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A REVIEW ON THE BIOACTIVE COMPOUNDS OF RHUS CHINENSIS MILL. NATIVE TO THE SIKKIM HIMALAYAS

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ABSTRACT

Background: The Sikkim Himalaya is home to the wild medicinal shrub *Rhus chinensis* Mill, which produces edible fruits. Traditionally, the fruit juice concentrate has been used to treat a variety of stomach issues. The plant is rich in phytoconstituents, including gallic acid (up to 130.4 ± 2.5 mg/g), methyl gallate, flavonoids, and tannins, which contribute to its traditional applications in managing conditions such as diarrhoea, dysentery, toothache, cough, and wounds. The total flavonoids and flavonol levels were quantified as rutin equivalents. The total phenolics were calculated as gallic acid equivalents. Through various *in vitro* antioxidant methods, including DPPH, Total antioxidant content, ABTS, and Hydrogen peroxide scavenging assays, the antioxidant capacity was determined. **Methodology:** This review combines data from numerous research studies and review articles that have elaborated on the various phytoconstituents, medicinal uses, and pharmacological properties of different Rhus species. **Results and Discussion:** This review provides a detailed description of multiple phytoconstituents, traditional uses, and medicinal applications of Rhus species. The quantitative findings from previous studies report the total phenolic content as 123.52±1.29 mg GAE/g. IC50 values through DPPH free radical scavenging assay and Hydrogen scavenging assay were 42.69±0.1% and 63.20±1.48% respectively. **Conclusion:** This review provides an in-depth description of various phytoconstituents, including gallic acid, citric acid, myricetin-3-O-rhamnoside, methyl gallate, quercetin-3-O-arabinoside, and protocatechuic acid, among others. These results provide concrete evidence to support the potential of *Rhus chinensis* Mill. as a source of bioactive compounds for the creation of new treatments.

INTRODUCTION

Rhus chinensis Mill is a wild medicinal plant that grows in the Sikkim Himalaya and produces edible fruits. Concentrated fruit juice has been utilized for decades to treat a range of digestive disorders. Many Rhus species are commonly used as herbal remedies, souring agents, flavorings, and ingredients in sauces and drinks. For instance, *R. chinensis* Mill., often known as Chinese sumac, has long been used by local people as a plant, vegetable, and natural souring agent [1]. Naturally occurring products of *R. chinensis* Mill. that have been isolated and identified from different plant parts (root, stem, or *Galla*

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chinensis), including gallic acid, gallicin, phenolics, glycosides, and compounds of the benzofuranone type [2]. However, systemic findings of various constituents of different sections of Rhus species are still lacking. Studies should focus on a broader range of phytoconstituents with their chemical and biological importance. Much stronger research has already been conducted on compounds from *Rhus chinensis Mill*, but it has not been distinctly categorized based on different parts, such as leaves, fruits, bark, and galls, leading to a lack of part-specific phytochemical profiles. Additionally, there is minimal exploration of the effects of geographical variations on chemical constituents. Additionally, connections between bioactive compounds and their therapeutic effects are often unclear, and few studies employ modern analytical tools or conduct clinical validations. This review aims to bridge these gaps by compiling part-wise phytoconstituent data, assessing methodological approaches, and highlighting areas for future pharmacological exploration suggesting future directions for drug development and clinical research.

Distribution and morphology

Bhakmilo-ko-Chuk, the water concentrated fruit juice of *Rhus chinensis* Mill plant, is used in traditional medicine to treat diabetes, diarrhoea, dysentery, and inflammation, and worm infections in cattle etc. Bhakmilo, or *Rhus chinensis* Mill., is found in the Sikkim Himalayan region which grows in between 300 and 1800 meters. When *Rhus chinensis* Mill. juice was phytochemically screened, it showed significant quantities of tannins, triterpenes, and carbohydrates and low levels of steroids and amino acids etc. According to economics, in the local market, the cost of Bhakmilo-ko-Chuk is Rs. 1000 L^{-1}. According to the marketing stats the rhus tree's fruit juice generated about Rs. 4,000 annually.

In the Sikkim Himalaya, the *Rhus chinensis* Mill. plant is found significantly between 300 and 1800 meters [3]. It is a subtropical plant that thrives on rocky and sandy hillside slopes, in dry to damp woods, and in both forest and farmed areas within agroforestry systems. A Chinese nutgall tree known as Chinese sumac [4]. This tree is native to China and has good moisture and shedding efficiency. In addition, it grows in moist temperate riverine environments and arid regions.

Folk medicine practitioners in the Sikkim Himalaya have long utilized the fruits. Rhus has a soft, semi-woody stem; green, simple, or compound leaves; small, brown flowers; and berries, which are classified as such because they are grouped in a single cluster and have small individual fruits. The deciduous rhus tree bears its first leaves in March or April at lower elevations, flowers from July to September, and bears fruit from October to December. Fresh Rhus fruits were gathered and transported to the lab for phytochemical screening [5]. After washing, slicing, and oven-drying at 60°C, the fruits reached a consistent weight. The samples were kept in a desiccator after being ground into a powder in a grinder. After being macerated in 250 millilitres of distilled water, fifty grams of powder were placed on an orbital shaker for forty-eight hours. Whatman filter paper and muslin clothing were used to filter the extract. These filtrates were lyophilized after being concentrated under vacuum at 50°C, allowed to cool to room temperature, and then incubated once more overnight at 80°C. To determine the phyto-constituents in the extract, preliminary chemical tests were conducted [2]**.**

TRADITIONAL MEDICINAL USE

Indigenous peoples have traditionally used Rhus species for medicinal applications, including *Rhus chinensis* Mill. and its gall, *Galla chinensis*. According to reports, the various parts of *Rhus chinensis* Mill., including the root, bark, stem, leaves, fruits, blooms, seeds, and gall, exhibit a range of intriguing medicinal qualities [5] .Several well-known applications include the identification of several Rhus species.

Various extracts have been investigated for *Rhus chinensis* Mill. are used to cure snake bites, fever, jaundice, coughing, diarrhoea, joint inflammation, liver disease, and malaria etc [6]. The extracts of *R. trilobata* have been utilized for the treatment of cancer and gastrointestinal disorders [7]. *Rhus coriaria* L. having anti-microbial and anti-fungal properties to treat skin inflammation [8]. Infected wounds, sore throats, diarrhoea, dysentery, and stomach ache can all be treated with *R. typhina* [9].

Different Parts of Plants and Their Constituents

Roots

A small, deciduous tree named *R. Javanica L. var. roxburghiana* is widely distributed in thickets and secondary forests at low-altitude areas across Taiwan [10]. Extensive research has been conducted on the qualitative evaluation of Rhus species, followed by the isolation and characterization of flavonoids [11,12], triterpenoids [13,14], phenolics [15], and tannins [16]

using infrared spectroscopy and nuclear magnetic resonance. Some new benzofuranone compounds were found in the different extracts of *Rhus chinensis* Mill. Apart from them 16 different bioactive compounds like 5-hydroxy-7 (3,7,11,15-tetramethylhexadeca-2,6,10,11-tetraenyl)-2(3H)benzofuranone, 3-oxo-6 beta-hydroxyolean-12 en-28-oic acid, and 3-oxo-6 beta-hydroxyolean-18 en-28-oic acid, moronic acid, betulonic acid, gallicin, dihydroxytoluene, and dimethylcaffeic acid were found also found from the extract of root stem of *Rhus chinensis* Mill [17]. The *Rhus chinensis* root's butanol extract includes phenol glycosides as well as lariciresinol-based lignan glycoside chemicals [18].

Leaves

The term *Galla chinensis* describes the gall that the Chinese aphid *Schlechtendalia chinensis* (Bell) produces on *Rhus chinensis'* leaves [19]. A particular kind of hydrolysable tannin, gallo-tannin, is abundant (50–70%) within the galls on *Rhus chinensis* leaves [20]. *Galla chinensis,* which has a variety of therapeutic actions and health advantages [21,22]. This plant produces a lot of volatile oils from its leaves, the primary ones including n-heptacosane, phytol, and palmitic acid [21].

The flavonoid glycoside in the leaves of *Rhus chinensis* was previously identified as only quercitrin, but additional analysis revealed that myricitrin and myricetin were also extracted [23,24]. *Rhus chinensis* Mill. leaves' infrared spectra showed distinctive absorption peaks that matched different functional groups. Near 3400 cm^{-1}, a broad and intense absorption peak suggested the presence of O-H bonds and the potential presence of phenols or alcohols.

The saturated C-H bonds from the stretching vibrations of the methyl group and methylene groups were identified as the source of two separate absorption peaks at about 2960 cm^{-1} and 2876 cm−1, respectively. The C=O bond produced a significant absorption peak at approximately 1650 cm^{-1}, indicating the presence of carbonyl molecules, such as aldehydes, ketones, or carboxylic acids. The skeletal vibrations of aromatic compounds were linked to overlapping peaks at about 1450 cm^{-1}. Furthermore, the presence of C-O-C bonds was indicated by two absorption peaks that were located at 1300 and 1030 cm. Overall, the leaf extracts' absorption maxima were centered in the regions between 3500 and 2750 cm and 1800 and 1000 cm^{-1}, indicating that a variety of functional groups have been identified in the leaves of *Rhus chinensis* Mill [25]. Spectral analysis, like GC-MS and LC-MS, has been done for the identification of active constituents Present in *Rhus chinensis* Mill. Different active constituents were identified, which were revealed to contain alkanes, phenols, alcohols, acids, esters, and other groups. Due to the active compounds that contain these functional groups and their roles as lipid hormones to control systemic metabolism, the food and drug industries utilize these chemicals. Among them, palmitoleic acid stands out. It can manage obesity-related diseases by affecting the development of fat, thereby reducing the risk of diseases such as atherosclerosis and liver disease. Furthermore, it has been demonstrated that palmitoleic acid controls the buildup of esters in plasma, which is linked to conditions including fatty liver and atherosclerosis [26].

Fruits

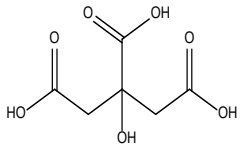
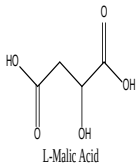
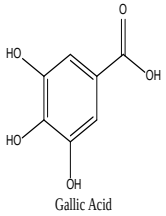
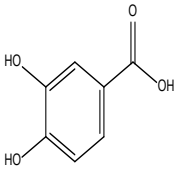
GC-MS and LC-MS analysis of the methanolic, ethanolic, and acetone extracts of *Rhus chinensis* Mill revealed the presence of 14 phenolics. These are gallic acid, myricetin-3-0-galactoside, methyl gallate, rutin, myricetin-3-o-rhamnoside, ellagic acid, luteolin-7-0-glucoside, methyl digallate, quercetin arabinoside, quercetin-3-o-rhamnoside, and luteolin, which are among the fruits that contain these compounds given in Table 1.

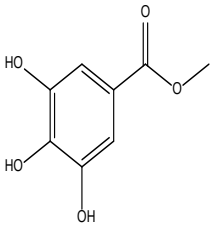
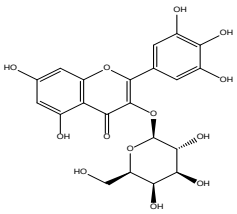
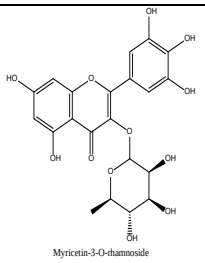
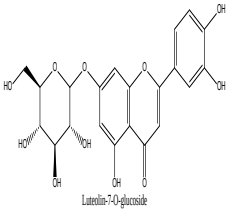
Citric acid, gallic acid, methyl gallate, myricetin-3-0-galactoside, syringic acid, rutin, myricetin-3-0-rhamnoside, ellagic acid, luteolin-7-0-glucoside, methyl digallate, quercetin arabinoside, quercetin-3-0-rhamnoside, luteolin, and quercetin are the fruits that UHPLC-ESI-HRMS/MS in negative ionization mode have identified, given in Table 2 [27].

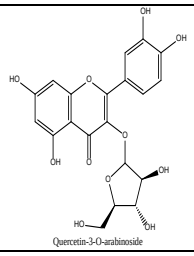
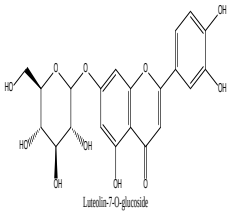
Table 1: Various phenolic compounds have been identified in the *Rhus chinensis* Mill. Fruit extracts [27].

Sl no	Name of the compounds
1	Mallic acid
2	Citric acid
3	Gallic acid
4	Protocatechuic acid
5	Methyl gallate
6	Myricetin-3-O-galactoside
7	Myricetin-3-O-rhamnoside
8	Luteolin-7-O-rhamnoside
9	Quercetin-3-O-arabinoside
10	Quercetin-3-O-rhamnoside

Table 2: Phytomolecules reported in various parts of *Rhus chinensis* Mill. and their *in vivo*, *in vitro*, and *in silico* experiments

Category	Name of Compound	Source (plant part)	Structure of Compound	Model Used	Findings	Ref
Antioxidant, Antiinflam-matory	Citric Acid	Fruits (Galls)	 Citric Acid	Spontaneously hypertensive rats (SHRs)	- Significant reduction in systolic and diastolic BP. - Relaxation of thoracic aorta - Effects reduced with endothelial removal - Citric acid rapidly absorbed and metabolized	[28]
Antioxidant, antimicrobial	L-Malic Acid	Fruits (Galls)	 L-Malic Acid	Potassium oxonate-induced *in vivo* hyperuricemia model.	- Significant inhibition of XO enzyme	[29]
Antioxidant, antimicrobia, Anti-inflammatory Anti-cancer	Gallic Acid	Fruits, Galls Leaves Bark	 Gallic Acid	Rat testicular torsion-detorsion model.	- Reduced lipid peroxidation (MDA levels). - Increased antioxidant enzyme activities (SOD, CAT, GSH) - Preservation of testicular structure and function - Decreased inflammation and apoptosis (lower TNF-α and Caspase-3 expression)	[30]
Antioxidant, anti-inflam Matory Neuro-Protective, anticancer	Protocate-chuic acid	Fruits Leaves	 protocatechuic acid	In vitro: TNF-α-induced hepatic stellate cell (HSC) model In vivo: Thioacetamide (TAA)-induced liver fibrosis in mice.	- Inhibited cell viability in TNF-α activated HSC-T6 cells (*in vitro*). - Reduced TAA-induced liver damage and fibrosis (*in vivo*) - Decreased liver fibrosis markers via TGF-β signaling pathway regulation.	[31]

Category	Name of Compound	Source (plant part)	Structure of Compound	Model Used	Findings	Ref
Antioxidant, anti-inflammatory Anti-cancer Hepatoprotective	Methyl gallate	Fruits (Galls)	 Methyl gallate	Zymosan-induced experimental arthritis	- Dose-dependent inhibition of arthritis (0.7–70 mg/kg). - Reduced edema, leukocyte migration, and inflammatory mediators (IL-1Beta, IL-6, TNF-Alpha, CXCL-1, LTB4, PGE2). - Inhibited neutrophil chemotaxis, adhesion, and macrophage activation. - Suppressed IL-6, NO, COX-2, and iNOS expression and intracellular calcium mobilization.	[32]
Antioxidant, anti-inflammatory, Neuro-protective,	Myricetin 3-O-beta-galactoside	Leaves		Influenza A virus (H1N1) in MDCK cell culture	Influenza A virus (H1N1) in MDCK cell culture	[33]
Antioxidant, antiinflam-matory, Anti diabetic	Myricetin-3-O-rhamnoside	Leaves	 Myricetin-3-O-rhamnoside	- skin Rat wound healing model.	Enhanced wound closure, collagen biosynthesis, reduced CRP and TNF-α levels, good elastase inhibition.	[34]
Antioxi-dant antiinflam-matory, anticancer	Luteolin-7-O-glucoside	Leaves	 Luteolin-7-O-glucoside	-Human Umbilical Vein Endothelial Cells (HUVEC) cultured *in vitro*. - Analysis of cholesterol hydroxylation pathways.	- Inhibited the STAT3 pathway in endothelial cells. - Exhibited antiproliferative and antioxidant activity in HUVEC cells. - Reduced ROS generation and transcriptionally repressed inflammatory cytokines and their receptors.	[35]

Category	Name of Compound	Source (plant part)	Structure of Compound	Model Used	Findings	Ref
					- Decreased cholesterol hydroxylated species (7-alpha-hydroxycholesterol and 7-beta-hydroxycholesterol). - Demonstrated anti-inflammatory effects, with potential cardioprotective benefits. - Implicated in reducing atherogenesis and cardiocirculatory diseases	
Anticancer, Antioxidant Antiinflam-matory	Quercetin-3-O-arabinoside	Leaves	 Quercetin-3-O-arabinoside	-In silico molecular docking, SARS-CoV-2	Highest binding affinity with papain-like protease (PLpro), potential as an anti-COVID-19 agent	[36]
Antioxi-dant antiinflam-matory, anticancer	Luteolin-7-O-glucoside	Leaves	 Luteolin-7-O-glucoside	-Human Umbilical Vein Endothelial Cells (HUVEC) cultured *in vitro*. - Analysis of cholesterol hydroxylation pathways.	- Inhibited the STAT3 pathway in endothelial cells. - Exhibited antiproliferative and antioxidant activity in HUVEC cells. - Reduced ROS generation and transcriptionally repressed inflammatory cytokines and their receptors. - Decreased cholesterol hydroxylated species (7-alpha-hydroxycholesterol and 7-beta-hydroxycholesterol). - Demonstrated anti-inflammatory effects, with potential cardioprotective benefits. - Implicated in reducing atherogenesis and cardiocirculatory diseases	[35]

A broad spectrum of both biological and pharmacological effects is demonstrated by *R. chinensis* extracts, as shown in Table 3.

1. Antidiarrheal activity

To test the methanol extract of the dried, ripe fruit of *Rhus javanica* or *Rhus semialata*, Swiss albino mice and Wister albino rats were employed as experimental models of castor oil-induced diarrheal [38,39]. Due to its high tannin content, it reduces intestinal fluid secretions and gut motility, contributing to its antidiarrheal activity. It also suppresses the release of pro-inflammatory mediators, including TNF-α, interleukin 1-β, through downregulating the NF-kB signalling pathway [40,41].

2. Antibacterial and Antimicrobial Activities

Gallic acid, phenolic compounds, methyl gallate, and gallotannins—all known antibacterial agents with positive effects on bacterial control are reported to be highly concentrated in the leaves of *Rhus chinensis* Mill [42].

3. Antioxidant activity

Water, ethanol, ethyl acetate, and ether extracts with varying polarities were used to evaluate the antioxidant, antibacterial, and antifungal properties of *R. chinensis* gallotannins. The extracts showed strong antioxidant activities in the hydroxyl radical scavenging, beta-carotene linoleic acid system, FRAP, and DPPH radical scavenging assays [43].

4. Anti- HIV activity

Different extracts of *Rhus chinensis* Mill. were used to evaluate (pet-ether, ethyl acetate, butanol, and aqueous extracts) the anti-HIV-1 effects. Petroleum ether extract was discovered to have the capacity to suppress the production of the HIV-1 p24 antigen and syncytium at non-cytotoxic concentrations. The therapeutic index and 50% effective concentration (EC50) were determined to be 100µg/ml, 0.91, and 0.71, respectively [44].

5. Antidiabetic activity

Alpha-glucosidase activity was examined in connection with the *R. chinensis* gall water extract (AEGRC). It was demonstrated that AEGRC inhibited Bacillus's alpha-glucosidase capacity. Additionally, it was found to be reversible and non-competitive following the administration of AEGRC as an inhibitor of the enzyme-substrate complex. An *in vivo* investigation using five groups of rats at graded dosages of 250–1000 mg/kg of AEGRC, with Acarbose (2.5 mg/kg) acting as the baseline, later confirmed this. Consequently, AEGRC has an antidiabetic impact by inhibiting the intestinal absorption of carbohydrates, which lowers the postprandial rise in blood glucose [45].

6. Hepatoprotective activity

The extract from *Rhus chinensis* Mill. fruits significantly reduced ALT, AST, TBIL, ALP, and MDA levels while decreasing the pro-inflammatory cytokines TNF-α, IL-6, and IL-1β, particularly at a dose of 800 mg/kg. It restored antioxidant markers such as GSH and SOD, activated the Nrf2 protein pathway, and inhibited CYP2E1 expression to reduce oxidative stress. Additionally, the extract upregulated BSEP and Mrp2 to regulate bile acid transport and alleviated cellular apoptosis by modulating the expression of Bax and Bcl-2 proteins. These findings suggest that *Rhus chinensis* Mill. fruits can prevent liver injury [46,47] induced by isoniazid and rifampicin in mice by regulating oxidative stress, apoptosis, and bile acid transport pathways [47]. Initiation of fatty acid oxidation through activation of AMPK and PPAR-α, *Rhus chinensis* Mill. shows liver protective effects, leading to reduced fatty acid accumulation. It also tends to inhibit fatty acid synthesis by downregulating the expression of SREBP-1 and FAS. Ethanol-induced oxidative stress in the rat model shows the prevention of alcoholic liver injury by inhibiting CYP2E1 through reducing the formation of reactive oxygen species [48].

7. Anticancer activity

It has been shown that *Rhus chinensis* extract has anticancer effects on carcinogenic Cdc25 phosphatases [49]. It has been established that several *Rhus chinensis* compounds, including pentagalloylglucose [45] and gallic acid, have anticancer properties [50]. It is being demonstrated that pentagalloylglucose possesses anticancer properties against lung cancer *in vivo*, and sarcoma [50] Inhibitory effects *in vitro* on the growth and/or invasion of breast cancer, leukaemia, melanoma, and liver cancer have been shown [51]. Through its ability to prevent angiogenesis, pentagalloylglucose [52] can have anticancer effects [53] and invasion of melanoma cells in metastasis [54].

8. Anti-inflammatory activity

Anti-inflammatory properties of *Galla chinensis* have been reported in both *in vitro* and animal models [55]. The immediate-type allergic reaction paradigm demonstrates that *Galla chinensis* can utilize multiple routes to dose-dependently regulate all inflammatory mediators, including lipid-derived

mediators, histamine, heparin, and other cytokines. The ethyl acetate fractions of the plant were separated and purified using activity-guided methods, which revealed that gallic acid was the main antiallergic component of *Galla chinensis* [56]. Fisetin, a well-known flavonoid compound of *Rhus chinensis* Mill roots have also been shown to dramatically reduce allergic reactions by reducing the production of mediators of inflammation from activated human mast cells[57,58]. Various in-vitro and in-vivo studies were conducted and it was found that pentagalloyl glucose, a polyphenolic compound has been shown to have strong anti-inflammatory effects [59,60]. Both the in- vitro and in-vivo experiments showed that the anti-inflammatory effects of *Rhus chinensis* Mill involves the downregulation of primary proinflammatory mediators including TNF-α, IL-1β, and IL-6. Generally these effects are due to inhibition of NF-κβ , MAPK signalling pathways. *Rhus chinensis* Mill. has the potential to targeting more than one pathway to neutralize inflammatory responses [61].

Table 3: The morphological features, key compounds and biological activities of different parts of *Rhus chinensis* Mill.

SL no	Plants parts	Morphological features	Key compounds	Respective Biological activity/ medicinal relevance	Ref
1	Fruits	Orange-red	terpenoids, polyphenols and Flavonoids	Antidiarrheal activity	[39,62]
2	Leaves	Green	Gallic acid, phenolic compounds, Methyl gallate, and gallotannins	Antibacterial and Antimicrobial activities	[42,63]
3	Arial parts	Green	Epicatechin-3-O-rhamnoside, Quercetin, Methyl gallate	antioxidant, antibacterial, and antifungal properties	[63]
4	Stem,Bark	Brown	Rhuspartin, Epicatechin-3-O-rhamnoside	Anti- HIV activity	[44]
5	Fruits	Orange-red	myricetin-3-O-rhamnoside, Quercetin-3-O-rhamnoside	Antidiabetic activity	[64]
6	Fruits	Orange-red	Quercetin and gallic acid.	Hepatoprotective activity	[65]
7	Fruits	Orange-red	Pentagalloylglucose, Gallic acid	Anticancer activity	[49,52]
8	Leaves	Brown	Tannin	Antibacterial, Antimicrobial	[66]

RESULT AND DISCUSSION

This review primarily focused on promising phytoconstituents, biological activities of *Rhus chinensis* Mill. but the comparison of different species of rhus can be established in view of bioactive compounds. Under the Rhus more than 250 species are available but only a small no of species undergoes phytochemical screening including *R. javanica, R. coriaria, Rhus chinensis* Mill., *R. tripartite, R. typhina L* etc. The bioactive compounds those shows promishing pharmacological including gallic acid, catechin 7-O-gallate, quercetin, quercetin 3-O-rhamnoside, myricetin, myricetin-3-O-β-glucoside, myricetin 3-rhamnoside, epicatechin-3-O-rhamnoside, Rutin etc given in table 4 [67]. *R. Japonica* contains various constituents like Naringenin (4',5,7-trihydroxyflavanone), eriodictyol, butin etc [63].Gallic acid, myricetin, kaempferol, and quercetin etc can be isolated from *Rhus coriaria* L. [68,69]. Rhuspartin, 2'',3''-dihydrohinokiflavone, 3′,8-Binaringenin, 2,3-Dihydro amentoflavone and many polyphenolic compounds can be isolated from *Rhus trilobata* [70]. *R. typhina L.* having well known primary bioactive compounds such as rutin, quercetin, gallic acid etc [71] so used as traditional medicine to treat cough, high blood pressure and worm infection , for cure diseases in respiratory and genital systems [72].

This review demonstrates the wide range of abundant bioactive substances like flavonoids, tannins, polyphenolics, etc across different sections of *Rhus chinensis* Mill. which contributes a vast range of pharmacological actions, aid to treat different pathological conditions. Previously conducted different research ensures these bioactive compounds have the potential to alleviate inflammatory response, show hepatoprotective activity , antiviral activity, antimicrobial activity etc. So, Rhus species are extensively used by rural people a traditional system of medicine to treat diarrhoea, worm infections in cattle, snake bites, respiratory infections etc in northeast region. Strong antibacterial and antimicrobial compounds like gallic acid,

methyl gallate are found in leaves, while other components like rhusparin in the stem and bark have anti-viral properties. Additionally, the aerial sections have antifungal and antioxidant properties. This section-wise distribution of chemicals emphasizes therapeutic applications. This review demonstrates that *Rhus chinensis* Mill. has promising pharmacological activities as it contains organic acids, phenolics, and flavonoids. The fruits, leaves, and galls contain a high concentration of gallic acid, citric acid, methyl gallate, myricetin, etc. Quantitative findings of malic acid, citric acid, gallic acid, quercetin-3-O-rhamnoside, and myricetin-3-O-rhamnoside were 144,520 ± 21, 651 µg/g and 135,453 ± 16,530 µg/g, 3791.02 ± 490.83 µg/g, 3592.77 ± 463.06 µg/g, and 525.43 ± 64.31 µg/g, respectively. These organic acids make significant contributions as potential antioxidants. Different gallic acid derivatives, such as digallic acid and trigalloyl glucose isomers, were present in low quantities, ranging from 108 to 327 µg/g. Luteolin-7-O-glucoside and quercetin were also identified at concentrations of approximately 81 µg/g and 173.38 µg/g, respectively. The quantitative data directly reflect the potential biological significance *of Rhus chinensis* Mill. The part-wise evaluation reveals that the fruits contain phenolics, including methyl gallate and Luteolin-7-O-glucoside, which have potent antioxidant and hepatoprotective properties. Leaves are rich in gallotannins and quercetin derivatives, showing antibacterial and anti-inflammatory activities. Galls contain a high amount of tannin, which has been shown to have antidiabetic and wound-healing effects through the NF-κB and AMPK pathways.

In vitro models, such as DPPH, ABTS, and FRAP, show IC50 values within 30-70 µg/ml for different extracts, strongly indicating a high capacity to neutralize free radicals. Methyl gallate exhibits suppression of zymosan-induced inflammation in the arthritis model at a dose of 0.7 mg/kg. Additionally, quercetin-3-O-arabinoside demonstrated a high binding affinity to SARS-CoV-2 PLpro in docking studies, suggesting potential antiviral properties. This thorough dissection highlights the unexplored medicinal potential of *Rhus chinensis* Mill.

Table 4: The key compounds and biological activities of Rhus species [63] **.**

Sl no	Rhus species	Major phytoconstituents	Biological activities
1	*R. chinensis*	Gallic acid, Betulonic acid, Lutein, Moronic acid, Benzofuranone	Antioxidant, antiviral, antimicrobial
2	*R. coriaria*	Quercetin, Rutin, Catechin, Gallic acid	Antioxidant, antifungal
3	*R. Glabra*	Epicatechin, Methyl gallate	Antioxidant, antimicrobial, astringent
4	*R. typhina*	Quercetin, Luteolin, Kaempferol, Rutin	Antioxidant, antimicrobial
5	*R. verniciflua*	Fustin, Butin, Methyl gallate	Antioxidant, antiviral, anticancer
6	*R. natalensis*	7-O-Methyl naringenin	Antibacterial, antioxidant, antimicrobial
7	*R. tripartita*	Myrecetin-3-O-glucoside	antioxidant, anti-inflammatory
8	*R. javanica*	Butin, sinapic acid	Antidiarrheal, antifungal
9	*R. copallinum*	Quercetin, Kaempferol, betulinic acid	Anticancer, antioxidant
10	*R. succedanea*	Robustaflavone, Amentoflavone	Antiviral, antioxidant
11	*R. retinorrhoea*	Eriodictyol	Anti-malarial, antioxidant
12	*R. mysorensis*	Fisetin, quercetin	Anti-inflammatory, antimicrobial
13	*R. pyroides*	Rhuschalcone-1	Antiviral, neuroprotective
14	*R. parviflora*	Agathisflavone	neuroprotective
15	*R. alata*	Friedelin	Antioxidant, antibacterial

CONCLUSION

However, the proper utilization and fulfillment of medicinal requirements of Rhus species require further extensive research to consolidate its medicinal applications. *Rhus chinensis* Mill. contains a broad range of phytochemicals, particularly flavonoids (quercetin, myricetin), phenolics (gallic acid, protocatechuic acid), and organic acids (citric acid, malic acid), having an IC50 of around 42.7%, showing anti-inflammatory, hepatoprotective, and antimicrobial effects. Evidence from qualitative analysis, preclinical bioassays, and spectral studies confirms the therapeutic efficacy of this compound. Future

research should focus on elucidating the molecular pathways responsible for biological activity, pharmaceutical kinetic profiles, standardizing extracts for bioactive fractions, *in vivo* validation, and advanced molecular docking. Furthermore, the clinical assessment and evaluation of new formulations based on *Rhus chinensis* Mill. may open the door for its incorporation into common pharmaceutical goods. However, there are some limitations in the existing research, as most current studies are based on preclinical research, which provides insufficient evidence to utilize Rhus species to treat diseases in humans, as they lack determination of safety and efficacy in human trials. By bridging the gap between ethnomedical use and scientific validation, *Rhus chinensis* Mill. can emerge as a robust source for drug development in inflammatory, infectious, hepatic, and metabolic disorders. Therefore, to utilize Rhus species as a medicinal product in the future, it is essential to address the present research gaps and restrictions. The Rhus species offer a valuable natural source for various therapeutic applications.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Sujan Banerjee and Surabhi Mandel contributed to conceptualization, data collection, editing, and drafting. Bhupendra Shrestha contributed to the conceptualization, editing the first draft, and revising the manuscript.

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