

Phytochemical Composition, Biological Activities, and Biomedical Applications of *Ruta graveolens* L.: A Review

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Ruta graveolens L. (Rutaceae) is a medicinal plant known for its diverse phytochemical composition and numerous reported biomedical and biological activities. This review provides an updated synthesis of its phytochemistry, alkaloid diversity, biological activities, mechanisms, safety profile, and biomedical relevance. A literature search identified 70 relevant research papers published between 2015 and 2026, covering chemical constituents and antioxidant, anti-inflammatory, antimicrobial, antiparasitic, insecticidal, and other biological effects. Evidence was considered according to experimental level, including *in vitro*, *in vivo*, animal, and traditional-use studies. The findings demonstrate substantial phytochemical diversity and promising biological activities; however, most evidence is derived from experimental models, with limited clinical validation. Reported phototoxic, hepato-renal, cardiovascular, reproductive, and embryotoxic effects also highlight important safety concerns. Further mechanistic, pharmacokinetic, toxicological, and clinical studies are needed to establish the efficacy and safety of *R. graveolens*. Overall, this review highlights its biological potential and biomedical relevance while emphasizing the limitations of current evidence and priorities for future research.

Keywords: Alkaloids; Antibacterial; Antioxidant; Cytotoxic; Phytochemicals; Plant; *Ruta graveolens* and Rutin.

Ruta graveolens is a small perennial shrub grown throughout the world in gardens as an ornamental plant in hot, dry and stony soils.¹ It's a Mediterranean native—specifically the Balkan Peninsula—now widely cultivated globally, particularly in Europe, Asia, South America, and North America.² Its growing season is spring especially from April to July in sandy soils³. Typically reaches a height of 50–100 cm, it possesses a taproot system and erect, cylindrical stems. It leaves are blue to green in color and have

a fern-like appearance.^{3,4} They contain translucent glands that secrete essential oils, which produce the strong characteristic odor of this species. The plant produces cluster of small yellow flowers that attract butterflies and other pollinating insects. The flowers of *Ruta* are characterized by five petals and five sepals.^{3,5} The sepals are concave and toothed, during the summer. The fruits are four-lobed capsules measuring approximately 7–9 mm in diameter and containing black, kidney-shaped seeds.^{6,7} It is densely covered with pellucid glands,

with each lobe containing several seeds. Seeds are blackish, wedge-shaped, approximately 2 mm long, rounded dorsally, and characterized by a minutely tuberculate surface. In genus *Ruta* there are 14 species, among them *R. graveolens* and *R. chalepensis* have been reported in the flora of Jordan.^{7,8} In many countries, *R. graveolens* is cultivated as a medicinal and ornamental plant and has traditionally been used to treat various disorders, as documented in the classical medical systems of Unani, Ayurveda and Homoeopathy.⁹

MATERIALS AND METHODS

A comprehensive literature search was conducted using electronic databases, including Google Scholar, Research Gate, and PubMed, supplemented by additional academic search engines and artificial intelligence-assisted literature search tools to identify relevant published studies. A total of 70 research papers were used as sources for this study. All of the selected papers were published between 2015 and 2026, ensuring that the research was based on recent and relevant scientific literature. The retrieved literature was screened for relevance to the study objectives, and pertinent articles were included to synthesize the current evidence. The selected studies provide a comprehensive overview of the topic and contribute to a well-supported analysis of the research problem. In addition, relevant publications by the authors were reviewed and incorporated, where appropriate, to provide additional context and support the interpretation and discussion of the findings.

AI-assisted tools were not employed as independent sources of scientific evidence. AI-assisted technologies were only utilized as supplemental tools to help with filtering and summarizing the literature, organizing obtained information, refining search keywords, and finding possibly relevant publications. Before being included in the review, every data retrieved using AI-assisted techniques was checked against the original publications.

Medicinal properties

Ruta graveolens produces a diverse range of secondary metabolites, including furanocoumarins, flavonoids, alkaloids, and

essential oils.^{10,11} These compounds contribute to its distinctive and potent odour.¹¹ *R. graveolens*, has been reported to possess a wide range of pharmacological and biological properties, including antiparasitic, antiseptic, hypotensive, antispasmodic, antimicrobial, insecticidal, anticancer, nematocidal, sedative, cytotoxic, diuretic, vasoprotective, venotonic activities and fungicidal properties.¹⁰⁻¹² Due to its diverse biological and pharmacological properties, *R. graveolens* has traditionally been used as a medicinal plant for various health conditions.¹¹ It has also been used to eliminate intestinal parasites and to manage circulatory disorders.^{10,12} It has traditionally been used to alleviate nervous disorders, menstrual cramps, digestive disturbances, vertigo, and headaches. In external applications, *R. graveolens* have been used in the treatment of rheumatism, scabies, earaches, vitiligo and other ailments.^{2,11}

Literature extensively reviews various traditional uses and pharmacological properties associated with this plant.^{11,13} Beyond medicinal applications, it finds utility in agriculture for its insecticidal and repellent characteristics, effectively managing pests like grasshoppers, ants, cutting insects, and aphids. Additionally, the plant serves as a nematocide, fungicide, and natural soil disinfectant.^{2,14}

However, despite its versatile applications, caution is emphasized in the literature regarding the dosage of the plant.^{2,15} Exceeding recommended values can lead to intoxication, resulting in symptoms such as diarrhea, headache, vomiting, stomach pain, abortion, bleeding, phototoxic burns and skin lesions.^{2,14,15} Therefore, careful consideration of dosage is crucial to harnessing the benefits of this plant without.

Phytochemical Constituents

Numerous studies have characterized the phytochemical composition of *R. graveolens*, revealing a diverse array of bioactive constituents. Phytochemical analyses of aerial parts extract have identified flavonoids, alkaloids, terpenoids, essential oils, glycosides and fatty acids.¹⁶⁻¹⁸ Furthermore, both qualitative and quantitative investigations have confirmed the presence of proteins, carbohydrates, free amino acids, phenolic compounds, steroids, alkaloids,

terpenoids, glycosides, and rutin, underscoring the complex phytochemical profile and potential pharmacological significance of this species.

Phenolics, Flavonoids, and Glycosides

Phenolic compounds are a class of chemical substances characterized by the presence of an aromatic ring bearing one or more hydroxyl groups. Compounds containing a single hydroxyl group are referred to as phenols, whereas those with multiple hydroxyl groups are termed polyphenols.^{11,19} This group also includes various functional derivatives, such as esters and glycosides. Phenolic constituents can be extracted using methanol from *R. graveolens*, yielding a range of secondary metabolites, including flavonoids, tannins, and glycosides.^{11,19,20}

These phytochemical constituents and bioactive compounds confer multiple therapeutic

properties to the extract, including antioxidant, scolicidal, and bactericidal activities, as well as potential applications in chemotherapeutic and adjuvant therapies for various disorders.^{18,20}

Flavonoids are among the major constituents identified in the methanolic extract of the aerial parts of *R. graveolens* (Table 2), including quercetin, procyanidin, apigenin, chrysin, isorhamnetin, kaempferol, myricetin, and vitexin.^{18,21}

Rutin, for instance, is a prominent flavonoid glycoside detected in the methanolic extract of *R. graveolens*.²² It exhibits a wide range of biological activities, including antimicrobial, antiparasitic, antilipidemic, antioxidant and anti-inflammatory.^{13,18–21,23}

Alkaloids

Alkaloids are a class of naturally organic compounds, heterocyclic bases that

Table 1. Classification of *Ruta graveolens*

Kingdom	Plantae	Plants
Phylum	Streptophyta	Vascular plants
Class	Equisetopsida	Flowering and dicot plants
Order	Sapindales	Woody, including trees and shrubs
Family	Rutaceae	Aromatic with glands and thorns on the leaves
Genus	<i>Ruta</i> L.	
Species	<i>graveolens</i>	

Taxonomic Authority Link URL: <https://npgsweb.ars-grin.gov/>

Table 2. Flavonoids constituents of *R. graveolens* extract

Flavonoid Name	Molecular Formula	Molecular Weight (g/mol)	References
1. Chrysin	C ₁₅ H ₁₀ O ₄	254.24	16–18,24
2. Procyanidin	C ₃₀ H ₂₆ O ₁₃	594.5	16,17,21,24
3. Apigenin	C ₁₅ H ₁₀ O ₅	270.24	11,16,17
4. Naringenin	C ₁₅ H ₁₂ O ₅	272.25	16,17,24,25
5. Myricetin	C ₁₅ H ₁₀ O ₈	318.23	11,16,17,25
6. Luteolin	C ₁₅ H ₁₀ O ₆	286.24	16,17,24
7. Acacetin	C ₁₆ H ₁₂ O ₅	284.26	13,16,17,25
8. Kaempferol	C ₁₅ H ₁₀ O ₆	286.24	16,17,24
9. Narcissoside	C ₂₈ H ₃₂ O ₁₆	624.5	16,17,24
10. Quercetin	C ₁₅ H ₁₀ O ₇	302.23	11,16,17
11. Isoquercetin	C ₂₁ H ₂₀ O ₁₂	464.4	7,16,17,25
12. Rutin	C ₂₇ H ₃₀ O ₁₆	610.5	11,16–18,24
13. Vitexin	C ₂₁ H ₂₀ O ₁₀	432.4	16,17,24,25
14. Hyperoside	C ₂₁ H ₂₀ O ₁₂	464.4	7,16,17
15. Isorhamnetin	C ₁₆ H ₁₂ O ₇	316.26	7,16,17,25

are synthesized by plants.²⁶ These compounds derived from amino acids, characterized by the presence of one or more nitrogen atoms within their structure.^{27,28} Alkaloids, along with other classes of phytochemicals, contribute significantly to the therapeutic properties of medicinal plants.^{16,17,29,30} Phytochemical analyses of *R. graveolens* have confirmed the presence of various alkaloids (Table 3), including isoquinoline and tropane alkaloids, as well as members of the acridone alkaloid group.^{16,17,29,30} In addition, alkaloids have been identified as the most abundant class of non-volatile chemical

constituents in *Ruta graveolens*. Among these, acridone and quinoline alkaloids are the most frequently reported. Furthermore, phytochemical analysis of the aerial parts of *R. graveolens* has led to the identification of a novel quinoline alkaloid³¹

Fatty Acids

Fatty acids are considered one of many important sources of energy and are the basic and essential components of structures like the cell membrane. They act as a signal and a substrate for different bioactive molecules.^{7,11,38,39}

Table 3. Alkaloids constituents of *R. graveolens* extract

Alkaloid classes	Molecular Formula	Molecular Weight (g/mol)	References
1. Isoquinoline	C ₉ H ₇ N	129.16	16,17,24,29
2. Tropane	C ₈ H ₁₅ N	125.21	16,17,30
Furoquinoline			
3. Dictamnine	C ₁₂ H ₉ NO ₂	199.2	17,30,31
4. Ptelein	C ₁₃ H ₁₁ NO ₃	229.23	16,17,30
5. Kokusaginine	C ₁₄ H ₁₃ NO ₄	259.26	17,30,31
6. Isoplatydesmine	C ₁₅ H ₁₇ NO ₃	229.24	17,24,32,33
7. Dihydroevocarpine	C ₂₃ H ₃₅ NO	341.5	4,7,32–34
8. Schinifoline	C ₁₇ H ₂₃ NO	257.37	17,24,31,34
9. Furoquinoline	C ₁₁ H ₇ NO	169.18	17,24,33,34
Acridone			
10. 1-Hydroxy-10-methylacridone	C ₁₄ H ₁₁ NO ₂	225.24	17,24,25,35
11. Arborinine	C ₁₆ H ₁₅ NO ₄	285.29	17,24,25,36
12. Graveoline	C ₁₇ H ₁₃ NO ₃	279.29	17,24,35,36
13. 1,4-Dihydroxy-2,3-dimethoxy-10-methylacridin-9(10H)-one	C ₁₆ H ₁₅ NO ₅	301.29	17,24,35,36
14. Graveolinine	C ₁₇ H ₁₃ NO ₃	279.29	17,24,25,35
15. Gravacridonol	C ₁₉ H ₁₇ NO ₄	323.3	17,24,25,36
16. Rutagravin	C ₁₉ H ₁₇ NO ₅	339.3	17,24,25,35
17. Gravacridonediol monomethyl ether	C ₂₀ H ₂₁ NO ₅	355.4	17,24,35,37
18. Gravacridondiol	C ₁₉ H ₁₉ NO ₅	341.4	17,24,35,37
19. Gravacridonetriol	C ₁₈ H ₁₇ NO ₆	357.4	17,24,25,37
20. Rutacridone	C ₁₉ H ₁₇ NO ₃	307.3	17,24,31,33–35
21. Isogravacridone chlorine	C ₁₉ H ₁₈ ClNO ₄	359.8	17,24,35,36
Quinolone			
22. Norgraveoline(2-(1,3-Benzodioxol-5-yl)quinolin-4(1H)-one)	C ₁₆ H ₁₁ NO ₃	265.26	17,24,25,35
23. 4-Methoxy-1-methylquinolin-2(1H)-one	C ₁₁ H ₁₁ NO ₂	189.21	17,24,25,37
24. 2-Heptyl-4(1H)-quinolone	C ₁₆ H ₂₁ NO	243.34	17,24,35,37
25. 2-Octyl-4(1H)-quinolone	C ₁₇ H ₂₃ NO	257.37	17,24,35,37
26. 1-Methyl-2-undecyl-4(1H)-quinolone	C ₂₁ H ₃₁ NO	313.5	9,17,24,37
27. 1-Methyl-2-dodecyl-4(1H)-quinolone	C ₂₂ H ₃₃ NO	327.5	17,30,31
28. 2-Nonyl-4(1H)-quinolone	C ₁₈ H ₂₅ NO	271.4	17,30,31
29. 4-Hydroxy-2-undecylquinoline	C ₂₀ H ₂₉ NO	299.4	9,17,24,37
Quinoline			
30. Quinoline	C ₉ H ₇ N	129.16	17,30,31

Table 4. Fatty acids constituents of *R. graveolens* extract

Fatty acid name	Chemical formula	Molecular weight (g/mol)	References
Palmitic acid	C ₁₆ H ₃₂ O ₂	256.42	7,11,25,40
Heptadecanoic acid	C ₁₇ H ₃₄ O ₂	270.5	7,11,25,40
Dodecanoic acid	C ₁₂ H ₂₄ O ₂	200.32	7,11,40
Linoleic Acid	C ₁₈ H ₃₂ O ₂	280.4	7,11,25,40
Decanoic acid	C ₁₀ H ₂₀ O ₂	172.26	7,11,25,40
Stearic acid	C ₁₈ H ₃₆ O ₂	284.5	7,11,25,40
Oleic acid	C ₁₈ H ₃₄ O ₂	282.5	7,11,25,40,41
Methyl oleate	C ₁₉ H ₃₆ O ₂	296.49	7,11,25,40
2,5-Octadecadiynoic acid	C ₁₈ H ₃₂ O ₂	280.5	7,11,25,40,41

Phytochemical analysis had identified multiple fatty acids present in *R. graveolens* (Table-4).

Nutritional Values

Ruta graveolens is an ancient culinary spice called (Hauajeh), and medicinal herb known for its intensely bitter flavor^{16,17} Due to its strong taste, it is used only in very small quantities¹⁶ Rather than serving as a significant source of calories, it is prized for its rich content of bioactive compounds, including carbohydrates, proteins, phenols, rutin, flavonoids, alkaloids, coumarins, glycosides, steroids, and terpenes which contribute to its potential health-promoting properties.²⁰ The moisture leaves were examined, and they contain a range of beneficial bioactive compounds, including vitamin C, calcium, sodium, magnesium, iron and anthraquinones.^{20,42}

Biological activities

Cytotoxic Activity

Several studies were reviewed to evaluate the toxicological effects of *R. graveolens* extract, higher concentrations of hydroalcoholic extracts resulted in a marked reduction in fibroblast proliferation, with an IC₅₀ value of approximately 65.68 mg/mL.¹¹ However, at low concentrations, *R. graveolens* extracts did not exhibit significant hepatotoxicity.^{17,43} Other studies reported toxic effects comparable to those associated with severe conditions such as sclerosing colitis, hemoglobin toxicity, and liver necrosis.^{1,11,43} Additionally, a rare clinical case of multisystem toxicity following *R. graveolens* use has been documented.^{1,11} *Ruta graveolens* possesses notable phototoxic and irritant properties that can lead to significant

dermatological adverse effects, particularly when combined with ultraviolet exposure.^{1,44,45}

R. graveolens exhibit significant hepato-renal and cardiovascular toxicity at high doses or with prolonged exposure.^{1,46} *R. graveolens* exhibit reproductive toxicity, including antifertility and embryotoxic effects to both maternal and fetal health, when used particularly at high doses or during pregnancy.^{1,47} The safety of *R. graveolens* is highly dependent on concentration, dosage, and method of preparation, so that, these findings strongly support avoiding its use in pregnant individuals or those attempting to conceive and emphasize the need for caution in its application.^{11,17,48}

When *R. graveolens* extract was tested on lymphoma and Ehrlich tumor cells, morphological changes such as cell shrinkage, rounding, and loss of the cell layer were observed.¹⁵ In another study, the extract was shown to reduce tumor size and improve the survival rate of affected animals.^{11,48} It also exhibited antioxidant activity at low concentrations, while demonstrating pro-oxidant effects at higher doses—an action that can be beneficial in targeting and killing cancer cells.⁴⁹ The essential oils of *R. graveolens*, along with their major constituents (2-nonanone and 2-undecanone), have demonstrated cytotoxic effects against several cancer cell lines, including breast cancer, cervical cancer, leukemia, metastatic cancer, and colon cancer.⁵⁰ At low concentrations, *hasraveolens* used in the homeopathic system have also shown cytotoxic activity against human lymphoma and fibroblastoma cells by regulating oxygen free

radicals and preventing lipid peroxidation in cell membranes.^{50,51}

The cytotoxic effects of *R. graveolens* extract containing silver nanoparticles (AgNPs) exhibited enhancing effects on normal rat splenic cells.^{52,53} Various constituents of *R. graveolens* extracts, including monoterpenes, graveoline, alkaloids, flavonoids, quinolone alkaloids and undecyl acetates may contribute to its cytotoxic activity.^{52,53} These effects are thought to be associated with the induction of DNA damage. The *R. graveolens* leaf extract, alone or with AgNPs, is biologically safe on animal cells and has antibacterial, insecticidal, and immunomodulation potentials.^{52,53}

Antioxidant activity

Ruta graveolens cultured under *in vitro* conditions represent a promising source of natural antioxidants such as quercetin and rutin (often reaching 40 mg to 1,010 mg per 100 g).^{16,17} Using several assays the antioxidant capacity was evaluated, the afuranocoumarin content of the extracts showed a strong correlation with free radical scavenging activity, transition metal reduction, and reducing power, whereas the total phenolic content was strongly correlated with nitric oxide scavenging potential, each gram of the leaf extract contains approximately 133 mg of rutin.^{54,55} Methanolic extract of *R. graveolens* exhibited the highest chelating property ($IC_{50} = 0.671 \pm 0.013$ mg/mL).¹³

The antioxidant capacity of *R. graveolens* methanolic extract was estimated using two methods FRAP and (DPPH) radical scavenging assay, in both methods *R. graveolens* extract shown the greatest potential of scavenging the DPPH radicals (100.8 ± 0.56 mg GA/g dry extract) and the antioxidant capacity measured by FRAP assay was also highest in the *R. graveolens* extract (91.2 ± 1.33 mg GA/g dry extract).^{16,17} The extract exhibited significant antioxidant activity compared with the standard antioxidant quercetin, the high rutin content may contribute to these effects, as rutin is known to protect blood vessels and help reduce inflammation.⁵⁵

Anti-inflammatory activity

Different extracts of *R. graveolens* have been determined to have anti-inflammatory activity.^{8,9,56,57} In an *in vitro* model, an extract of rue (which has high concentration of rutin)

showed anti-inflammatory activity by inhibiting the production of nitric oxide and oxide synthase.^{9,56,57} In another study done on *R. graveolens* extract, skimmianine, an alkaloid found in rue, showed better anti-inflammatory activity than diclofenac by inhibiting the function of multiple proinflammatory enzymes like COX-2 and 5-LOX, and by inhibiting proinflammatory, chemicals like TNF- α , IL-6, PGE2, and nitric oxide.^{6,57,58} This result comes to an agreement with another study which also showed the rue methanolic extracts had higher anti-inflammatory activity than diclofenac sodium.^{8,58,59} Another methanolic extract showed that rue extract can be effective against allergic asthma, which reduced IL-17, TGF- β , IL-4 levels, and increased the level of IFN- γ in an *in vivo* model.⁵⁶ *R. graveolens* leaf methanol extract demonstrated significant analgesic and anti-inflammatory activities in mice. It reduced acetic acid-induced writhing by 54%, increased the response latency to thermal stimulation, and significantly inhibited carrageenan-induced oedema. Moreover, combining sub-effective doses of the extract with indomethacin enhanced both analgesic and anti-inflammatory effects, suggesting a potential synergistic interaction.⁶⁰

Antilipidemic activity

Ruta graveolens flavonoids extract has anti-lipidemic activities like anti-triglycerides, antihyperglycemia, hypolipidemic, and antihyperlipidemia as flavonoids gave the extract these powerful properties.^{24,61} Flavonoid-containing food products showed in multiple clinical trials beneficial modifications of LDL and HDL ratio.^{24,61} It was also shown that rue flavonoid extract reduces cholesterol levels in diabetic and healthy individuals.²⁴ In another study, methanolic extract of *R. graveolens* showed a significant decrease in LDL-c levels and cholesterol but no significant changes were seen in triglycerides, VLDL-c, HDL-c values and glucose.^{24,62} *In vivo* study shown the methanolic extract of *R. graveolens* significantly reduced body weight, obesity index, subcutaneous fat thickness, lipid profile, fasting blood glucose, leptin and adiponectin levels and significantly increased HDL-C levels with $p < 0.05$, compared to the negative control group.⁶³

Neuroprotective activity

Ruta graveolens and its metabolite flavonoid rutin have neuroprotective activity by

enhancing the ischemic damage and improving different neurological performances.⁶⁴ Also, low doses of rue extract showed significant reduction in neurological deficits compared with the intermediate and high dose of the same extract.⁶⁵ A study showed that *R. graveolens* plays a role in the treatment of Parkinson's disease by inhibiting enzyme monoamine oxidase B (MAO-B).^{11,64,66,67} Differently, studies showed that *R. graveolens* aqueous extract can cause death in different glioblastoma (a multiform brain tumor) cells like: U87MG, C6, and U138.^{66,67} Treatment of Alzheimer's disease has been also suggested by using *R. graveolens* containing rutin.⁶⁴ Studies have shown successful application of *Ruta graveolens* in an *in vivo* model with Alzheimer's disease by inhibiting acetylcholinesterase (AChE).^{11,64,67} Rutin has also demonstrated efficacy in both rat and *Caenorhabditis elegans* models of Huntington's disease.⁶⁴

Antiparasitic Activity

The crude extract of *R. graveolens* at a concentration of 100 mg/mL, induced 100% mortality in adult *S. mansoni* worms and eggs within 24 hours and significantly reduced parasite motor activity.³⁰ The alkaloid-rich fraction (Rg-FAE) of *R. graveolens* demonstrated potent schistosomicidal activity without detectable cytotoxic effects on mammalian cells.^{30,68} The *R. graveolens*, essential oil, is suggested to disrupt tegument integrity and interfere with key metabolic enzymes of the parasite.³⁰ *In vivo*, treatment mice with *R. graveolens* extract exhibited a reduction in liver granuloma formation and improved histopathological architecture compared to untreated controls.^{68,69}

Ruta graveolens exhibits significant antischistosomal activity, likely mediated by its alkaloid and essential oil constituents, supporting its potential as a safe and effective therapeutic candidate against *S. mansoni* infection.^{68–70} The safety of plant extract may warrant further investigation.

The extracts of *R. graveolens* inhibited the growth of *L. major* promastigotes in a dose-dependent manner.^{68,70} Fractions rich in alkaloids and furanocoumarins exhibited pronounced antileishmanial activity through disruption of parasite membrane integrity and interference with

mitochondrial function without significant toxicity to host cells.^{30,68,70}

Ruta graveolens extracts used as antiparasitic activity against *Entamoeba histolytica* trophozoites, the methanolic extract of *R. graveolens* significantly reduced trophozoite viability compared to the negative control ($P < 0.05$).³⁰ However, its antiparasitic activity was lower than that of metronidazole, achieving approximately 19.8% of the drug's effect.³⁰ The bioactivity of *R. graveolens* is attributed to its phytochemical composition, including rutin, quercetin, isoquinoline, acridone derivatives, coumarins, and hydroxybenzoic acids.^{17,30}

When *R. graveolens* extracts were used to evaluate the antiparasitic activity against *Giardia lamblia* trophozoites, the extract of *R. graveolens* exhibited a reduction in trophozoite viability, although the effect was significantly weaker than that observed with metronidazole.³⁰ The observed effects are likely associated with the presence of phytochemicals such as flavonoids (e.g., quercetin and rutin), tropane alkaloids, and coumarins.^{17,30} When *R. graveolens* extracts were used in the treatment of cystic echinococcosis caused by *Echinococcus granulosus*, the extract exhibited a significant reduction in the number, size, and weight of hydatid cysts. Saponins can affect the permeability of the parasite's cell membrane inducing vacuolization and tegument disintegration causing a decrease in the sizes and weights of cysts.^{16,17,30} Histological analysis revealed notable damage to the germinal layer, a key component for parasite survival and reproduction.^{16,17,30} Furthermore, the extract enhanced host immune response by increasing IFN- α levels while decreasing IL-4 and IL-10 levels, indicating a shift toward a Th1-type immune response.^{16,17,30}

Insecticidal Potentials

Ruta graveolens have been widely studied as a natural insecticide for the protection of crops against agricultural pests. Its bioactive compounds exhibit insecticidal, repellent, and reproductive inhibitory activities against a broad range of insect species.⁵² Laboratory and field studies have demonstrated the effectiveness of *R. graveolens* against several important pests, including *Agrotis ipsilon*, *Diabrotica speciosa*, *Ephesia kuehniella*, *Acanthoscelides obtectus*,

and *Sitophilus zeamais*.^{41,52} In addition, both the ethanolic leaf extract of *R. graveolens* and its silver nanoparticle (AgNP)-loaded formulation have shown significant insecticidal activity against *Culex pipiens* mosquitoes, further highlighting its potential for vector control applications.⁷¹

The essential oil extracted from the aerial parts of *Ruta graveolens* exhibited significant insecticidal activity against fourth-instar larvae of *Culiseta longiareolata*. At the LC₅₀ and LC₉₀ concentrations, the essential oil induced a marked reduction in larval body volume and significantly altered the levels of major biochemical constituents, including proteins, carbohydrates, and lipids. Furthermore, exposure to the essential oil appeared to activate the larval detoxification system, as indicated by an increase in glutathione S-transferase (GST) activity accompanied by a reduction in glutathione (GSH) levels.⁷²

Antimicrobial activities

Various studies have exhibit strong antimicrobial activity of methanol, ethanol, ethyl acetate and petroleum ether extracts of *Ruta graveolens* against Gram-positive bacteria such as *Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus*, *Streptococcus mutans*, *Streptococcus sobrinus* and *Micrococcus luteus*,⁷³ as well as Gram-negative bacteria such as *Escherichia coli* and *Salmonella typhimurium*.^{73,74} *R. graveolens* methanolic extract showed the potent inhibitory effect against all pathogenic bacterial strains isolated from hydatid cysts fluid such as *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, *Enterobacter aerogenes*, *Enterobacter amnigenus*, *Achromobacter xylosoxidans*, and *Escherichia coli*.^{16,17,30} The 70% ethanolic aerial parts extraction of *R. graveolens* exhibited potent antibacterial activity against *Helicobacter pylori*, as evidenced by inhibition zones (ZOIs) of 22 mm and minimum inhibitory concentrations (MICs) of 5 mg/mL. In comparison, the reference antibiotics azithromycin, clarithromycin, metronidazole, and amoxicillin produced ZOIs of 30, 25, 14, and 14 mm, respectively.¹¹

The volatile oil extracted from the leaves of *R. graveolens* demonstrated broad-spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria, with inhibition zones (ZOIs) ranging from 8.30 to 25.60 mm and minimum inhibitory concentrations (MICs) of 0.75–1.40 µg/mL. The weakest inhibitory effect was

observed against *P. aeruginosa*, whereas *B. cereus* and *S. aureus* exhibited the highest susceptibility ($P < 0.01$), with inhibition zones for *B. cereus* and *S. aureus*, the ZOIs were 25.60 ± 0.03 and 22.00 ± 0.06 mm, respectively, while the corresponding MIC values were 1.0 ± 0.04 and 1.0 ± 0.08 µg/mL, respectively.¹¹

CONCLUSION

Ruta graveolens L. is a medicinal plant characterized by a diverse phytochemical composition, including flavonoids, alkaloids, coumarins, furanocoumarins, and essential oils. These constituents have been associated with a broad range of biological activities, including antioxidant, anti-inflammatory, antimicrobial, antiparasitic, insecticidal, and cytotoxic effects. However, the available evidence is predominantly derived from in vitro experiments and animal models, while clinical evidence remains limited. Therefore, the findings cannot yet be directly translated into established therapeutic applications. Safety is also an important consideration in the potential biomedical application of *R. graveolens*. Safety is also an important consideration in the potential biomedical application of *R. graveolens*, the safety profile of different extracts and isolated compounds may vary according to their chemical composition, concentration, and route of administration. Future research should focus on the use of standardized extracts and well-characterized isolated compounds, together with detailed mechanistic, pharmacokinetic, and toxicological investigations. Well-designed clinical studies are also required to determine the efficacy, safety, appropriate dosage, and therapeutic relevance of *R. graveolens*. Further research should establish stronger links between specific phytochemical constituents and their biological effects.

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Data Availability Statement

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Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

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This research does not involve any clinical trials.

Permission to reproduce material from other sources

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Author Contributions

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REFERENCES

- Adel-Mehraban, M. S. *et al.* Exploring the Genus *Ruta*: Traditional Uses, Pharmacology, and Safety Concerns. *Planta Med.* (2025).
- Shahrajabian, M. H. A candidate for health promotion, disease prevention and treatment: common rue (*Ruta graveolens* L.), an important medicinal plant in traditional medicine. *Current reviews in clinical and experimental pharmacology* 19, 2–11 (2024).
- Abou Auda, M. M. An updated comprehensive review, systematics and biological activity of medicinal plants used in traditional medicines and their common uses in the Gaza Strip. *Palestine Adv Environ Biol* 19, 1–43 (2025).
- Cisternas, E., Solari, C., Torres, A. & Osman, A. M. Registro de *Agonoscena succincta* (Heeger, 1856) (Hemiptera: Aphalaridae) en *Ruta chalepensis* L. (Sapindales: Rutaceae) en Chile. *Revista chilena de entomología* 50, 409–413 (2024).
- Geertsma, I. P., Françoze, M., van Anel, T. & Rodríguez, M. A. What's in a name? Revisiting medicinal and religious plants at an Amazonian market. *J. Ethnobiol. Ethnomed.* 17, 9 (2021).
- Burga, L. Methyltransferases from *Ruta graveolens* L.: molecular biology and biochemistry. (2005).
- Parray, S. A. *et al.* *Ruta graveolens*: from traditional system of medicine to modern pharmacology: an overview. *Am J Pharm Tech Res* 2, 239–252 (2012).
- Kannan, R. & Babu, U. V. Identity and pharmacognosy of *Ruta graveolens* Linn. *Anc. Sci. Life* 32, 16 (2012).
- Reza, M. S., Ahmad, M. R., Rahman, M. N. & Alam, M. T. Suddab (*Ruta graveolens* Linn.) the Blessed Medicinal plant of Unani System of medicine: Literature Review. *AMERICAN JOURNAL OF PHARMACY* 8, 52–57 (2020).
- Ellis, L. T. *et al.* New national and regional bryophyte records, 41. *J. Bryol.* 36, 306–324 (2014).
- Luo, P., Feng, X., Liu, S. & Jiang, Y. Traditional uses, phytochemistry, pharmacology and toxicology of *Ruta graveolens* L.: a critical review and future perspectives. *Drug Des. Devel. Ther.* 6459–6485 (2024).
- Aliotta, G. & Cafiero, G. Biological properties of rue (*Ruta graveolens* L.): Potential use in sustainable agricultural systems. in *Principles and practices in plant ecology* 551–563 (CRC Press, 2023).
- Szewczyk, A., Marino, A., Molinari, J., Ekiert, H. & Miceli, N. Phytochemical characterization, and antioxidant and antimicrobial properties of agitated cultures of three rue species: *Ruta chalepensis*, *Ruta corsica*, and *Ruta graveolens*. *Antioxidants* 11, 592 (2022).
- Reyes-Vaquero, L. *et al.* Biological activity evaluation against *Fusarium oxysporum*, *Fusarium circinatum*, and *Meloidogyne incognita* of bioactives-enriched extracts of *Ruta graveolens* L. *Molecules* 30, 2240 (2025).
- Kumar, A., Sharma, M., Prajapati, S. & Gupta, P. Adjuvant approach to mitigate the adverse effects of cancer treatments using homeopathic medicines. *Curr. Cancer Ther. Rev.* 18, 252–261 (2022).
- Al Qaisi, Y., Alfarrayeh, I., Alsarayreh, A., Khleifat, K. & Abu-Nwas, N. Assessment of antioxidant potential, cytotoxicity, and anticancer activity of methanolic extracts from selected wild medicinal plants. *Phytomedicine plus* 4, 100534 (2024).
- Al Qaisi, Y. T., Khleifat, K. M., Alfarrayeh, I. I. & Alsarayreh, A. Z. In vivo therapeutic effect of some medicinal plants' methanolic extracts on the growth and development of secondary hydatid cyst infection. *Acta Parasitol.* 67, 1521–1534 (2022).

18. El-Saadony, M. T. *et al.* Medicinal plants: bioactive compounds, biological activities, combating multidrug-resistant microorganisms, and human health benefits-a comprehensive review. *Front. Immunol.* 16, 1491777 (2025).
19. Mokhtar, M. *et al.* Phenolic Content and in Vitro Antioxidant, Anti Inflammatory and antimicrobial Evaluation of Algerian *Ruta graveolens* L. *Chem. Biodivers.* 19, e202200545 (2022).
20. Elsherif, K. M., Sulaiman, M. A. & Mlitan, A. *Ruta graveolens* L. Leaves as a Potential Source of Natural Antioxidants and Phytochemicals: A Study from Msallata, Libya. *Baghdad Journal of Biochemistry and Applied Biological Sciences* 7, 155–163 (2026).
21. Amer, A. & Shahin, A. In Vitro Production of Flavonoids. *Plant Specialized Metabolites: Phytochemistry, Ecology and Biotechnology* 1267–1315 (2025).
22. Polya, G. *Biochemical Targets of Plant Bioactive Compounds: A Pharmacological Reference Guide to Sites of Action and Biological Effects.* (CRC press, 2003).
23. Hao, B., Yang, Z., Liu, H., Liu, Y. & Wang, S. Advances in flavonoid research: sources, biological activities, and developmental perspectives. *Curr. Issues Mol. Biol.* 46, 2884–2925 (2024).
24. Noori, M., Jafari, M., Azimi, H. & Node-Farahani, M. Effects of *Ruta graveolens* total and flavonoids extracts on rat blood glucose, cholesterol, triglycerides and urea comparing synthetic drugs. *Nusantara Bioscience* 11, 23–29 (2019).
25. Information, N. C. for B. PubChem compound summary. Preprint at (2021).
26. Adefegha, S. A., Oboh, G. & Oluokun, O. O. Food bioactives: the food image behind the curtain of health promotion and prevention against several degenerative diseases. *Studies in natural products chemistry* 72, 391–421 (2022).
27. Wieczorek, P. P. *et al.* Bioactive alkaloids of hallucinogenic mushrooms. *Studies in natural products chemistry* 46, 133–168 (2015).
28. Chaturvedi, S. & Gupta, P. Plant secondary metabolites for preferential targeting among various stressors of metabolic syndrome. *Studies in natural products chemistry* 71, 221–261 (2021).
29. Sharma, D. A brief review of *Ruta graveolens* plant in homoeopathic system of medicine. *Indian Journal of Integrative Medicine* 1–5 (2022).
30. Al Qaisi, Y. T. *et al.* *Ruta graveolens*, *Peganum harmala*, and *Citrullus colocynthis* methanolic extracts have in vitro protoscolocidal effects and act against bacteria isolated from echinococcal hydatid cyst fluid. *Arch. Microbiol.* 204, 228 (2022).
31. Salib, J. Y. *et al.* New quinoline alkaloid from *Ruta graveolens* aerial parts and evaluation of the antifertility activity. *Nat. Prod. Res.* 28, 1335–1342 (2014).
32. Liu, Y., Wei, K. & Yang, J. 4, 8-Dimethoxyfuro [2, 3-b] quinoline (â-fagarine). *Structure Reports* 67, o1907–o1907 (2011).
33. Ahmad, A. H. & Amabeoku, G. J. Involvement of gamma aminobutyric acid in the anticonvulsant effect of the leaf methanol extract of *Ruta graveolens* L. (Rutaceae) in mice. (2013).
34. Nebo, L. *et al.* Phytotoxicity of alkaloids, coumarins and flavonoids isolated from 11 species belonging to the Rutaceae and Meliaceae families. *Phytochem. Lett.* 8, 226–232 (2014).
35. Sampaio, O. M. *et al.* Evaluation of alkaloids isolated from *Ruta graveolens* as photosynthesis inhibitors. *Molecules* 23, 2693 (2018).
36. Nahrstedt, A., Wray, V., Engel, B. & Reinhard, E. New furoacridone alkaloids from tissue culture of *Ruta graveolens*. *Planta Med.* 51, 517–519 (1985).
37. Kostova, I., Ivanova, A., Mikhova, B. & Klaiber, I. Alkaloids and coumarins from *Ruta graveolens*. *Monatshefte für Chemie/Chemical Monthly* 130, 703–707 (1999).
38. Lichtenstein, A. Fats and oils: an overview. *Encyclopedia of human nutrition* 201–208 (2014).
39. Tokuyama, S. & Nakamoto, K. Pain as modified by polyunsaturated fatty acids. *Omega-3 Fatty Acids in Brain and Neurological Health* 131–146 (2014).
40. Ghabbari, M. *et al.* Behavior-modifying and insecticidal effects of plant extracts on adults of *Ceratitis capitata* (Wiedemann) (Diptera Tephritidae). *J. Pest Sci.* (2004). 91, 907–917 (2018).
41. Jammal, R. M. *et al.* Micropropagation and in Vivo Antibacterial Activity of Different Extracts of Rue (*Ruta graveolens* L.). *Jordan J. Biol. Sci.* 19, 35 (2026).
42. de Souza, M. R. R., da Silva Lima, R. C., Dantas, L. G. & Frensch, G. Bioinsecticides based on neem (*Azadirachta indica*) and rue (*Ruta graveolens*) against *Agrotis ipsilon*. *Communicata Scientiae* 16, e4272–e4272 (2025).
43. Drissi, B. *et al.* Cubeb (*Piper cubeba* Lf): A comprehensive review of its botany, phytochemistry, traditional uses, and pharmacological properties. *Front. Nutr.* 9, 1048520 (2022).

44. Grosu, C. *et al.* New insights concerning phytophotodermatitis induced by phototoxic plants. *J. Pharm. Med.* 14, 1019 (2024).
45. Laghari, Z. *et al.* Role of chlorpyrifos in experimentally based rats. *Haya: Saudi J Life Sci* 5, 220–225 (2020).
46. Sharma, V., Sharma, R. & Sharma, V. L. *Andrographis paniculata* mitigates first-line anti-tubercular drugs-induced nephrotoxicity in Wistar rats. *Biomarkers* 27, 325–337 (2022).
47. Alinia-Ahandani, E., Boghazian, A. & Alizadeh, Z. New approaches of some herbs used for reproductive issues in the world: Short review. *J Gynecol Women's Health* 16, 555927 (2019).
48. Preeethi, K. C., Kuttan, G. & Kuttan, R. Anti-tumour activity of *Ruta graveolens* extract. *Asian Pacific Journal of Cancer Prevention* 7, 439 (2006).
49. Nahar, L., El-Seedi, H. R., Khalifa, S. A. M., Mohammadhosseini, M. & Sarker, S. D. *Ruta* essential oils: Composition and bioactivities. *Molecules* 26, 4766 (2021).
50. Abdoul-Latif, F. M. *et al.* Essential oil of *Ruta chalepensis* L. from djibouti: chemical analysis and modeling of in vitro anticancer profiling. *Separations* 9, 387 (2022).
51. Khan, K. A. *et al.* Plant (*Cinnamomum Camphora*) Mediated Silver Nanoparticles: Their Characterization, Mosquito Larvicidal Efficacy, And Biological Activities. *Fresenius Environ. Bull* 30, 338–348 (2021).
52. Ghramh, H. A. *et al.* Silver nanoparticle production by *Ruta graveolens* and testing its safety, bioactivity, immune modulation, anticancer, and insecticidal potentials. *Bioinorg. Chem. Appl.* 2020, 5626382 (2020).
53. Mahmoud, E. A., Elansary, H. O., El-Ansary, D. O. & Al-Mana, F. A. Elevated bioactivity of *Ruta graveolens* against cancer cells and microbes using seaweeds. *Processes* 8, 75 (2020).
54. Diwan, R., Shinde, A. & Malpathak, N. Phytochemical composition and antioxidant potential of *Ruta graveolens* L. in vitro culture lines. *J. Bot.* 2012, 685427 (2012).
55. Eldalawy, R. Quantitative estimation of rutin in rue (*Ruta graveolens* L.) cultivated in Iraq with the evaluation of its antioxidant activity. *Asian journal of pharmaceutical and clinical research* (2017).
56. Jianu, C. *et al.* Chemical profile of *Ruta graveolens*, evaluation of the antioxidant and antibacterial potential of its essential oil, and molecular docking simulations. *Applied Sciences* 11, 11753 (2021).
57. Sandhiutami, N. M. D. *et al.* In vitro assesment of anti-inflammatory activities of coumarin and Indonesian cassia extract in RAW264. 7 murine macrophage cell line. *Iran. J. Basic Med. Sci.* 20, 99 (2017).
58. Bai, R. *et al.* Discovery of natural anti-inflammatory alkaloids: Potential leads for the drug discovery for the treatment of inflammation. *Eur. J. Med. Chem.* 213, 113165 (2021).
59. Ratheesh, M., Shyni, G. L. & Helen, A. Methanolic extract of *Ruta graveolens* L. inhibits inflammation and oxidative stress in adjuvant induced model of arthritis in rats. *Inflammopharmacology* 17, 100–105 (2009).
60. Loonat, F. & Amabeoku, G. J. Antinociceptive, anti-inflammatory and antipyretic activities of the leaf methanol extract of *Ruta graveolens* L.(Rutaceae) in mice and rats. *African Journal of Traditional, Complementary, and Alternative Medicines* 11, 173 (2014).
61. Koshy, A. S. & Vijayalakshmi, N. R. Impact of certain flavonoids on lipid profiles—potential action of *Garcinia cambogia* flavonoids. *Phytotherapy Research* 15, 395–400 (2001).
62. Toserkani, A., Razi Jalali, M. & Najafzaheh, H. Changes of lipid profiles, glucose, and hemogram after administration of *Ruta graveolens* extract in diabetic rats. *Comp. Clin. Path.* 21, 1587–1592 (2012).
63. Kusumaningrum, S., Mudigdo, A., Purwanto, B. & Indarto, D. The effects of methanol extract of rue leaves (*Ruta graveolens*) on body weight, lipid profile, adipokine levels, TCPTP, and perilipin-1 expression in obesity model rats. *Trends in Sciences* 22, 10407 (2025).
64. Colucci-D'Amato, L. & Cimaglia, G. *Ruta graveolens* as a potential source of neuroactive compounds to promote and restore neural functions. *J. Tradit. Complement. Med.* 10, 309–314 (2020).
65. Campanile, M. *et al.* *Ruta graveolens* water extract (RGWE) ameliorates ischemic damage and improves neurological deficits in a rat model of transient focal brain ischemia. *Biomedicine & Pharmacotherapy* 154, 113587 (2022).
66. Agil, M., Kusumawati, I., Muslikh, F. A. & Ma'arif, B. Neuroprotective activity of Indonesian traditional herbal medicine: A systematic review. *J. Appl. Pharm. Sci.* 13, 14–30 (2023).
67. García, M. C. *et al.* Using computer modeling to find new LRRK2 inhibitors for parkinson's disease. *Sci. Rep.* 15, 4085 (2025).
68. Carvalho, L. S. A. de *et al.* In Vitro Schistosomicidal Activity of the Alkaloid Rich Fraction from *Ruta graveolens* L.(Rutaceae) and Its Characterization by UPLC QTOF MS. *Evidence Based Complementary and Alternative*

- Medicine* 2019, 7909137 (2019).
69. Azevedo, C. M. *et al.* Therapeutic potential of natural products in the treatment of schistosomiasis. *Molecules* 28, 6807 (2023).
 70. Samkhaniani, E., Ale-Ebrahim, M., Hajikhani, R., Mortazavi, P. & Alibeik, H. Therapeutic potential of *Ruta graveolens* extract: Protecting against liver fibrosis and oxidative stress in cholestatic conditions in male Wistar rats. *Arab Journal of Gastroenterology* (2025).
 71. Al-Shaeri, M. A. Cytotoxicity and Genotoxicity Effects of Green Silver Nanoparticles in Mosquito *Aedes Aegypti* and *Culex pipiens* Larvae. (2026).
 72. Bouabida, H. & Dris, D. Effect of rue (*Ruta graveolens*) essential oil on mortality, development, biochemical and biomarkers of *Culiseta longiareolata*. *South African Journal of Botany* 133, 139–143 (2020).
 73. Mounir, S. & Belhattab, R. Exploring the Antibacterial and Antioxidant Activities of *Ruta chalepensis* Before, During and After Flowering. *Fabad Eczacılyk Bilimler Dergisi* 50, 583–596 (2025).
 74. Salman, H. A., Venkatesh, S., Senthilkumar, R., Kumar, B. S. G. & Ali, A. M. Determination of antibacterial activity and metabolite profile of *Ruta graveolens* against *Streptococcus mutans* and *Streptococcus sobrinus*. *J. Lab. Physicians* 10, 320–325 (2018).