Traditional uses, Pharmacology and Phytochemistry of National flower of Nepal Rhododendron arboreum: A Review

Md. Parwez Ahmad, Sheeza Ali, Shadma Wahab, Tarannum Perveen, Naiyer Shahzad, Dabal Bahadur Dhami

INTRODUCTION

The tree Rhododendron arboreum coming from family Ericaceae and found in Nepal, India, North America, Europe, Australia, Myanmar, Sri Lanka, Bhutan, Pakistan, China, Tibet and Thailand. This remarkable plant designated as the state flower of Nagaland, official flower of Chin state, also known as Nepal national flower and Uttarakhand state tree. It contains numerous nutrients, minerals and used for varieties of condition like energizing drinks, food colouring agent, decorations and firewood. Conventionally, it has been used for the correction of many ailments such as liver disorders, dysentery, epistaxis, heart and visual problem, asthma, stomachache, fever, diabetes, gout, oughs and hemorrhoids. In this review, we have an attempt to focus on ethnopharmacology, nutrition profile, Phytochemistry, and pharmacological activities. The different type of phytochemical substances was present in this plant like phenolics, flavonoids, flavonal glycosides, triterpenoid and steroids. The unprocessed extracts and extracted plant mixture showed several pharmacological actions such as hypoglycemic, reduce stress and anxiety, cytotoxic, decreased intestinal motility, antiinvasive, antioxidant and anti-inflammatory activity.

TRADITIONAL USES

Flowers of Rhododendron arboreum used conventionally for preparing adjuvant of a frozen dessert. Local sherbet was considered to be highly effective for the prevention of altitude sickness in hilly areas specially in mountain climbers are at the risk of developing altitude sickness. The plant also used as ancient medicine for various ailments such as diarrhoea, headache, stomach-ache, nasal bleeding, fever, and mental retardation. Nepali people use their flowers to prepared pickle. Fresh flower is used in many diseases like dysentery and dyspepsia, and roasted flowers petal in ghee are also sometimes were used as a medicine for dysentery. The juice or squash of flowers is highly useful in chronic disease like diabetes and heart diseases, and also for women ailment. Fresh or dried flower petals are also used for taking out fish bone in the gullet. The wood of the plant is used for charcoal and fuel. The grained wood of these plant is prepared for making khukri handles, pack saddles, gift-boxes, gunstocks and posts. Flowers and leaves of these plants are fixed in long ropes made of munja grass and also used to decorate the house and temple.
PHARMACOLOGICAL ACTIVITIES

Antioxidant activity

Ajaz Ahmad et al., were performed to find out the antioxidant potential of these plant (RAP) by using different specification in the animal model. The different doses of RAP were administered orally pre-treatment of animals for one week and then given by lipopolysaccharide (LPS) injection and were assessed the different behavioural parameters like open field changes, body temperature and burrowing. After 6 hours of LPS administration liver and renal function test were done. Oxidative stress markers such as SOD, CAT and MDA were measured in tissue and also measured the concentration of inflammatory markers like interleukin-6 (IL-6) interleukin-1beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) as well as VEGF, a specific sepsis marker. The test drug given group were significantly restored all the markers of liver and renal functions, antioxidant markers and also normalized plasma pro-inflammatory cytokines, thus preventing the multi-organ and tissue damage in LPS induced rats 15-16.

Anti-inflammatory activity

There were assessed the effect of R. arboreum bark for anti-inflammatory property and also done comparative studies of different fractions like chloroform, n-hexane, ethyl acetate, n-butanol and aqueous fractions of this plant. The ethyl acetate fraction showed the maximum analgesic effect (82%) seen in (200 mg/kg i.p.) in acetic acid-induced writhing, and not as much effective by both crude extract and chloroform fraction at a dose of 200 mg/kg i.p. and its fractions showed a dose-dependent recovery in carrageenan-induced mouse paw oedema and an anti-inflammatory activity for all time-courses (1-5 hrs). For the active portion (200 mg/kg i.p.), after 5 hour of carrageenan injection the maximum effect was observed 17.

Antiviral activity

Maneesh Lingwan et al., were assessed antiviral action of active constituents of these plant against varieties of virus by using both vitro and vivo, which prompted us to test against SARS-CoV-2. In vitro assays of hot aqueous extract R. arboreum petals confirmed the declined in viral load of SARS-CoV-2 in infected Vero E6 cells in dose dependent manner 18.

Antitumor activity

Methanolic solvent used for extraction of active moiety from bark of R. arboreum and successively partitioned into hexane, dichloromethane and ethyl acetate fractions, respectively. The novel cytotoxic agent, 15-oxoursolic acid extracted from ethyl acetate fraction by using column chromatography. For structure explanation of new compound were used different spectroscopic techniques i.e., IR, MS and 1D and 2D NMR. The cytotoxic studied there is specified human cancer cell lines [renal cell carcinoma (A498), non-small cell lung (NCI-H226), squamous cell carcinoma (H157) and human ovarian carcinoma (MDR-2780AD)] were used at the doses of 5-100 μM for a period of 72 h. Various wide spectroscopic techniques used for extracted ingredient for confirmation as 15-oxoursolic acid. There is 15-Oxursolic acid showed significant anticancer activity. The confirmation of polyphenol in Rhododendron arboreum leaves (MEL) and flowers (MEF) extract were used different type of chromatography.

There are 20 active constituents in leaves and 17 in the flowers established by GC-MS, while, amino acid analyzer revealed leaves contain 11 amino acids and flowers contain 10 amino acids. The analysis of extracts for antioxidant activity in vitro assays, antimitogenic activity in Ames assay and cancer cell growth inhibition activity by MTT (3-(4,5-dimethylthiazol-2,5-diphenylethrazolium bromide) assay. The extract revealed that have antimitogenic and anticancer potential 19-20.
Antidiabetic activity
There are four fractions of *Rhododendron arboreum* were used in control and streptozotocin induced diabetic rats for small duration and with fraction three for study for long term treatment completion, different type of biochemical parameters was tested including haemoglobin A1C, body weight, fasting glucose, plasma protein, insulin secretion, lipid profile and carbohydrate metabolism regulating enzymes of liver.

There is an active fraction exhibited a substantial decreased in haemoglobin A1C and blood glucose level at a dose of 200 mg/kg after the treatment in the diabetic rats in short term study. rats resulted in a significant decreased in haemoglobin A1C, blood glucose level, serum urea and creatinine while increase in insulin level similar to standard drug glybendamide after ingestion of active fraction (200 and 400 mg/kg) once daily for 30 days in streptozotocin induced diabetic rats.

Antihyperlipidemic activity
Neeraj Verma *et. al*, determined the Active fraction of *Rhododendron arboreum* extract administered in streptozocine induced diabetic rat. Significant fall in bad cholesterol like serum total cholesterol, triglycerides, low density lipoprotein cholesterol and very low-density cholesterol levels and increased in high-density lipoprotein cholesterol observed in the diabetic rats after treatment of test drug and its revealed antihyperlipidemic activity as demonstrated by.

Hepatoprotective activity
There is ethyl acetate fraction of *Rhododendron arboreum* of different dose was administered orally once daily for 14 days in CCl4 induced hepatotoxicity. The determination of liver function tests was calculated.

Increased serum enzymatic activities of SGOT, SGPT, SALP, γ-GT, and bilirubin and decreased activities of GST and glutathione reductase due to CCl4 treatment. After administration of test drug were restored the liver function parameters towards normal in a dose-dependent manner. Silymarin known hepato-protective effect, here it is used as reference drug also exhibited significant hepatoprotective activity after treatment against CCl4-induced hepatotoxicity in rats. After biochemical observations and histopathological assessment of rat liver sections showed strongly indicate that has a liver protection potential against CCl4-induced hepatotoxicity found in only ethyl acetate fraction.

Antimicrobial activity
Ethanol and methanolic extracts of *Rhododendron arboreum* were tested where using against Gram-negative, Gram-positive bacteria mainly *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica*, *Shigella sonnei*, *Staphylococcus aureus* and *Listeria innocua* respectively and also assessed the effect on fungal (*Candida albicans*) and viruses like yellow fever, chilangunya and enterovirus. Test drug was found dose dependent anti-bacterial, antifungal and anti-viral activity.

Anti-hypercholesterolemic activity
flower juice of *Rhododendron arboreum* Linn was tested in laboratory induced hypercholesterolemic rabbits and estimate the lipid profile like triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), atherogenic index (AI), high-density lipoprotein (HDL), and high-sensitivity c-reactive protein (CRP). Atorvastatin where used as standard drug. In this experiment four groups of rabbits were made to different treatments schedule for 8 weeks: First group was control group, second group was CHOL group (1% w/w cholesterol for 8 weeks), third group was S+R group (cholesterol 1% w/w and Arborium Plus for 8 weeks), and fourth group was (cholesterol 1% w/w and atorvastatin for 8 weeks). The results revealed that all the parameters were normalized in hypercholesterolemic rabbits in arboreum group.

Cardioprotective activity
Ethanol extract of *Rhododendron arboreum* its leaves showed protective effect in the myocardial ischemia induced by isoproterenol. Significantly decreased in the concertation of LDH (lactate dehydrogenase), ALT (alanine aminotransferase), and AST (aspartate aminotransferase) was in the rat serum for after pretreatment of these plant extract for 42 days in a dose-dependent manner as compared with disease group. Beside with the cardioprotective effect and have antioxidant potential might be due to the presence of flavonoids.

Antidiarrheal Activity
Neeraj Verma *et. al*, reported that oral administration of ethyl acetate fraction of *Rhododendron arboreum* (EFRA) flowers at different doses exhibited dose-dependent and highly significant antidiarrheal potential in castor oil and magnesium sulfate-induced diarrhea. Different doses of doses of EFRA (100, 200 and 400 mg/kg) also produced significant dose-dependent reduction in propulsive movement in castor oil-induced gastrointestinal transit using charcoal meal in rats. EFRA was reduced significantly weight and volume of colonic content in castor oil-induced experimental animals, its proofed antienteropoothing property of *Rhododendron arboreum*.

Immunomodulatory activity
The ethanol leaf extract treated mice showed significant conquest to the immune response. The ethanol extract test drug treated group was more effective compare to levamisole treated and control group. There was insignificant difference found in hepatic marker like Alanine transaminase (ALT), Aspartate transaminase (AST), serum total bilirubin and the weight of spleen and liver. Rawat *et. al* reported that TMS-10 (ursolic acid), CMS-3 (kaempferol) and RAM fr2 fraction, showed 79.67±0.57%, 67.67±2.08% and 40.3±1.5% stimulation respectively towards the phagocytic activity of neutrophils and also stimulated the phagocytosis in killed Candida albicans. The 1mg/ml concentration of TMS-10, CMS-3 and RAM fr2 had 7, 6.7 and 6.3 mean particle numbers respectively.

Adaptogenic activity:
The methanolic extract of *Rhododendron arboreum* showed potent anti-stress activity due to the presence of flavonoid to hydroethanol and aqueous extract as revealed by HPTLC analysis. The confirmed compounds may be accountable for the activity.

Anti fungal activity
The studied of different type extract of *R. arboreum* on multiple type of fungus and calculate the zone have inhibition. For ethanol flower extract the zone of inhibition at concentration 50 mg/ml as, (10mm) for *Aspergillus flavus* (9mm) *Candida albicans*, (8mm) *Aspergillus parasiticus* and for the water extract, (10mm) for *Candida albicans*, (9mm) *Aspergillus parasiticus* and (8mm) for *Aspergillus flavus53*. The methanolic extract revealed 17mm, 25mm, 28mm, 29mm, 32mm and the ethyl acetate extract 16mm, 22mm, 24mm, 25mm, 28mm, 28 mm of inhibition against *F. solani*, *M. niger*, *M. canis*, *C. flavus*, *C. albican* and *D. glabera* respectively at 50μg/ml. On the ground of zone of inhibition *Rhododendron arboreum* extracts revealed the antifungal activity.
PHYTO-CHEMISTRY

Various active constituents extracted from flowers, bark and leaves of Rhododendron arboreum contains flavonoids, alkaloids, terpenoids, glycosides, steroids, anthraquinones, saponins and tannins but phenols and flavonoids are main active compounds of Rhododendron arboreum. Some polyphenol like Rutin, quercetin, quercetin-3-rhamnose, coumaric acid and amino acids are present in flowers. It barks contain betulinic acid, ursolic acid acetate, leucopelargonidin, teraxerol, terpenoids, and steroids. Stem and root contain few alkaloids, anthraquinones, terpenoids, reducing sugars, saponins and tannins.

CONCLUSION:

On the basis of literature R. arboreum is abundant with minerals, nutrients and utilized in an extensive range of traditional treatments. Various pharmacological activities are reported by its active ingredients like anti-inflammatory, antimicrobial, anti-diabetic, adaptogenic, antidiarrheal, antinoceptive, antioxidant, anticancer, cardioprotective, hepatoprotective, and immunomodulatory which supports its use in different ailments and health benefits. Within the present and past, most of the pharmacological activities are done on mixture, only some are on isolated compounds and their mechanisms not to be clear, so further studies should be required to lighten the how does it work and to make sure their suitability to be used as medicines. Different type of chromatography profiling revealed the many type of medicinal entity like flavonoids ester, hydrocarbon alkane, steroids and terpene are present in R. arboreum, which have different pharmacological, industrial and national importance. Few of the active ingredients like phenolics, flavonoids, flavonoid glycosides, sterol and terpenoids have already been reported from leaves, flowers and bark and also the rest are yet to explore, so further study is essential on the purification and isolation of the compounds from R. arboreum, which can increase scientific based use within the world.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES


