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Rhododendron Arboreum Phytochemistry, Medicinal Applications and Pharmacology: A Review

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ABSTRACT

Rhododendron is a tiny evergreen tree with deep red or pastel pink blossoms from the Ericaceae family. The species is extensively distributed between 80°N and 20°S and is the national flower of Nepal and state flower of Himachal Pradesh (India). Besides its horticultural function, it's utilized as an attractive plant in gardens, roadways, and vessels. Because of its phytochemical potential, it's used to treat ailments. Mountain people use this plant's flowers to create pickle, juice, jam, syrup, honey, squash, etc., and to treat diarrhoea, headache, and inflammation, bacterial and fungal illnesses. The present review highlights Rhododendron's medicinal, nutritional, and prospective capabilities by developing value-added goods to improve the rural tribal population's livelihood and work chances.

Keywords- Rhododendron, Fungal illnesses, Phytochemical, Inflammation, Diarrhoea.

I. INTRODUCTION

It has been discovered that India is a country with a high biodiversity and an amazing resource of herbal plants. Because of this, India is sometimes referred to as the medical garden of the globe. In the form of medicines, plants are magnificent resources that are of immeasurable value and have been used for centuries to cure a variety of disorders. (1) The rhododendron is one example of the kind of plant that has a history of being employed in the practise of traditional medicine in India as well as in other nations. The Rhododendron genus is quite extensive, and within it are several species that have come to occupy a distinct niche not only in the cultural but also in the economic lives of the people. (2) There are around 80 species, 10 subspecies, and 14 variations of Rhododendrons in India. The majority of them may be found in various sections of the Himalayas at elevations ranging from 1500 to 5500 metres. (3) The name Rhododendron comes from the Greek word rhodon, which means 'rose,' and dendron, which means 'tree.' The specific epithet arboreum means 'tree-like,' and the generic name Rhododendron comes from the Greek word. (4) The Rhododendron arboreum, which belongs to the Ericaceae family, is considered to be one of the most stunning species of Indian Rhododendrons. In traditional medicine, it is employed in the management of inflammatory problems, gastrointestinal disorders, pain, the common cold, asthma, and various skin diseases, among other ailments. Rhododendrons are well-known for their ability to be poisonous, and certain species have long been employed in medicinal and poisonous preparations. (1) Despite the fact that it is poisonous, it has been utilised in several traditional medicinal practises throughout history, including Ayurvedic and traditional Chinese medicine, as well as in folk medicine practised in North America and Europe. This plant also holds the record for the largest rhododendron in the world, according to the Guinness Book of World Records. (5, 6) It is also included in the Ayurvedic formulation known as "Ashokaarishtha," which is known to exhibit estrogenic and oxytocic properties. The plant is native to the north-central part of India and may be found across the Himalayas, from Kashmir to Bhutan, as well as in the hills of Assam and Manipur at elevations between 1200 and 1400 metres. One of the species that is found the most frequently is the Rhododendron arboreum, which has a wide distribution and can be found in northeast India, the western ghats (subsp. nilagiricum), Bhutan, Nepal, China, Thailand, and Myanmar. many subspecies of Rhododendron arboreum can be found in various geographic locations. Red blossoms of this plant, which are both aesthetically appealing and have some religious significance, attract the attention of visitors to the plant and entice them toward it. They are presented as part of the devotion that takes place in monasteries and temples because of the high regard with which they are held. It is the national flower of Nepal, as well as the state flower of Nagaland in India and the state tree of Sikkim in Sikkim, both of which are in India. (7)

II. MORPHOLOGICAL CHARACTERS

About five to ten metres in height, the Rhododendron arboreum can be an evergreen or, less commonly, a deciduous shrub or small tree. (8, 9) The trunk is branching, and the bark is fuzzy, scaly, and a

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rusty brown colour. The leaves are normally monomorphic or very rarely dimorphic, oblong and lanceolate, rounded to cuneate at the base, acute, acuminate to obtuse at the apex, crowded at the end of branches, dark green in colour (10-15 x 2-4 cm), and have strongly impressed lateral veins (12-18 pairs). The indumentum may be glandular or have hairs that are branching. In most cases, the blooms will be arranged in a raceme or a corymb (Figure No. 1). The form of the corolla can range from shallowly lobed to polypetalous, and the inflorescence is seldom axillary. It has 10–20 flowers with a funnel-shaped corolla that is pink to deep crimson red in colour. The calyx has a slight split and is 1–2 centimetres long. Filaments are filiform, the style is capitate, and the anthers are oblong. The ovary is superior, white tomentose, or glandular (5-15 locular). The capsule is concave and partitioned quite precisely (3-4 x 1-2 cm). The seeds are often compressed and spindle-shaped to ellipsoid or flattened minute in form. They have a thin obvolute membrane and, in some circumstances, appendages on both ends. (10,11,12)

Fig: 1 Rhododendron arboreum plant

Table-1 Subspecies of rhododendron arboreum[13]

SUBSPECIES	CHARACTERISTICS AND DISTRIBUTION
Rhododendron arboreum spp. Arboreum	Red flower, found in Western Himalayas
Rhododendron arboreum spp. Cin-namomeum	White, pink or red flower, found in Central Himachal
Rhododendron arboreum spp. Delavayii	Red flower, found in Eastern Himalayas
Rhododendron arboreum spp. Nilagiricum	Red flowers, found in Nilgiri
Rhododendron arboreum spp. Zeylancium	Orange red flowers, found in Sri Lanka

III. PHYTOCHEMISTRY

Chemical Present in Plant part

Rhododendron blooms are a rich source of an abundance of different nutrients, many of which are considered to be important. It is believed that the presence of water and fat-soluble pigments in flowers gives flowers their substantial antioxidants capability. Flowers have a total carotenoids concentration of 2685 micrograms per 100 millilitres and a total anthocyanins content of 154.8 milligrammes per litre. Because they contain a considerable amount of flavanols and total flavonoids (respectively 286.7 mg/100 ml and 1276.5 mg/ml), they have a lot of applications in the field of pharmacology. Because their total ash level is at about 2.30 percent, including them in a diet will contribute to a decent mineral profile. Rhododendrons also have a very high concentration of sodium (385 mg/L), iron (405 mg/L), manganese (50.2 mg/L, and zinc (32mg/L), all of which are elements that are highly vital to the upkeep of biological processes that are necessary for a healthy existence(14-15).

As a result, they are able to make a contribution toward the elimination of mineral deficiencies in populations. According to the findings of Devi and Vats (2017), the calcium and iron levels of Rhododendron flowers range between 16.64 and 27.29 mg/100g and between 5.62 and 6.25 mg/100g, respectively, from two separate locations of Himachal Pradesh. When Madhvi et al. (2019) investigated the phytochemistry and pharmacology of the plant using the methanol extraction method, they found results that were comparable to those found here. It was noticed that there was a minor difference in the protein content of flowers, ranging from 4.85 to 5.59 percent (16,17). These findings are attributed to the fact that the geographical region causes slight changes in the protein content of flowers. The factors that have come to light for this may include shifts in the quality of the soil and fluctuations in temperature. Although the blooms are valued for their aesthetic characteristic, there is evidence that they also contain sixteen distinct types of amino acids (18, 19).When consumed as part of a diet, the phytochemicals and secondary metabolites found in rhododendron, which include alkaloids, flavonoids, glycosides, saponins, tannins, and steroids, are abundantly present in rhododendron and hence add to the overall anti-oxidant content of the plant. Rhododendron arboreum is said to have a significant amount of polyphenolic chemicals, as stated by Sonar et al. (2012). In addition to that, it has saponins, steroids, and flavonoids(20,21).During the extraction process, the author also mentioned quercetin, a polyphenolic molecule, as being one of the physiologically active chemicals. According to the research, the quantity of phytochemicals is not restricted to the flowers of the plant; rather, the bark, root, and stem are all good sources of phytochemicals(22,23).

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Bark

The petroleum ether extract of the bark showed the presence of a single triterpenoid compound, which was identified as taraxerol (C30H50O), in addition to ursolic acid acetate (C32H50O4). The identification of betulinic acid was revealed by the ether extract of the bark that was performed after the petroleum ether extraction (C30H48O3). The chemical known as leuco-pelargonidin was derived from an acetone extract of the bark (C15H14O6) (24, 25).

Leaves

Glucoside, ericolin (arbutin) (C12H16O7), ursolic acid (C30H48O4), -amyrin (C30H50O), epifriedelinol (C30H52O), a novel triterpenoid called campanulin, quercetin, and hyperoside (C21H20O12) are some of the compounds that have been found in green leaves (Orwa et al., 2009). Chemical examination of the leaves of R. arboreum var. nilagiricum indicated the presence of the compounds hyperoside (3-D - galactoside of quercetin), ursolic acid, and epifriedelinol, which is a triterpenoid complex (Rangaswamy & Sambamurthy, 1959). According to some reports, the leaves also contain flavone glycoside, dimethyl ester of terephthalic acid, and other flavonoids (26, 27).

Flowers

According to Rangaswamy and Sambamurthy's 1960 research, the blooms of this particular species contain a crystalline chemical component called quercetin-3-rhamnoside. Through the use of high-performance thin-layer chromatography, it was discovered that the flowers of R. arboreum contain three phenolic compounds that are physiologically active. These chemicals include quercetin (C15H10O7), rutin (C27H30O16), and coumaric acid (C9H8O3) (HPTLC).

Table 2- Phytochemicals present in Rhododendron arboreum plant

Sr. no.	Part of plant	Compound	References
1.	Bark	Triterpenoids	[28,51]
		Ursolic acid acetate	
		Betulinic acid	
		Leuco-pelargonidin	
2.	Leaves	Glucoside	[29,52]
		Ericolin	
		Ursolic acid	
		Quercetin	
		Hyperoside	
		Flavone glycosides	
		Flavonoids	
3.	Flowers	Quercetin-3-rhamnoside	[30,31]
		Phenolic compounds: Rutin Coumaric acid	

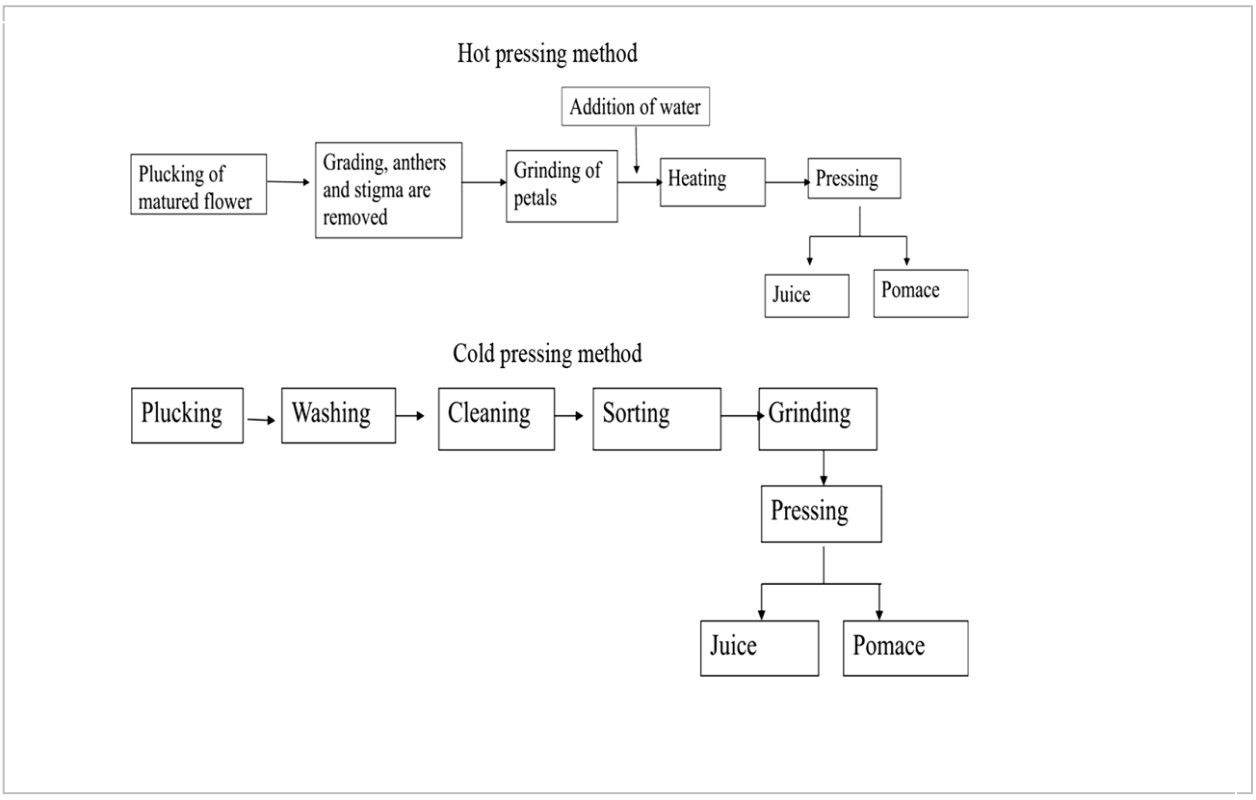

Figure-2 Methods of Rhododendron flower juice extraction (hot and cold pressing)

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Pharmacology activity of Rhododendron arboretum:

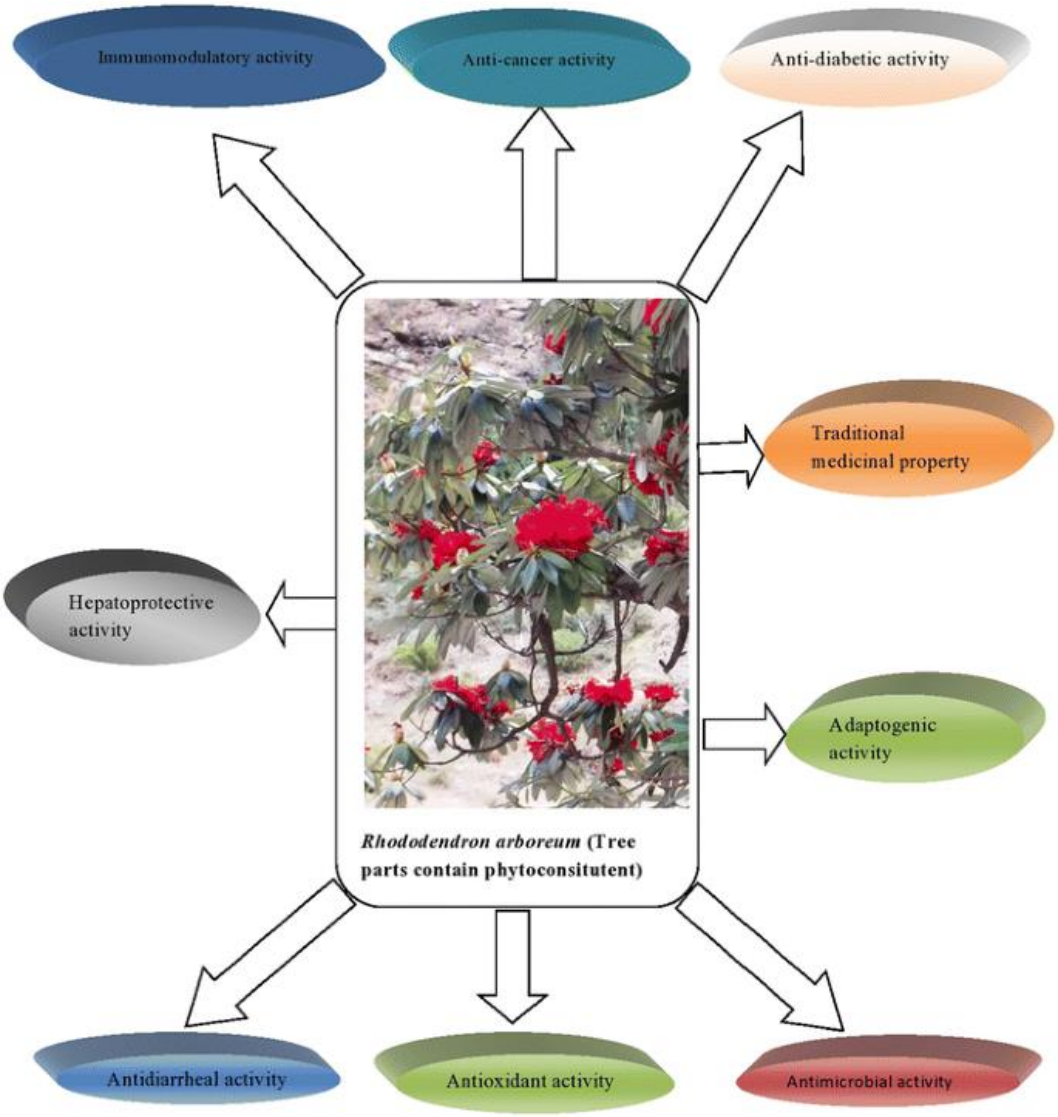

Fig: 3 Pharmacological Activity of Rhododendron arboretum

Anti-microbial activity:

Researchers have demonstrated that both aqueous and ethanolic extracts of Rhododendron arboretum flowers possess antibacterial properties. They investigated the anti-microbial efficacy of the isolated chemical, quercetin, against seven different microorganisms, however they only discovered that it was effective against Staphylococcus aureus and Escherichia coli. Up to a dosage of 12.5 mg/ml, it displayed some level of action. Lal et al. 2017 evaluated the anti-microbial activity of a plant extract from Rhododendron arboreum on six different bacterial pathogens: S. Typhi, Shigella, E. coli, S. aureus, and B. cereus. According to the findings of the least inhibitory concentration results, an even lower concentration of the extract was adequate to prevent the development of all harmful bacteria. These findings were discovered by analysing the data from the test. It was discovered that ethanolic extract was efficient against S. aureus but not against any other bacterium, but methanolic extract was effective against all bacteria other than Shigella. (32, 53)

Hepatoprotective activity:

In both preventative and curative models, the ethyl acetate fraction of Rhododendron arboreum showed considerable hepatoprotective capability against carbon tetrachloride (CCl4)-induced liver damage. In CCl4-treated groups, fraction at doses of 100, 200, and 400 mg/kg was given orally once day for a period of 14 days (II, III, IV, V and VI). The levels of glutamic oxaloacetic transaminase (SGOT), glutamate pyruvate transaminase (SGPT), alkaline phosphatase (SALP), glutamyltransferase (-GT), and bilirubin in the blood were measured, together with the activities of glutathione S-transferase (GST), glutathione reductase,

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he In a dose-dependent manner, normalcy was returned to the significantly raised blood enzymatic activity of SGOT, SGPT, SALP, -GT, and bilirubin that were caused by CCl4 therapy. During this time, the activities of GST and glutathione reductase, which had been reduced, were also brought back up to normal levels. In a dose-dependent way, the ethyl acetate fraction not only greatly inhibited the rise of hepatic malondialdehyde production, but it also protected the depletion of reduced glutathione level in the liver of CCl4-intoxicated rats. (33, 54)

Anti-diabetic activity:

In this study, the anti-diabetic potential of the Rhododendron arboreum Sm flower was investigated, and active chemicals were extracted from the bloom. (34) It was discovered that an aqueous methanolic extract of the flower of Laligurans had action that was inhibitory on the rat intestinal -glucosidase. (35) The water-soluble and ethyl acetate-soluble sections of the aqueous methanolic extract had inhibitory actions on -glucosidase, with the ethyl acetate-soluble component displaying a greater level of activity than the water-soluble portion. Through the use of enzyme-assay guided separation, the beta-glucosidase inhibitor quercetin-3-O—D-galactopyranoside (hyperin) was successfully extracted from the fraction that was soluble in ethyl acetate. The chemical that was obtained exhibited a dose-dependent -glucosidase inhibitory action, with IC50 values of 1.66 mM for sucrase and 0.76 mM for maltase, respectively. According to the findings of this research, the flower possesses antidiabetic potential, a quality that might be useful in the development of pharmaceutical formulations, nutraceuticals, or functional foods for diabetes and the difficulties associated with it.(36,37)

Adaptogenic and Anti-oxidant activity:

The presence of flavonoids in the leaves of Rhododendron arboreum confers anti-oxidant action, according to research published in 2007 by Prakash and colleagues. (Swamidasan et al. 2008) discovered that an ethanolic extract of Rhododendron arboreum has adaptogenic effects on mice and rats. These effects were observed to mitigate the effect of acute and chronic stress-induced biochemical and physiological disturbance. For the purpose of determining adaptogenic activity, researchers employed a variety of approaches, including swimming endurance tests, models of resistance to anoxic stress, and models of immobilisation stress. In addition, treatment with ethanolic extract at dosages of 250 and 500 mg/kg led to improvements in anaerobic stress tolerance as well as an increase in swimming endurance time. (38, 39, 40)

Anticancer activity:

The ethanolic leaves extract showed dose-dependent efficacy against Agrobacterium tumefaciens-induced potato disc tumours. Leaf extract was statistically significant compared to TAM, while floral extract was not. Quercetin and rutin may have anticancer activity71. 15-oxoursolic acid had IC50 values of 32.81.54M, 10.30.01M, 9.20.23M, 4.90.02M, and 2.30.04M against A498, NCI-H226, H157, Hep G2, and MDR 2780AD cell lines. Cytotoxicity caused by OH at carbon 3, carbonyl at carbon 17. 5000g/ml of aqueous leaf extract was non-cytotoxic against S. cerevisiae, strain BY4741. The extract decreased Vero and HELA cell growth by 75.3% and 87.6%, respectively, and lowered HIF-1 and VEGE expression by 0.332 and 0.24-fold, respectively.(41,42)

Cardioprotective activity:

The whole plant ethanolic extract of R. arboreum dose-dependently decreased ALT, AST, LDH enzyme activity, decreased MDA in serum and heart tissue, and elevated SOD, catalase, GPx, and GSH activity in isoproterenol-treated rats. Ethanolic extract improved vacuolation, myocardial degeneration, and inflammatory cell infiltration. Parcha et colleagues observed that ethanolic flower extract was more effective than aqueous extract at reducing lactate dehydrogenase and creatine kinase release in albino rats, while the n-butanol fraction of ethanolic extract showed the most cardioprotective activity.(43)

Hypolipidemic effect:

Arboreum plus (300 mg/kg) lowered total cholesterol, triglycerides, LDL, and atherogenic index. Rabbits given arborium plus and atorvastatin (5mg/kg/d) showed no meaningful difference. R. arboreum flower juice lowered serum LDL, TG, TC, AL, hsCRP and elevated HDL in hypercholesteremic New Zealand rabbits (1 percent w/w cholesterol +10 percent v/w groundnut oil).

Immunomodulatory activity:

Ethanolic leaf extract suppressed the immunological response in mice. Ethanolic extract was more effective than levamisole and control. Serum glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, serum total bilirubin, and spleen and liver weight were not significantly different . Rawat et al reported that TMS-10 (ursolic acid), CMS-3 (kaempferol), and RAM fr2 fraction increased neutrophil phagocytosis by 79.670.57%, 67.672.08%, and 40.31.5%, respectively. They also stimulated phagocytosis in dead Candida albicans. TMS-10, CMS-3, and RAM fr2 at 1mg/ml showed 7, 6.7, and 6.3 mean particle counts.(44,45)

Toxicity study:

Oral treatment of 2000 mg/kg floral fractions and 200 mg/kg hyperin was innocuous in acute toxicity studies of Wistar rats, whereas intraperitoneally induced 300 mg/kg ethanolic leaf extract was hazardous in albino mice. Nisar et al. observed that R. arboreum methanolic extracts were poisonous to Artemia salina at 1000 g/ml. Leaves (LD50=20 g/ml) and flowers (LD50=64.23 g/ml) have high cytotoxicity; stem, roots, and bark have minimal cytotoxicity (LD50=545ug/ml). Extract action may be due to glycosides, alkaloids, and flavonoids.(46)

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Antibacterial activity:

Flower, leaf, stem, and root methanolic extracts of R. arboreum were active against B. subtilus, Salmonella typhi, and S. aureus98. The lowest effective concentrations against E. coli and S. aureus69 were 12.5 mg/ml, 50 mg/ml, and 25 mg/ml, respectively. In another investigation, 50mg/ml ethanolic floral extract inhibited E. coli, S. epidermidis, and S. aureus by 201mm, 191mm, and 171mm, respectively. Methanolic leaf extract was more efficient against gram-positive bacteria than acetone99, according to Prakash et al. Chauhan et al. found that methanolic leaf extract inhibited S. aureus growth 60-40% and methanolic floral extract 50-50%. Leaf extract was good, then floral extract100. S. aureus, Klebsiellapneumoniae, Streptococcus pyogene, and E. coli were inhibited by methanol and aqueous leaf extracts at 12.501.10a, 11.500.90c, 11.500.50 b, 11.000.80d, and 6.500.10d, 8.000.50c, 8.500.55b.(47)

Antifungal activity:

Saklani & Chandra reported the zone of inhibition at 50 mg/ml for ethanolic floral extract as 10mm for Aspergillus flavus, 9mm for Candida albicans, and 8mm for Aspergillus parasiticus53. The methanol extract inhibited F. solani, A. niger, M. canis, C. flavus, C. albacan, and D. glaberata at 50g/ml. 3-acetoxyurs-11, 12-epoxy-13, 28-olide inhibit, 39 mm, 32 mm, 42 mm, 28 mm, 41 mm, 44 mm; Lupol inhibit, 32 mm, 28 mm, 38 mm, 17 mm, 40 mm, 36 mm; Betulin inhibit, 40 mm, 23 mm, 43 mm, 35 mm, 44 mm, 39 mm; against D. glaberata, F. High-activity substances (betulin and 3-acetoxyurs11, 12-epoxy-13) may be hydrophilic74. Trichodermaviride and Candida albicans had 9.000.50a and 8.000.40b zone of inhibition for methanol extract and 5.000.30a and 4.000.20b for aqueous leaves extract, respectively.(48,49,50)

IV. CONCLUSION

Rhododendron plants provide a lot of health advantages, as well as actions that are antibacterial, and they have the potential to be used in the food and beverage business. Researchers have more room to investigate this plant since it is not currently being used to its full potential and is not being adequately kept to ensure that it is accessible throughout the year. The authors have made an effort to review the medicinal properties of Rhododendron flower in addition to exploring different horizons for its utilisation, and they are hoping that this review will attract researchers to conduct research in this field for the value addition, which may help in the enhancement of employment and economy for the upcoming generation. In addition, the authors have reviewed the medicinal properties of Rhododendron flower and explored different horizons for its utilisation. The cultivation of plants for medicinal purposes is of extreme antiquity. The potential of herbs & crude drugs as source of newer compounds for management of various diseases & disorders is rapidly accelerating. Plants of hilly regions have always captured the attention of botanists & horticulturist urging them to unleash new dimensions in medical treatment. There are abundant plants all over the world which are yet to be explored & investigated for their biological activity & pharmacological potency. The detailed survey of literature revealed that Rhododendron arboreum is important plant of hilly region with extensive medicinal & commercial uses. The plant exhibited antiinflammatory, hepatoprotective, anti-diarrhoeal, antidiabetic, anti-cancer, anti-hyperlipidaemic cardio protective antioxidant properties due to presence of flavonoids, saponins, tannins & other phytochemicals. Fresh petals are processed to prepare sub-acidic jelly & sharbat a famous market commodity. Young leaves are poisonous cause intoxication in large quantities.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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