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Review Article

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

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Abstract



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Methods: This review provides scientific grounds in the literature for the phytochemical and pharmacological activities of *Rhododendron arboreum*, from 2010- 2021. Chiefly three bibliographic databases were used as the main sources of information (Google scholar, PubMed, and Science Direct). The keywords used in this research are as follows: "Phytochemical", "National flower", "Bioactive compounds", "Pharmacology" and "*Rhododendron arboreum*".

Results: Various studies were included in this review according to the required criteria, including phytochemical and traditional uses. *Rhododendron arboreum* contains flavonoids alkaloids, terpenoids, glycosides, steroids, anthraquinones, saponins and tannins. Pharmacological and traditional uses of this plant on the basis of presence of above active ingredients.

Keywords: Bioactive compounds, National flower, *Rhododendron arboreum*

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 ¹. This remarkable plant designated as the state flower of Nagaland ², official flower of Chin state ³, also known as Nepal national flower and Uttarakhand state tree ⁴. 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, coughs and hemorrhoids ⁴⁻⁵. 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, flavonols, flavonol glycosides, triterpenoid and sterols ⁶⁻¹¹. The unprocessed extracts and extracted plant mixture showed several pharmacological actions such as hypoglycemic, reduce stress and anxiety, cytotoxic, decreased intestinal motility, antinociceptive, 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 ¹². 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 ¹². The wood of the plant is used for charcoal and fuel. The grained wood of these plant is prepared for making khukri handles, packsaddles, gift-boxes, gunstocks and posts ¹³. Flowers and leaves of these plants are fixed in long ropes made of munja grass and also used to decorate the house and temple. ¹⁴.



Figure 1: Flower of *Rhododendron arboreum*

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-1-beta (IL-1 β) 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 spectroscopy i.e., IR, MS and 1D and 2D NMR. For 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 μ M for a period of 72 h. Various wide spectroscopic techniques used for extracted ingredient for confirmation as 15-oxoursolic acid. There is 15-Oxoursolic 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, antimutagenic activity in Ames assay and cancer cell growth inhibition activity by MTT (3-(4,5 dimethylthiazol-2,5 diphenyltetrazolium bromide) assay. The extract revealed that have antimutagenic and anticancer potential ¹⁹⁻²⁰.

Antidiabetic activity

There are four fractions of *R. 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 hemoglobin A1C, blood glucose level, serum urea and creatinine while increase in insulin level similar to standard drug glybenclamide after ingestion of active fraction (200 and 400 mg/kg) once daily for 30 days in streptozotocin induced diabetic rats.²¹

Antihyperlipidemic activity

Neeraj Verma *et. al*, determined the Active fraction of *R. arboreum* extract administered in streptozotocin 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 by²¹.

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 fraction²².

Antimicrobial activity

Ethanollic and methanollic 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, chikungunya and enterovirus. Test drug was found dose dependent anti-bacterial, antifungal and anti-viral activity²³.

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 group²⁴.

Cardioprotective activity

Ethanollic extract of *Rhododendron arboreum* its leaves showed protective effect in the myocardial ischemia induced by isoproterenol. Significantly decreased in the concentration 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 flavonoids²⁵.

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 antienteropooling property of *Rhododendron arboreum*²⁶.

Immunomodulatory activity

The ethanollic leaf extract treated mice showed significant conquest to the immune response. The ethanollic 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 $\pm$ 0.57%, 67.67 $\pm$ 2.08% and 40.3 $\pm$ 1.5% stimulation respectively toward 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 respectively²⁷.

Adaptogenic activity:

The methanollic 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 activity²⁸.

Antifungal activity

The studied of different type extract of *R. arboreum* on multiple type of fungus and calculate the zone have inhibition. For ethanollic 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 flavus*⁵³. The methanollic extract revealed 17mm, 25mm, 28mm, 28mm, 29mm, 32mm and the ethyl acetate extract 16mm, 22mm, 24mm, 25mm, 28mm, 28 mm of inhibition against *F. solani*, *A. niger*, *M. canis*, *C. flavus*, *C. albican* and *D. glabrata* respectively at 50 μ g/ml. On the ground of zone of inhibition *Rhododendron arboreum* extracts revealed the antifungal activity²⁹.

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-rhamnoside, coumaric acid and amino acids are present in flowers³⁰. 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 tannins³¹⁻³⁵.

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, antidiabetic, adaptogenic, antidiarrheal, antinociceptive, 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.

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