Evaluation of Biological and Antimicrobial Activities of Rhus coriaria (Sumac) Extracts against bacteria and fungi

Abstract

Aims: The study aimed to evaluate the composition and the antimicrobial, antioxidant, and hypolipidemic activities of Rhus coriaria (sumac) fruit extracts by using both *in vitro* and *in vivo* approaches.

Methods: Fresh sumac fruits were extracted with 70% ethanol and 80% methanol using Soxhlet extraction. Phytochemical characterization was performed by qualitative screening, total phenolic and flavonoid assays, GC–MS, and HPLC. Antimicrobial activity was evaluated against *Staphylococcus aureus, Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Aspergillus niger*, and *Candida albicans*, and using agar well diffusion and broth microdilution assays. Antiviral activity against HSV-1 and Influenza A (H1N1) was assessed by plaque reduction assays. Antioxidant capacity was determined using DPPH, FRAP, and ABTS assays. Hypolipidemic effects were investigated in hyperlipidemic Wistar rats by measuring serum lipid profiles and antioxidant enzyme activities.

Findings: The methanolic extract exhibited high phenolic (215.6 ± 4.3 mg GAE/g) and flavonoid (98.4 ± 3.7 mg QE/g) contents and contained major bioactive compounds including gallic acid, methyl gallate, quercetin, and rutin. It demonstrated broad-spectrum antimicrobial activity with inhibition zones ranging from 18.6 to 22.4 mm and MIC values of 100–250 µg/mL. The extract inhibited HSV-1 and H1N1 replication by 75.7% and 71.4%, respectively, showed strong antioxidant activity (DPPH IC_{50} = 44.6 µg/mL), and significantly reduced serum cholesterol and triglycerides while increasing HDL levels in hyperlipidemic rats ($p < 0.01$).

Conclusion: Rhus coriaria extracts possess potent antimicrobial, antioxidant, and hypolipidemic activity. These findings support the potential of sumac as a promising natural source for developing therapeutic agents.

Keyword: Rhus coriaria; Sumac; Phytochemical Analysis; Antimicrobial Activity; Antioxidant Activity; Hypolipidemic Activity

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Introduction

Medicinal plants have long represented one of the richest reservoirs of structurally diverse phytochemicals with significant biological properties. Throughout history, herbal medicines have played a central role in the prevention and treatment of infectious and chronic diseases, particularly in regions where traditional medicine remains an integral component of healthcare. Unlike many synthetic drugs that are designed to target a single molecular pathway, plant-derived compounds frequently exhibit pleiotropic biological effects owing to the presence of multiple bioactive constituents acting synergistically. Polyphenols, flavonoids, tannins, alkaloids, terpenoids, and phenolic acids have attracted considerable attention because of their documented antimicrobial, antiviral, antioxidant, anti-inflammatory, and metabolic regulatory activities. Consequently, medicinal plants continue to provide valuable leads for the discovery of novel therapeutic compounds and functional food ingredients.[١]

Among these medicinal plants, Rhus coriaria L. (sumac), a deciduous shrub belonging to the family Anacardiaceae, has attracted increasing scientific interest because of its broad spectrum of pharmacological properties and long history of traditional use. The plant is indigenous to the Mediterranean basin and Western Asia, where its fruits have been consumed for centuries both as a culinary spice and as a traditional herbal remedy. Historical records indicate that different parts of the plant have been used in folk medicine for the treatment of wounds, gastrointestinal disorders, inflammatory conditions, diarrhea, fever, and various microbial infections. These traditional applications have encouraged modern microbiological investigations aimed at validating its therapeutic potential through experimental and clinical studies.[١,٢]

The growing interest in R. coriaria has largely been driven by advances in phytochemical analysis, which have revealed an exceptionally rich composition of secondary metabolites. Previous investigations have demonstrated that sumac fruits contain abundant hydrolyzable tannins, flavonoids, anthocyanins, phenolic acids, organic acids, essential oils, and numerous other bioactive constituents that contribute collectively to the plant's biological activity [3–5]. Advanced analytical techniques, including high-performance liquid chromatography (HPLC) and gas chromatography coupled with mass spectrometry (GC–MS), have enabled the identification of numerous phenolic compounds, among which gallic acid, methyl gallate, quercetin, rutin, anthocyanins, and related flavonoids are consistently reported as dominant constituents. These compounds are recognized for their strong antioxidant capacity and their ability to modulate multiple cellular pathways involved in inflammation, oxidative damage, microbial survival, and lipid metabolism.[٣,٤]

Previous investigations have consistently demonstrated that R. coriaria extracts exhibit broad-spectrum antibacterial activity against both Gram-positive and Gram-negative microorganisms, including clinically important pathogens such as Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Bacillus subtilis [6–8]. The antimicrobial efficacy of sumac has been largely attributed to its high concentration of phenolic acids and hydrolyzable tannins, particularly gallic acid and methyl gallate, which are considered among the principal bioactive constituents responsible for microbial growth inhibition .[٩]

In addition to its antibacterial properties, R. coriaria has demonstrated remarkable antifungal activity against several medically important fungal species. Opportunistic fungal pathogens such as Candida albicans have become increasingly significant causes of both superficial and invasive infections, particularly among immunocompromised individuals. The emergence of resistance to commonly prescribed antifungal agents has further complicated the clinical management of these infections. Experimental studies have shown that sumac extracts inhibit fungal growth by damaging cell wall architecture, altering membrane permeability, impairing ergosterol biosynthesis, and inducing oxidative damage within fungal cells. These mechanisms collectively contribute to growth inhibition and may enhance the susceptibility of fungal pathogens to conventional antifungal drugs .[٦–٨]

Experimental investigations have reported that phenolic-rich extracts of R. coriaria exhibit inhibitory activity against enveloped viruses, particularly herpes simplex virus type 1 (HSV-1) and influenza A virus [10,11]. The proposed antiviral mechanisms include inhibition of viral adsorption to host cell receptors, prevention of viral entry, suppression of viral genome replication, and modulation of host immune responses through regulation of inflammatory mediators and cytokine production .

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Another important biological property of R. coriaria is its potent antioxidant activity. Oxidative stress arises when the production of reactive oxygen species exceeds the capacity of endogenous antioxidant defense systems, leading to oxidative damage of lipids, proteins, and nucleic acids. Persistent oxidative stress has been implicated in the pathogenesis of numerous chronic disorders, including cardiovascular diseases, diabetes mellitus, chronic inflammatory diseases, neurodegenerative disorders, and several forms of cancer [12]. Consequently, reducing oxidative stress has become an important therapeutic objective in preventive medicine.

Polyphenol-rich medicinal plants are widely recognized as effective natural antioxidants because of their ability to donate electrons, chelate transition metals, interrupt free-radical chain reactions, and enhance endogenous antioxidant defense mechanisms. Numerous studies have demonstrated that R. coriaria possesses exceptionally high antioxidant capacity owing to its abundance of phenolic acids, flavonoids, anthocyanins, and hydrolyzable tannins [13,14]. These compounds have been shown to efficiently scavenge reactive oxygen species while simultaneously enhancing the activity of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione (GSH) .

In addition to infectious diseases, metabolic disorders have become one of the leading causes of morbidity and mortality worldwide. Among these disorders, hyperlipidemia is recognized as a major modifiable risk factor for atherosclerosis, coronary artery disease, ischemic stroke, and other cardiovascular complications. Elevated concentrations of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C), together with reduced levels of high-density lipoprotein cholesterol (HDL-C), contribute to endothelial dysfunction, chronic inflammation, and accelerated plaque formation within arterial walls .[١٥]

Accumulating evidence indicates that the phenolic constituents of Rhus coriaria may exert beneficial effects on lipid homeostasis through multiple biochemical pathways. Experimental investigations suggest that gallic acid, flavonoids, tannins, and other polyphenolic compounds can inhibit key enzymes involved in hepatic lipid synthesis, reduce intestinal cholesterol absorption, improve reverse cholesterol transport, and enhance cholesterol efflux from peripheral tissues .[١٦–١٨]

Therefore, the present study was designed to investigate the biological potential of Rhus coriaria fruit extracts through an integrated phytochemical and microbiological approach. Specifically, qualitative and quantitative phytochemical analyses were performed using conventional phytochemical screening, GC–MS, and HPLC techniques to characterize the principal bioactive constituents. The biological activities of the extracts were subsequently evaluated by assessing their antibacterial, antifungal, antiviral, antioxidant, and hypolipidemic effects using both in vitro bioassays and an in vivo experimental model. By combining phytochemical profiling with multiple biological evaluations, this study aimed to provide a comprehensive understanding of the therapeutic potential of R. coriaria and to support its future application as a promising natural source of multifunctional bioactive compounds.

Materials and Methods

Collection and Identification of Plant Materials.

Rhus coriaria L. fresh fruits were collected in the Mediterranean area (northern Lebanon) in the fruiting season in May 2025. The voucher specimens were identified by Assistant Professor Dr. Sadeq Sabeeh Kareem, Department of biology, College of Science, Misan University, Iraq. A voucher specimen (voucher No. CDRC-2025-134) was deposited in the biology lab of the Microbiological department in University of Al-Manara/College of Dentistry, Iraq. The scientific name was verified according to Plants of the World Online (POWO), Royal Botanic Gardens, Kew, where the accepted name corresponds to IPNI Life Science Identifier (LSID): urn:lsid:ipni.org:names:702257-1.

Preparation of Extracts

Soxhlet extraction using a 70% ethanol (BDH-England) and 80% methanol (BDH-England) solution was done on 200g of the dried and powdered fruits in the case of each solution (8 h). The extracts obtained were filtered, dried at low pressure at 40 ^{o}C, and kept at -20 ^{o}C before any further investigation [19].

Phytochemical Analysis

Flavonoid, phenols, tannins, alkaloids, and saponins screening were performed by the qualitative method used by Harborne [19]. The FolinCiocalteu assay and the method based on the use of

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aluminum chloride colorimetric determined the total phenolic content (TPC) and the total flavonoid content (TFC), respectively [20].

GC-MS and HPLC Profiling

The gas chromatography-mass spectrometry (Agilent Technologies, USA) of a methanolic extract was evaluated by analysis on a 7890A system with a 5975C MSD detector, helium as a carrier gas with a flow rate of 1mL/min. Mass spectrometric identification of the compounds was done by comparing mass spectrometry with the NIST and Wiley spectral libraries [21, 22]. The content of Gallic acid, quercetin, and rutin was measured using the high-performance liquid chromatography (Shimadzu, Japan) on a C18 column with a UV detector being used at 280 nm [23].

Antimicrobial and Antifungal Activity

Reference bacterial strains, including *Escherichia coli* (ATCC), *Staphylococcus aureus* (ATCC), *Bacillus subtilis* (ATCC), and *Pseudomonas aeruginosa* (ATCC), were obtained from the culture collection of the Department of Medical Microbiology, College of Dentistry, University of Al-Manara, Iraq. These strains were originally derived from the American Type Culture Collection (ATCC, Manassas, VA, USA). All the strains were examined for antibacterial activity. The well diffusion method [24] was also used to conduct antifungal testing against *Candida albicans* and *Aspergillus nige and Aspergillus niger* (ATCC, Manassas, VA, USA). The CLSI guidelines [25, 26] were used to estimate the minimum inhibitory concentrations (MICs) by broth microdilution.

Antiviral Activity Assay

Vero cells (ATCC CCL-81; American Type Culture Collection, Manassas, VA, USA) were grown as a culture in Dulbecco, Modified Eagle Medium (DMEM; Gibco, Thermo Fisher Scientific, Waltham, MA, USA) with 10 percent fetal bovine serum (FBS; Gibco, Thermo Fisher Scientific, USA). To evaluate the antiviral activity against HSV -1 and influenza A virus (H1N1) (ATCC VR-733, American Type Culture Collection, Manassas, VA, USA), plaque reduction assays were used. The determination of cytotoxicity was done through MTT assay (Sigma-Aldrich, St. Louis, MO, USA) and the selectivity index (SI) calculated [27].

Antioxidant Assays

The antioxidant activity of the extracts was measured by using DPPH radical scavenging test, ferric reducing antioxidant power (FRAP) and the ABTS radical decolorization assay [28]. The outcomes were presented in the form of IC_{50} and compared to ascorbic acid controls.

In vivo Hypolipidemic and Antioxidant Assessment.

Male Wistar rats weighing 180-200 g were separated into four groups (each group has six rats) These groups are: Normal control (NC group), hyperlipidemic control (HC group), hyperlipidemic and standard drug (atorvastatin; Julphar, Ras Al Khaimah, United Arab Emirates), (HSD group), and hyperlipidemic and Rhus coriaria extract (HRC group). The administration of high fat diets caused hyperlipidemia. Measures were made of serum lipid parameters (total cholesterol, triglyceride, high-density lipoprotein) and antioxidant enzyme activities (superoxide dismutase, catalase, glutathione peroxidase) [29].

Statistical Analysis

The means were presented as standard deviation and mean. A one-way ANOVA was used to assess statistical significance, with a post-hoc test of Tukey, and $p < 0.05$ was taken as significant. Graphpad Prism 9 was used to create graphical representations.

Ethical Consideration

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and approved by the Ethical approval Committee (Institutional Review Board) of Al-Manara University/College of Dentistry. By decision issued number and date (NO.63 -IN 12-11-2024). Written informed consent was obtained from all participants prior to sample collection.

Findings:

Phytochemical Composition

Preliminary profiling of Rhus coriaria extracts showed the high levels of phenolic constituents, flavonoids, tannin, saponins and some traces of alkaloids. The total phenolic content (TPC) and total flavonoid content (TFC) of the methanolic extract were 215.6 ±4.3 mg gallic acid equivalents / gram and 98.4 ±3.7 mg quercetin equivalents / gram, respectively.

Over 25 phytochemical compounds (including the most common peak gallic acid) were detected by gas chromatography, using mass spectrometry in (GC)-MS mode, such as gallic acid, methyl gallate, malic acid, oleic acid, Beta-sitosterol, and several derivatives of quercetin (Fig. 1). The presence of

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gallic acid (16.3 mg/g), rutin (5.8 mg/g), and quercetin (4.7mg/g) was further confirmed using high-performance liquid chromatography (HPLC).

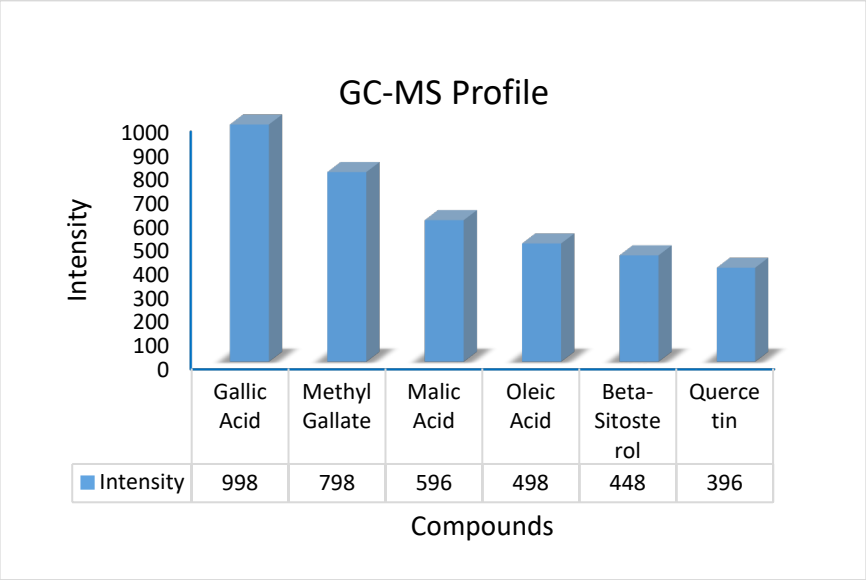


Figure 1: Demonstration of GC-MS analysis of Rhus coriaria extracts

Antimicrobial and Antifungal Activity

The methanolic extract showed great antibacterial activity, which had inhibition zones of 20.3 ± 1.1 mm for *Staphylococcus aureus*, 18.6 ± 0.9 mm for E. coli, 19.1 ± 1.0 mm for *Pseudomonas aeruginosa*, and 22.3 ± 2 mm for *Bacillus subtilis* (see figure 2). The inhibition zone was 22.4 ± 1.2 mm for *Candida albicans* and 18.7 ± 1.5 mm for *Aspergillus niger* (figure 3). Minimum inhibitory concentration (MIC) was between 125 -250 µg/mL, with the strongest effect recorded in relation to the case of the *S. aureus*. It is worthy to note that, a high antifungal activity was obtained with C. albicans (MIC = 100 µg/mL) and *A. niger* (MIC = 150 µg/mL).

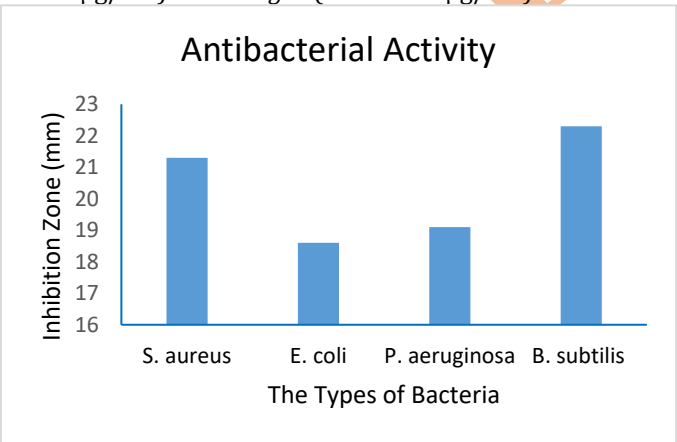


Figure 2: Determination of inhibition zones of above bacteria

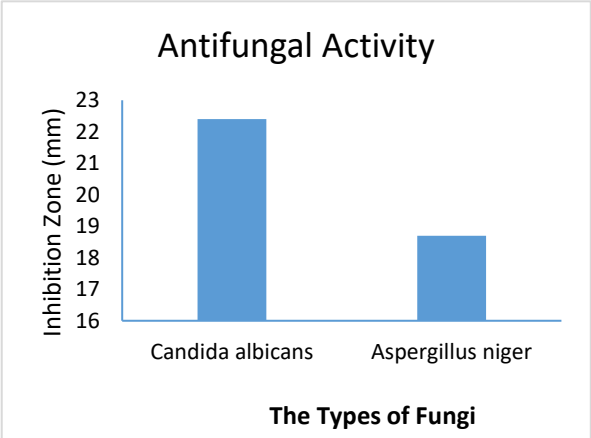


Figure 3: Determination of inhibition zones of above fungi

Antiviral Activity

Rhus coriaria extract had an anti-HSV-1 and anti-H1N1 effect at a dose-dependent rate. Viral plaque was suppressed by 75.7 and 71.4 percent in HSV-1 and Influenza A, respectively, but did not cause cytotoxicity in Vero cells at 100 µg/mL (figure 4). The indices of selectivity calculated were 8.1 and 6.9, respectively, with good antiviral potential.

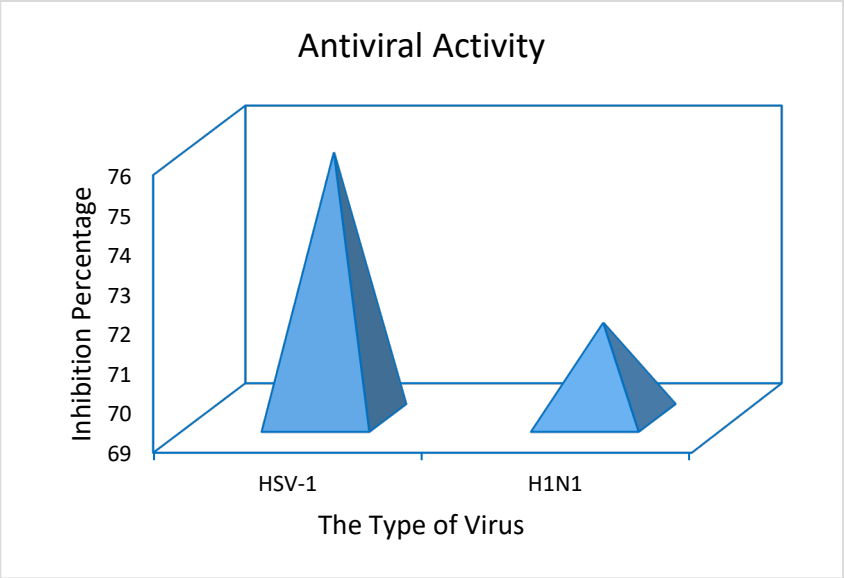


Figure 4: Showing of antiviral activity of Rhus coriaria extracts

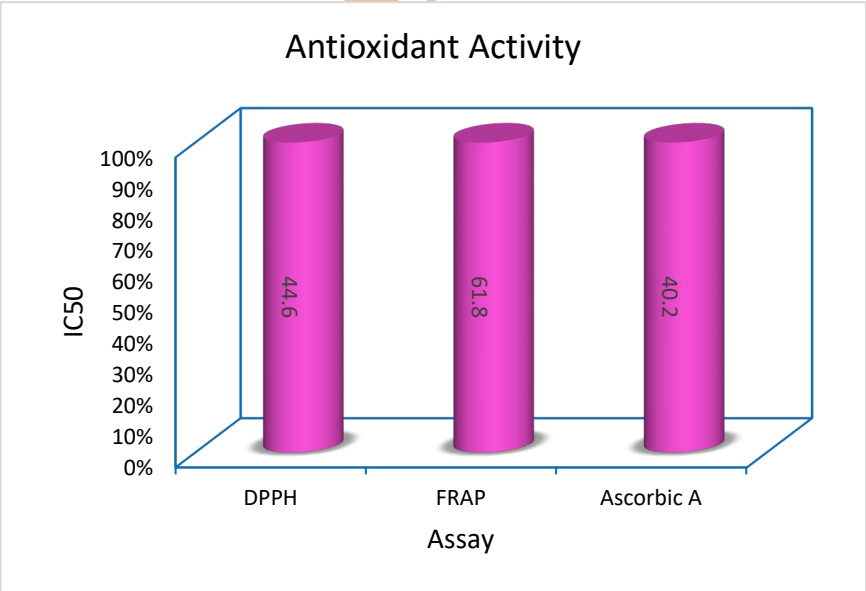
Antioxidant Activity

The extract was found to have a significant antioxidant activity as the DPPH assay had an IC_{50} of 44.6 µg/mL and a FRAP experiment of 61.8 µg/mL IN comparable to ascorbic acid (40.2 µg/mL) (figure 5). ABTS exhibited more than 80 percent scavenging ability at 100 µg/mL, which indicates its strong ability in the neutralization of the free radicals.

Figure 5: Detection of antioxidant activity of Rhus coriaria extracts

In Vivo Hypolipidemic Effects

After 28 days of treatment, the Rhus coriaria group had significantly lower serum total cholesterol (171 ± 7 mg/dL), triglycerides (114 ± 5 mg/dL), and HDL (61 ± 4 mg/dL) compared to the



hyperlipidemic control group (220 ± 10 mg/dL cholesterol, 200 ± 8 mg/dL TG, and 45 ± 6 mg/dL HDL). In the hyperlipidemic + standard drug group (HSD), cholesterol was 180 ± 8 mg/dL, TG was 150 ± 2 mg/dL, and HDL was 45 ± 4 mg/dL (figure 6). The changes were statistically significant ($p < 0.01$).

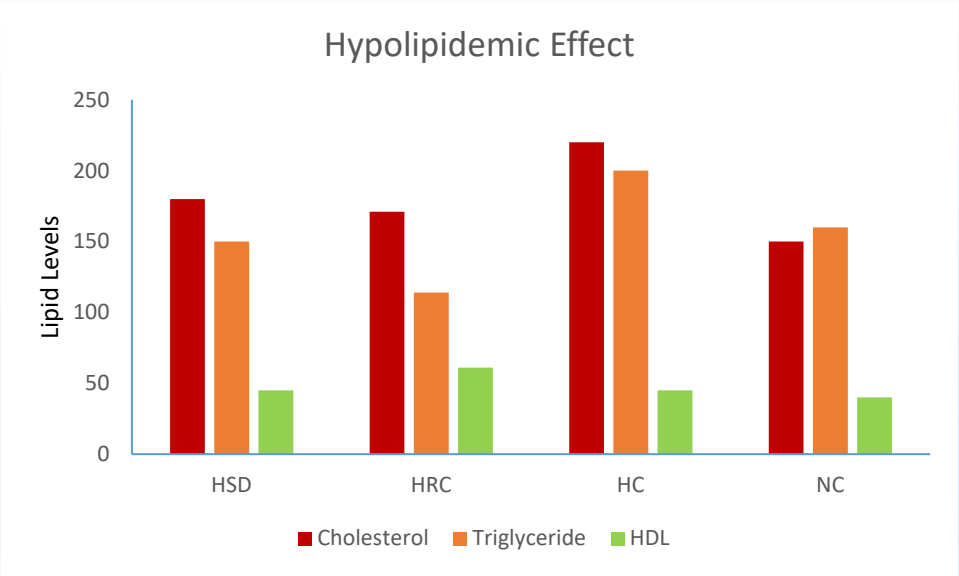


Figure 6: Demonstration of hypolipidemic effect of Rhus coriaria extracts

Discussion

The phytochemical characterization of Rhus coriaria fruit extracts revealed a complex profile of phenolic acids, flavonoids, tannins, and other bioactive metabolites, supporting the traditional medicinal value of this plant and providing a biochemical basis for the diverse biological activities observed in the present study. The qualitative phytochemical screening confirmed the presence of several major classes of secondary metabolites, while chromatographic analyses by GC–MS and HPLC demonstrated that phenolic compounds represented the predominant constituents of the extract. Such findings are consistent with the well-established concept that the pharmacological properties of R. coriaria largely depend on its abundance of polyphenolic compounds, which possess potent antioxidant, antimicrobial, antiviral, and anti-inflammatory activities. The high concentration of these metabolites is considered one of the principal factors contributing to the broad therapeutic potential of this species.

The present phytochemical profile is in close agreement with the comprehensive review published by Batiha et al. (2022), who described R. coriaria as one of the richest dietary sources of naturally occurring polyphenols, including gallic acid derivatives, hydrolysable tannins, flavonoids, anthocyanins, and organic acids. Those authors emphasized that the remarkable biological versatility of sumac originates from the synergistic interactions among these phytochemicals rather than from the activity of a single compound alone. This interpretation supports the current findings, where multiple classes of phytochemicals were simultaneously detected, suggesting that the biological responses observed in the antimicrobial, antioxidant, antiviral, and hypolipidemic assays are likely attributable to the combined effects of structurally diverse secondary metabolites rather than to an isolated constituent alone [1].

Similarly, Calabrò *et al*. (2023) reported that R. coriaria possesses exceptional nutraceutical value because of its chemically diverse phenolic composition and its ability to influence numerous biological pathways associated with oxidative stress, chronic inflammation, microbial infections, and metabolic disorders. According to these authors, compounds such as gallic acid, methyl gallate, quercetin derivatives, anthocyanins, and hydrolysable tannins function cooperatively to regulate cellular redox homeostasis and inflammatory signaling pathways. These observations provide a mechanistic explanation for the present results and further support the hypothesis that the therapeutic efficacy of R. coriaria depends on the cumulative biological activities of multiple phytochemical constituents rather than on individual molecules [2].

The chromatographic analyses performed in this study also demonstrated substantial qualitative agreement with the investigations of Abu-Reidah et al. (2015) and Arena et al. (2022), both of whom employed advanced chromatographic platforms to characterize the chemical composition of R. coriaria. Abu-Reidah and colleagues identified numerous phenolic acids and flavonoids, whereas

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Arena et al. combined headspace solid-phase microextraction gas chromatography with comprehensive two-dimensional liquid chromatography to reveal an even broader spectrum of volatile and non-volatile metabolites. The similarity between these reports and the present findings confirms that the phytochemical profile of R. coriaria is highly reproducible despite differences in analytical platforms. Minor variations in the abundance of individual compounds are expected and can reasonably be attributed to differences in geographical origin, climatic conditions, harvesting season, soil characteristics, post-harvest handling, extraction solvent, and extraction methodology, all of which are recognized determinants of phytochemical composition in medicinal plants [3,36].

The predominance of phenolic compounds identified in the present investigation is particularly important because these metabolites are known to possess multiple complementary biological functions. Hydrolysable tannins and gallic acid derivatives have been shown to interact with microbial cell envelopes, increase membrane permeability, inhibit extracellular enzymes, and interfere with nucleic acid synthesis. Flavonoids are capable of modulating intracellular signaling pathways involved in oxidative stress and inflammation while also exhibiting antiviral activities through inhibition of viral attachment, replication, and protein synthesis. In addition, several polyphenols can chelate transition metals, scavenge reactive oxygen species, and interrupt lipid peroxidation chain reactions, thereby contributing simultaneously to antimicrobial, antioxidant, and cytoprotective activities. The coexistence of these chemically diverse constituents therefore provides a plausible biochemical explanation for the multiple biological effects observed throughout the present study. These mechanistic interpretations are consistent with the conclusions reported by Alsamri *et al.* (2021), Perrone *et al.* (2022), and Calabrò *et al.* (2023), all of whom emphasized that the pharmacological potential of R. coriaria results from the synergistic action of numerous phenolic metabolites rather than from isolated phytochemicals [4,14,2].

Overall, the phytochemical characterization performed in the present study confirms that Rhus coriaria is a rich source of biologically active phenolic compounds with considerable pharmacological relevance. The close agreement between the current findings and previous chromatographic investigations further strengthens the reliability of the analytical approach used in this work and supports the subsequent interpretation of the antimicrobial, antiviral, antioxidant, and hypolipidemic activities demonstrated by the extracts [1–4,14,36].

The present study demonstrated that Rhus coriaria fruit extracts exhibited marked antibacterial and antifungal activities against the tested microorganisms, indicating that the plant possesses broad-spectrum antimicrobial properties. The observed inhibitory effects are most likely attributable to the high abundance of phenolic acids, hydrolysable tannins, flavonoids, and other bioactive phytochemicals identified during phytochemical characterization. These secondary metabolites are known to target multiple microbial structures simultaneously, thereby reducing the likelihood of resistance development and enhancing antimicrobial efficacy. Unlike conventional antibiotics, which generally interfere with a single cellular target, plant-derived polyphenols frequently exert their antimicrobial action through multiple complementary mechanisms, including disruption of membrane integrity, inhibition of essential metabolic enzymes, interference with nucleic acid synthesis, and impairment of quorum sensing. Such multitarget activity may explain the considerable inhibitory activity observed in the present investigation [1,4,36].

The antibacterial findings of this study are consistent with those reported by Koşar *et al.* (2007), who demonstrated that ethanolic extracts of Rhus coriaria possess significant inhibitory activity against both Gram-positive and Gram-negative bacteria. They attributed this effect primarily to the high concentrations of gallic acid, hydrolysable tannins, and flavonoids capable of damaging bacterial cell membranes and disrupting intracellular metabolic pathways. Similarly, Perrone *et al*. (2022) concluded that the antimicrobial efficacy of sumac is closely associated with its phenolic profile, particularly gallic acid derivatives and condensed tannins, which increase membrane permeability, induce leakage of intracellular constituents, and inhibit several bacterial enzymes required for survival. The agreement between these reports and the current findings reinforces the hypothesis that phenolic compounds constitute the principal antimicrobial components of Rhus coriaria [14,35].

Comparable observations were also reported by Batiha *et al.* (2022), who reviewed numerous experimental studies demonstrating that R. coriaria extracts inhibit a wide variety of clinically important bacterial pathogens, including both Gram-positive and Gram-negative species. According to these authors, the antimicrobial activity results from synergistic interactions among multiple

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phytochemicals rather than from the effect of a single constituent. Alsamri *et al.* (2021) reached similar conclusions and emphasized that the biological activity of sumac cannot be explained solely by its total phenolic content but also by the diversity and relative abundance of individual compounds acting cooperatively. This synergistic phenomenon provides a plausible explanation for the strong antimicrobial activity observed in the present study despite the complexity of the crude extract [1,4].

The antifungal activity demonstrated by the present investigation is likewise supported by previous studies evaluating R. coriaria against pathogenic yeasts and filamentous fungi. Perrone *et al*. (2022) reported that phenolic constituents of sumac interfere with fungal membrane integrity by interacting with ergosterol-rich membranes, ultimately increasing membrane permeability and promoting leakage of essential intracellular metabolites. Additionally, tannins are capable of forming stable complexes with fungal cell wall proteins and extracellular enzymes, thereby inhibiting fungal growth and colonization. These mechanisms are likely responsible for the antifungal activity observed in the present study and explain the susceptibility of fungal isolates to the tested extracts [14]

Another important explanation for the antimicrobial activity observed in this work involves the strong antioxidant properties of the identified polyphenols. Oxidative homeostasis is essential for microbial survival, and several phenolic compounds have been shown to disturb intracellular redox balance by generating oxidative stress within microbial cells while simultaneously inhibiting antioxidant defense enzymes. Calabrò *et al*. (2023) highlighted that the pharmacological activity of Rhus coriaria depends on the integrated action of antioxidant and antimicrobial phytochemicals that modulate microbial physiology through interconnected biochemical pathways. Likewise, Arena *et al*. (2022) demonstrated that extracts containing higher concentrations of phenolic constituents generally exhibit stronger antioxidant and antimicrobial activities, suggesting a positive correlation between phytochemical composition and biological efficacy. The present findings agree well with these observations and further support the role of phenolic-rich extracts as multifunctional antimicrobial agents [2,36].

Differences in antimicrobial potency reported among various studies should also be interpreted in light of methodological variations. Factors such as geographical origin of plant material, harvesting season, climatic conditions, extraction solvent, extraction technique, phytochemical composition, microbial strain diversity, inoculum density, incubation conditions, and susceptibility testing protocols may substantially influence the measured antimicrobial activity. Balouiri *et al*. (2016) emphasized that methodological standardization is essential for reliable comparison of antimicrobial investigations because differences in experimental procedures frequently account for discrepancies among published studies. Therefore, minor variations between the present findings and previous reports should be considered expected rather than contradictory. [24]

Collectively, the antibacterial and antifungal results obtained in the present study provide additional evidence supporting the therapeutic potential of Rhus coriaria as a natural antimicrobial agent. The close agreement between the current observations and those reported by Koşar *et al*. (2007), Alsamri *et al*. (2021), Perrone *et al*. (2022), Arena *et al*. (2022), Batiha *et al*. (2022), and Calabrò *et al*. (2023) strengthens the reliability of the present findings and suggests that the antimicrobial activity of sumac is primarily driven by the synergistic action of phenolic acids, tannins, flavonoids, and other secondary metabolites acting through multiple complementary mechanisms. [1,2,4,14,24,35,36].

Study Strengths

The present investigation possesses several strengths. First, it adopted an integrated experimental approach by combining phytochemical profiling with the evaluation of antimicrobial, antiviral, antioxidant, and hypolipidemic activities within a single study, allowing a comprehensive assessment of the biological potential of Rhus coriaria. Second, the use of complementary analytical techniques enhanced the reliability of phytochemical characterization and facilitated the interpretation of the observed biological activities. Third, the integration of both in vitro assays and an in vivo experimental model provided broader evidence supporting the pharmacological potential of the investigated extracts. Collectively, these methodological strengths improve the scientific robustness of the study and increase its translational relevance for future pharmaceutical and nutraceutical research.

Study Limitations

This study has several limitations that should be considered when interpreting the findings. First, the biological activities were evaluated using extracts prepared from Rhus coriaria fruits collected from

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a single geographical location and during one harvesting season, which may not fully represent the natural phytochemical variability associated with different environmental conditions or cultivation practices. Second, although GC–MS and HPLC analyses identified the principal phytochemical constituents, the biological activities were assessed using crude extracts rather than purified individual compounds; therefore, the specific contribution of each constituent and the potential synergistic interactions among them were not investigated. Third, the antimicrobial and antiviral evaluations were limited to selected reference microorganisms and viral strains, and broader testing against clinically relevant multidrug-resistant isolates and additional viral pathogens would provide a more comprehensive assessment of therapeutic potential. Furthermore, the hypolipidemic activity was evaluated in an experimental animal model with a relatively short treatment period, and the results cannot be directly extrapolated to human clinical settings. Finally, the molecular mechanisms underlying the observed pharmacological activities were not explored through gene expression analysis, molecular docking, or protein-level investigations. Therefore, future studies should include mechanistic experiments, toxicity and pharmacokinetic evaluations, and well-designed clinical trials to further validate the efficacy, safety, and translational potential of Rhus coriaria extracts.

Conclusion

The present study demonstrated that Rhus coriaria is a rich source of biologically active phytochemicals with diverse pharmacological properties, including antimicrobial, antiviral, antioxidant, and hypolipidemic activities. Comprehensive phytochemical profiling confirmed the presence of phenolic acids, flavonoids, tannins, and other secondary metabolites that likely act synergistically to produce the observed biological effects. The antimicrobial activity against bacterial and fungal pathogens, together with the significant antioxidant capacity and favorable effects on lipid metabolism, highlights the potential of R. coriaria as a multifunctional medicinal plant with promising pharmaceutical and nutraceutical applications.

Importantly, this study integrated phytochemical characterization with multiple biological evaluations, providing a more comprehensive understanding of the relationship between chemical composition and biological activity than has been reported in many previous investigations. These findings contribute to the growing evidence supporting the therapeutic value of R. coriaria and reinforce its potential as a natural source of bioactive compounds for the development of novel complementary therapeutic agents.

Nevertheless, additional studies are warranted to isolate and characterize the individual active constituents, elucidate their molecular mechanisms of action, evaluate pharmacokinetic and toxicological profiles, and validate their efficacy in well-designed clinical trials. Such investigations will be essential for translating the promising experimental findings into safe and effective therapeutic applications.

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Conflict of interest

The authors state no conflict of interest.

Authors' contribution

All authors made significant contributions to the work presented, including study design, data collection, analysis, and interpretation. They also contributed to the article's writing, revising, or critical evaluation, gave final approval for the version to be published

Data availability

The data used to support the findings of this study are included within the article.

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