REVIEW ARTICLE

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, ecilliate 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

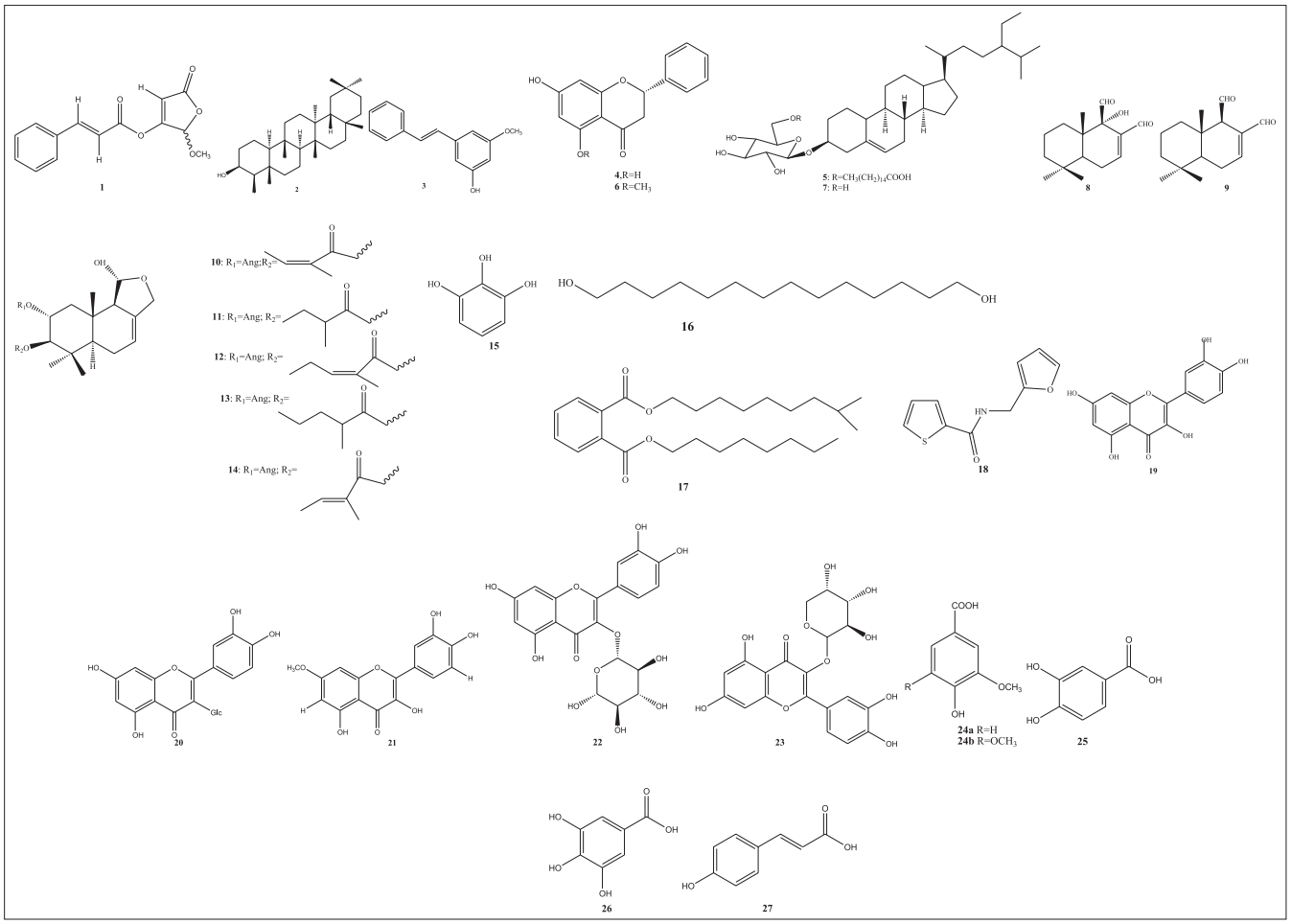
Analgesic effect of aqueous extract of leaves of *P. glabrum* was performed in albino rats and mice of either sex by the tail-flick latent period, formalin-induced paw licking in rat, and hot plate reaction time and acetic acid-induced writhing test in mice. Aspirin (25 mg.kg^{-1}, i.p.), pentazocine (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 adjutant-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 adjutant-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 (CCl_4)-induced hepatotoxicity in rats was examined. CCl_4 (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 CCl_4 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 CCl_4 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 CCl_4 intoxicated rats.[35] *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% (IC_{50}) 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.[35] 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 showed 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 IC_{50} 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-HIV1 activity against HIV1UG070 (X4, subtype D) and HIV1VB59 (R5, subtype C). Which have been evaluated using TZMbl cell lines with IC_{50} in the range of 15.68-22.43 µg.mL^{-1}. The methanol extract showed TI with IC_{50} 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 IC_{50} 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, pancreatic PANC-1 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 IC_{50} values of 1.88-11 μg.mL^{-1} aligned with HeLa, A549, Panc1, THP1, and MCF7 cell lines.[29]

Antileishmanial activity

In vitro antileishmanial activity of aqueous extract of the whole plant of *P. glabrum* was performed against *Leishmania tropica.* 96 healthy flat bottoms enzyme-linked immunosorbent assay plate were used for incubation at 25°C for 72 h. At concentration of 500 μg.mL^{-1}, lethal concentration 50% (LC_{50}), LC_{90}, and R^2 values were found to be 7.25, 227.4, and 0.97 μg.mL^{-1} while to amphotericin B (standard drug) values of LC_{50}, LC_{90}, and R^2 were found to be 0.35, 9.49, and 0.91 μg.mL^{-1}, respectively.[43]

Molluscicidal and anthelmintic activity

Invitro molluscicidal activity of pure anthelmintic stuff has been isolated from the aqueous and crude extract of leaves of *P. glabrum* has been evaluated against *Biomphalaria glabrata* and *Lymnaea truncatula* Mull. Crude extract showed 100% and 40% mortality against *B. glabrata* and *L. truncatula,* respectively, whereas pure anthelmintic stuff showed 100% mortality against *P. glabrata* and *L. truncatula* at 10.5 and 21 ppm, respectively after exposure of 1 day. *In vivo* anthelmintic activity of leaves of *P. glabrum* was performed against *Hymenolepis nana* var *fraternal* of the mouse at dose of 200-600 mg·kg^{-1}. At this dose level gave no

Table 1: Phytoconstituents of *P. glabrum*

Plant part	Nature	Extract	Compound	Reference
Aerial parts	Butenolide cinnamate	Methanol extract	2-methoxy-2-butenolide-3-cinnamate (1), *β*-hydroxyfriedalanol (2), 3-hydroxy-5-methoxystilbene (3), pinocembrin (4), sitosterol-(6′-*O*-palmitoyl)-3-*O*-*β*-*d*-glucopyranoside (5), pinocembrin-5-methyl ether (6) sitosterol-3-*O*-*β*-d-glucopyranoside (7)	[29]
Leaves	Sesquiterpenes	Aqueous methanol extract	Warburganal (8), polygodial (9), 2*α*,3*β*-diangeloyloxyisodrimeninol (10), 2*α*-Angezoytoxy-3*β*-2’ methylbutanoyfoxyisodrimeninol (11), 2*α*-angeloyloxy-3*β*-2’-methylpent-2’enoyloxyisodrimeninol (12), 2*α*-Angeloyloxy-3*β*-2’ methyl-pentanoyloxyisodrimeninol (13), 2*α*,3*β*-ditigloyloxyisodrimeninol (14)	[30]
Leaves	Fatty acids and esters	Petroleum ether	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-methoxycarbonylethyl-6-gamma-methylenecarbonyl-porphine (14) hexadecanoic acid, methyl ester (14) 1,2-benzenedicarboxylic acid, isodecyloctyl ester (15)	[31]
Leaves	Flavonol-glycoside	Ethanol extract	Quercetin (19), rutin (20), rhamnetin (21), quercitrin (22), avicularin (23)	[2]
Whole Plant	Pyrogallol, alcoholic, and sulfur compound	Ethanol extract	1,2,3 benzene triol (16) 1, 14 tetradecanediol (17), thiophene-2-carboxamide, N-(2-furfuryl) (18)	[32]
Stem and seeds	Polyphenols	Ethanol extract	Vanillic (24a), syringic (24b), protocatechuic acid (25), gallic (26), and *cis* and *trans* -pcoumaric acids (27)	[33]
Flowers	Glycosides	Ethanol extract	Delphinidin-3,5-diglucoside and cyanidin-3,5 diglucoside	[34]

P. glabrum: Polygonum glabrum

Table 2: Ethnomedicinal uses of *P. glabrum*

Place/country	Part (s) used	Preparations	Ethnomedical uses	References
Jharkhand/India	Whole plant	decoction	Fever and colic pain	[4]
Maharashtra/India	Root	Paste	Contraceptive	[5]
Mahabubnagar, Andhra Pradesh/India	Whole plant	Juice	Bone fracture for bone setting	[6]
Tamil Nadu/India	Root	Decoction	Piles, Jaundice, constipation	[7]
Mumbai/India	Leaves	Infusion	Relieve in colic pain	[8]
Chota Nagpur/India	Leaves	Stitch up	Wound	[8]
Assam/India	Leaves	Decoction	Fever	[8]
Tirumala Hills, Andhra Pradesh/India	Whole plant	Decoction	Jaundice, throat pain, headache, scorpion sting, burns, cuts	[9,10]
Tirunelveli, Tamil Nadu/India	Whole plant	Paste mixed with oil	Cuts and wounds	[11]
Khyber Pakhtunkhwa/ Pakistan	Whole plant	powder	Fish hunting	[12]
Jhalod Taluka, Gujarat/India	Root	Mixture of fennel seeds, candy sugar with powder	Progeny less	[13]
Mangalore/India	Root stocks	Decoction	Piles, jaundice debility, and consumption	[14,15]
Kumar Parvatha, Karnataka/ India	Leaves	Infusion	Febrifuge	[15]
Kalinjar Hillock/India	Leaves, roots	Decoction	Piles	[16]
Wayanad, Kerala/India	Leaves	Juice	Skin disorder (ectoparasites)	[17]
Sudan	Leaves	Juice	Anthelminthic, antimalarial	[18]
Gondia/India	Whole plant	Boiled paste	Cuts and wounds	[19]
Arunachal Pradesh/India	Root	Juice	Jaundice	[20,21]
Bahawalpur/Pakistan	Leaves	Infusion	Astringent, diuretic, rheumatism, and poison ivy rash	[22]
Eastern Ghat of Orissa/India	Leaves	Paste of leaves with *Piper longum* is given with honey	Fever and colic pain, unlock bone	[23,24]
Bihar, Uttar Pradesh/India	Leaves	Juice	Pneumonia	[25,26]
Latehar, Jharkhand/India	Leaves	Infusion	Vegetable	[27]
Chitral/Pakistan	Peels (stems)	Paste	Rheumatism	[28]

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}.[44]

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.[45]

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

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 $mg \cdot kg^{-1}$, 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 $mg \cdot kg^{-1}$, p.o.) and a standard drug (glibenclamide) administered at a dose of (10 $mg \cdot kg^{-1}$) 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.[46]

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 LC_{50} value 0.74 ± 0.045 $\mu g.mL^{-1}$.[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-5methoxystilbene, and pinocembrin [Table 1] isolated from the methanol extract of the aerial parts of *P. glabrum,* in which only pinocembrin showed antiproliferative 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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