·kg\(^{-1}\), i.p.) are used as the standard drug. At doses 25, 50 and 100 mg·kg\(^{-1}\) of aqueous extract of leaves of *P. glabrum* were shown higher latency of percentage protection than standard drug. At a dose of 100 mg·kg\(^{-1}\), 80.35% inhibition was found in acetic acid-induced writhing in mice, whereas in tail-flick model, hot plate, the highest enhanced reaction time was observed at 100 mg·kg\(^{-1}\) 12.95 ± 0.24 at 4 h, 4.11 ± 0.16 at 3 h at 100 mg·kg\(^{-1}\) aqueous extract of leaves of *P. glabrum* reduce licking time formalin-induced paw licking was found to be 19.02 ± 2.36 as compared to standard (35.33 ± 2.12).\(^{[35]}\)

**Anti-inflammatory activity**

The anti-inflammatory activity of the aqueous and ethanol extract of the stems of *P. glabrum* was evaluated by carrageenan-induced paw edema, cotton pellet-induced granuloma, formaldehyde-induced arthritis, and adjuvant-induced poly-arthritis tests to determine its effects on acute and chronic phase of inflammation models in rats. Aqueous extract and ethanol extract at a dose of 200 mg·kg\(^{-1}\) i.p. route showed maximum inhibition (0.12 ± 0.02, 0.15 ± 0.01). Oral administration of aqueous extract at the dose of 400 mg·kg\(^{-1}\) and ethanolic extract at the dose of 600 mg·kg\(^{-1}\) exhibits considerable reductions in Carrageenan induced pedal oedema. In the chronic model, croton oil-induced granuloma, formaldehyde-induced arthritis, and ethanol extract of the stem of *P. glabrum* showed maximum inhibition (73.4% and 60.4% at 4 h) at a dose of 50 mg·kg\(^{-1}\). After 18 h of injection for adjuvant-induced polyarthritis showed significant inhibition 49.7%.\(^{[36]}\)

**Antipyretic activity**

Methanol extract of the rootstocks of *P. glabrum* was evaluated for its antipyretic potential on brewer’s yeast-induced hyperpyrexia in albino rats. Yeast suspension (10 ml·kg\(^{-1}\))
increased rectal temperature 18 h after subcutaneous injection. Methanol extract of the rootstocks of *P. glabrum* at doses of 200 and 400 mg·kg⁻¹, p.o. produced a significant reduction in yeast induced an elevated temperature in a dose-dependent manner. The effect extended up to 3 h after the drug administration. The antipyretic effect of methanol extract of rootstocks of *P. glabrum* was found comparable to that of standard drug paracetamol (400 mg·kg⁻¹, p.o.).[37]

**Hepatoprotective activity**

Protective and curative effect of ethanol extract of leaves of *P. glabrum* against carbon tetrachloride (CCl₄)-induced hepatotoxicity in rats was examined. CCl₄ (1 ml·kg⁻¹) given through intraperitoneal route caused liver damage in rats manifested by considerable rise in serum enzymes levels, turn down in reduced glutathione (GSH) level, and increase in malondialdehyde (MDA) levels. The oral administration of ethanol extracts of leaves of *P. glabrum* in a dose of 400 mg·kg⁻¹ to CCl₄ intoxicated rats produced significant percentage increase in the reduced GSH levels with noteworthy decrement in MDA as well as transaminase levels. Histopathological change of liver sections confirmed that prophylactic and healing treatments with ethanol extract of leaves of *P. glabrum* resulted in a comparatively excellent protection against CCl₄ intoxicated rats.[38]

**Antioxidant activity**

Pretreatment with ethanol leaves extract of *P. glabrum* at doses 200 and 400 mg·kg⁻¹ for 8 days illustrated significantly higher levels of catalase, superoxide dismutase, and GSH in accumulation to significant lower levels of hepatic MDA as evaluated to CCl₄ intoxicated rats.[39] *In vitro* antioxidant activity of methanol leaves extract of *P. glabrum* was performed. Methanol leaves extract of the *P. glabrum* exhibited strong scavenging effects on 2,2-diphenyl-2-picryl hydroxyl free radicals, with inhibitory concentration 50% (IC₅₀) were 79.81 µg·mL⁻¹, respectively.[39]

**Antifungal activity**

The antifungal activity of the methanol extracts of leaves of *P. glabrum* was tested against *Candida albicans* and *Candida tropicalis*. Methanol extracts of *P. glabrum* did not show any noteworthy inhibition in the concentration range tested.[39]

**Antimicrobial activity**

The antibacterial activity of the methanol leaves extracts of *P. glabrum* exhibited restrained activity against all the tested pathogens such as *Staphylococcus aureus*, *Micrococcus luteus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, with a highest zone of inhibition of 11, 10, 10, and 11 mm, respectively.[40] In another activity, the antibacterial activity of a different part and extract of *P. glabrum* was tested against three Gram-positive (*Bacillus subtilis*, *Bacillus cereus*, and *S. aureus*) and one Gram-negative (*Proteus vulgaris*) bacterial strain. Ethyl acetate extract of leaves of *P. glabrum* showed 8 mm of zone of inhibition aligned with *B. subtilis* and *P. vulgaris*. Methanol extract of *P. glabrum* stem illustrated 8 mm of zone of inhibition against *B. subtilis*, whereas methanol extract of the flower and leaves of *P. glabrum* showed 12 mm and 10 mm zone of inhibition against *P. vulgaris*. Each and every extract of *P. glabrum* did not show inhibition against *B. cereus*.[40] The ethanol extract of the leaves of *P. glabrum* was evaluated against two Gram-positive bacteria (*S. aureus* and *Bacillus subtilis*) and three Gram-negative bacteria (*E. coli*, *P. vulgaris*, and *P. aeruginosa*). The ethanol extract of *P. glabrum* showed a major activity against Gram-positive bacteria with inhibitory action almost similar to 40 µg·mL⁻¹ of gentamycin and against Gram-negative bacteria with inhibitory action almost similar to 10 µg·mL⁻¹ of standard drug (gentamycin) with showed no any effect against *E. coli*.[41]

**Toxicity Study**

Crude ethanol extract of *P. glabrum* was evaluated for toxicity effect. Hematological test showed a normal range between blood parameter, sample, and control. Liver and kidney function tests showed no significant difference excluding creatinine ranges which have showed a significant difference with control.[41]

**Antimalarial activity**

*In vitro* study of ethanol extract of the leaves of *P. glabrum* against *Plasmodium falciparum* was showed a significant effect with IC₅₀ 6.6 µg·mL⁻¹.[41]

**Nephroprotective activity**

The nephroprotective effect of the methanol extract of whole plant of *P. glabrum* was evaluated in cisplatin- and gentamycin-induced albino rats. Rats were administered whole plant of methanol extract (200 and 400 mg·kg⁻¹ for 14 and 8 days, respectively) by the oral route. While control drugs (cisplatin 12 mg·kg⁻¹ and gentamycin 80 mg·kg⁻¹) were given through intraperitoneal route. Treatment with extract at a dose of 200 and 400 mg·kg⁻¹ bw showed a significant enhancement in body weight, serum, urine urea, uric acid, total protein, and creatinine when compared with control. Histopathological examination showed that methanol extract of the whole plant of *P. glabrum* protected the glomerular and tubular tissue from cisplatin- and gentamycin-induced damage enormously.[42]

**Anti-HIV activity**

Compound 2-methoxy-2-butenolide-3-cinnamate isolated from methanol extract of the aerial parts of *P. glabrum* confirmed promising *in vitro* anti-HIVI activity against HIV1UG070 (X4, subtype D) and HIV1VB59 (R5, subtype C). Which have been evaluated using TZMbl cell lines with IC₅₀ in the range of 15.68-22.43 µg·mL⁻¹. The methanol extract showed TI with IC₅₀ in the range of 10.90-15.55 µg·mL⁻¹.[29]
Anti-mycobacterium activity

Compound 2-methoxy-2-butenolide-3-cinnamate, 3-hydroxy-5-methoxystilbene and pinocembrin isolated from methanol extract of the aerial parts of *P. glabrum* revealed *in vitro* anti-Mycobacterium activity aligned with *Mycobacterium tuberculosis* H37Ra with IC50 values of 1.43, 3.33, and 1.11 μg.mL⁻¹ in immature phase and 2.27, 3.33, and 1.21 μg.mL⁻¹ in active phase, respectively.[29]

Antiproliferative activity

Compound pinocembrin isolated from methanol extract of the aerial parts of *P. glabrum* was evaluated on cell growth in acute monocytic leukemia cell line THP-1, lung A549 adenocarcinoma, cervix adenocarcinoma HeLa, and MCF7 human mammary gland/breast adenocarcinoma epithelial cell line by a standard 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay for measuring cellular proliferation. Isolated compound was found to be the most active antiproliferative with IC50 values of 1.88-11 μg.mL⁻¹ aligned with HeLa, A549, Panc1, THP1, and MCF7 cell lines.[29]

### Table 1: Phytoconstituents of *P. glabrum*

<table>
<thead>
<tr>
<th>Plant part</th>
<th>Nature</th>
<th>Extract</th>
<th>Compound</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerial parts</td>
<td>Butenolide cinnamate</td>
<td>Methanol extract</td>
<td>2-methoxy-2-butenolide-3-cinnamate (1), β-hydroxyfriedalanol (2), 3-hydroxy-5-methoxystilbene (3), pinocembrin (4), sitosterol-(6'-O-palmitoyl)-3′-O-β-α-glucopyranoside (5), pinocembrin-5-methyl ether (6) sitosterol-3-O-β-α-glucopyranoside (7)</td>
<td>[29]</td>
</tr>
<tr>
<td>Leaves</td>
<td>Sesquiterpenes</td>
<td>Aqueous methanol extract</td>
<td>Warburganal (8), polygodial (9), 2α,3β-diangeloyloxyisodrimeninol (10), 2α-Angeloxytoxy-3′β,2′-methylbutanoyloxyisodrimeninol (11), 2α-angeloyloxy-3′β-2′-methylpent-2′enoyloxyisodrimeninol (12), 2α-Angeloxyloxy-3′β-2′ methyl-pentanoyloxyisodrimeninol (13), 2α,3β-ditigloyloxyisodrimeninol (14)</td>
<td>[30]</td>
</tr>
<tr>
<td>Leaves</td>
<td>Fatty acids and esters</td>
<td>Petroleum ether</td>
<td>3, 4-Bis (3,4,5 trimethoxyphenyl)-1-[2-(4-methoxyphenyl) ethyl] pyrrole-2,5-dicarboxylic acid, (15) (2RS)-1,3,8-trimethyl-4-propyl-5-ethyl-2-(1-hydroxyethyl)-7-methoxycarbonyl-6-gamma-methylene carboxyl-7-porphine (14) hexadecanoic acid, methyl ester (15) 1,2-benzenedicarboxylic acid, isodecylcoyloxy ester (15)</td>
<td>[31]</td>
</tr>
<tr>
<td>Leaves</td>
<td>Flavonol-glycoside</td>
<td>Ethanol extract</td>
<td>Quercetin (19), rutin (20), rhamnetin (21), quercitrin (22), avicarlin (23)</td>
<td>[2]</td>
</tr>
<tr>
<td>Whole Plant</td>
<td>Pyrogallol, alcoholic, and sulfur compound</td>
<td>Ethanol extract</td>
<td>1,2,3 benzene triol (16) 1, 14 tetradecanediol (17), thioephene-2-carboxamide, N-(2-furfuryl) (18)</td>
<td>[32]</td>
</tr>
<tr>
<td>Stem and seeds</td>
<td>Polyphenols</td>
<td>Ethanol extract</td>
<td>Vanillic (24a), syringic (24b), protocatechuic acid (25), gallic (26), and cis and trans -p coumaric acids (27)</td>
<td>[33]</td>
</tr>
<tr>
<td>Flowers</td>
<td>Glycosides</td>
<td>Ethanol extract</td>
<td>Delphinidin-3,5-diglucoside and cyanidin-3,5 diglucoside</td>
<td>[34]</td>
</tr>
</tbody>
</table>

*P. glabrum: Polygonum glabrum*
positively significant results, but it has been observed that a good tolerance of isolated substance was found in white mice at a dose of 400 mg·kg$^{-1}$.

Antidepressant and brain neurotransmitters activity

Aqueous extract of leaves of *P. glabrum* was evaluated preclinically for its recognized antidepressant activity in rodents. The aqueous extract of *P. glabrum* was evaluated by depression of animal models including behavioral despair and tail suspension test; L-dopa induced hyperactivity along with aggressive behavior model. At doses of 50, 100, and 200 mg·kg$^{-1}$, p.o. for 3 repeated days has significantly decreased the period of immobility in the behavioral despair and tail suspension test in rats and mice, respectively, as compared to the standard drug imipramine (15 mg·kg$^{-1}$, i.p.). In the tail suspension test, antidepressant effect of elevated dose (200 mg·kg$^{-1}$ p.o.) of *P. glabrum* was found more significant than standard drug. *P. glabrum* has revealed a dose-related increase in L-dopa-induced hyperactivity. A significant increase in the levels of dopamine and serotonin and a decrease in the levels of norepinephrine have been reported.

Antidiabetic activity

Antidiabetic activity of methanol extract of leaves of *P. glabrum* was estimated in alloxan-induced diabetic rats. Alloxan-induced diabetic rats were administered methanol leaves extract (200 and 400 mg·kg$^{-1}$, p.o.) of the plant drug or vehicle (water) or standard drug glibenclamide (10 mg·kg$^{-1}$) for 28 days. Sample of blood was collected by retro-orbital
Sharma and Gautam: Phytochemistry and pharmacology of Polygonum glabrum

puncture technique and was evaluated for blood glucose level on days 0, 7, 14, 21, and 28, whereas serum glucose level, lipid profile, and histopathological changes in the pancreas were checked after 28 days. For oral glucose tolerance tests, glucose (2 g·kg⁻¹, p.o.) was received to non-diabetic control rats treated with glibenclamide (10 mg·kg⁻¹, p.o.) and methanol leaves extract of *P. glabrum*. The Methanol extract of leaves of *P. glabrum* was evaluated for anti-diabetic activity in alloxan-induced diabetic rats. The diabetic rats were administered methanol leaves extract at a dose of 200 and 400 mg·kg⁻¹, p.o.) and a standard drug (glibenclamide) administered at a dose of (10 mg·kg⁻¹) for 28 days. Blood samples were collected by retro-orbital puncture and were analyzed for serum glucose level using glucose oxidase-peroxidase reactive strips. Methanol leaves extracts of *P. glabrum* at a dose of 400 mg/kg showed the reduction in the fasting blood glucose levels whereas the histopathological studies of the rat pancreas showed recovery of the alloxan-induced damage of the insulin-secreting beta pancreatic cells. In the oral glucose tolerance test, methanol extract of *P. glabrum* increased the glucose tolerance.¹⁴⁶

**Cytotoxic activity**

Methanol extract of leaves of *P. glabrum* and its fractions were evaluated for cytotoxic activities against artemia salina for a 1 day. Vincristine sulfate was used as positive control. Among all fractions, the crude methanol extract showed significant cytotoxic activity having LC₅₀ value 0.74 ± 0.045 μg.mL⁻¹.²²

**Membrane stabilizing activity**

Methanol extract of leaves of *P. glabrum* and its fractions were screened for membrane stabilizing activity. At concentration 1 mg.mL⁻¹, different fractions of *P. glabrum* protected the hemolysis of red blood cell induced by hypotonic solution and heat as compared to the standard drug (aspirin). The crude methanol extracts inhibited 79.21 ± 0.44% (hypotonic solution) and 84.87 ± 0.23% (heat induced) of hemolysis of red blood cell induced by hypotonic solution and heat as compared to 71.9 ± 0.73% and 42.12 ± 0.37% by standard drug, respectively.²²

**Thrombolytic activity**

Methanol extract of leaves of *P. glabrum* and its fractions were evaluated for thrombolytic activity using streptokinase as the standard substance. At 100 μL, standard drug showed 65.16 ± 0.48% lysis of clot after subsequent incubation for 90 min at 37°C. On the other hand, distilled water was treated as negative control which exhibited a negligible percentage of lysis of clot 2.41 ± 0.27%. In this study, methanol extract of *P. glabrum* exhibited highest thrombolytic activity (35.17 ± 0.42%).²²

**CONCLUSION**

In the present study, data gathered on ethnopharmacology, phytochemistry, and pharmacology of the different plant parts of *P. glabrum* up to February 2016. Literature review revealed that more than 27 compounds isolated from the different plant parts of *P. glabrum*. Most of the compounds isolated from the leaves and aerial part of *P. glabrum* belong to flavonoids category which has a wide range of biological activities. 2-methoxy-2-butenolide-3-cinnamate, 3-hydroxy-Smexoxystilbene, and pinocembrin [Table 1] isolated from the methanol extract of the aerial parts of *P. glabrum*, in which only pinocembrin showed antiprofibrerative activity, whereas all three compounds were showed antimycobacterium activity. Literature survey revealed that *P. glabrum* is an important medicinal plant [Table 2]. Additional clinical study of isolated compounds may be performed to get prospective candidates for the treatment of cancer, liver disorders, malaria, and cardiovascular, neurological, and renal diseases.

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