

## Antimicrobial Activity and Bioactive Compounds of *Juniper phoenicea*: A Mini Review

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### Abstract

In recent decades, natural plants have been increasingly used to improve human health. The genus of *Juniper* has been widely used in the treatment of certain diseases as a traditional medicinal herb. *Juniperus phoenicea* stands as an attractive subject of study within botany and pharmacology domains due to its ecological flexibility in the Mediterranean area and bioactive compound diversity. Many studies have shown that plant parts of *Juniperus phoenicea* store various of bioactive chemicals which display significant antimicrobial activity. Therefore, this study aims to provide a review of the bioactive compound within the *Juniperus phoenicea*, explore the antimicrobial activity effects, and discuss the potential use of this species in the controlling of pathogenic microbes.

**Keywords:** *Juniperus phoenicea*; Antimicrobial Activity; Bioactive Compounds

### Introduction

The World Health Organization (WHO) reports that over 80% of the global population depends on traditional medicine for their primary healthcare. With rising microbial resistance to chemically synthesized drugs, attention has turned toward medical plants. Literally, thousands of phytochemicals from plants are found to be safe and widely effective alternatives with less adverse effect [70]. *Juniper sp.* is one of the medicinal plants that belong to family of *Cupressaceae* [37]. *Cupressaceae* family is the largest family of conifers in terms of genera and the third in terms of species [43]. The genus *Juniperus* occupies an important place in the *Cupressaceae* family, with about 67 species and 28 varieties (distinguished by their hardiness and dynamism), and more than 220 cultivars [37,48]. Commonly, *Juniperus sp.* found in the Mediterranean region, the Northern Hemisphere, including Europe, Asia, and Central America. *Juniper spp.* are evergreen plants, some species used as ornamental plants due to their variety in form, color, and arrangement of their leaves [25]. *Juniperus phoenicea* is one of the Libyan flora, and the currently accepted taxonomic nomenclature for this taxon is *Juniperus turbinata* Guss [8]. The red or Phoenician juniper (*Juniperus phoenicea*) is a bushy shrub or monoecious tree, standing 1 - 8m high (Figure 1A) [53]. Plant leaves are small, opposite, scale-like, its fruit is a berry-like globes cone, lustrous, that is dark reddish-brown and can measure up to 1.5 cm in diameter, containing 3 to 6 seeds (Figure 1B) [53]. Typically appears from February to April, as a green shrub plant (evergreen) grow up to 10 m high, coniferous, aromatic, grow in arid and semi-arid climates, often found on rocky slopes and coastal areas [53].



**Figure 1:** (A): The red or Phoenician juniper (*Juniperus phoenicea*) (B): Plant leaves and fruit.

Recently, juniper forests have been greatly reduced due to both natural factors; like wildfires, and human activities such as uncontrolled forest exploitation (agricultural expansion and wood cuttings) [51,53,66]. Additionally, climate change may have adversely affected the distribution and population sizes of *juniper species*. It is well known that increased temperatures and seasonal drought periods with decreased rainfalls for a long time can be considered the main reasons behind the death of *juniper trees* [21,47]. Moreover, several studies indicated that the natural habitats of some *Juniperus sp.* including *Juniperus chinensis*, *Juniperus excelsa*, creeping juniper (*Juniperus horizontalis*), cade juniper (*Juniperus oxycedrus*) are greatly reduced [73]. Additionally, some populations of *Juniperus communis* in Turkey are considered at risk due to their limited regeneration ability [22,33,51]. In General, Some *Juniper species* are currently classified as rare or endangered and require immediate conservation measures to protect its habitats. In Libya, *Juniperus phoenicea* is one of the species that ecologists concern about the main reason behind the danger of extinctions. Few studies have conducted in Libya to figure out the reasons that lead to its death like climatic changes, human impacts, and fires [53].

Many studies have been reported *Juniper sp.* as diuretic, having anti-inflammatory properties [68], antimicrobial activity [69], analgesic activity [1], hepatoprotective activity [21], antidiabetic and antihyperlipidemic activity [51], antioxidant activity [41] as well as a cure to treat asthma and dysmenorrhea [47]. The chemical compounds of *Juniperus sp.* vary greatly depending on the plant organ, geographical distribution, and phenological stage. *Juniper sp.* berries are well known as sources of various pharmaceutical preparations and for flavoring gain [47].

*Juniperus phoenicea* has gained scientists attention due to its diverse bioactive compounds, including essential oils, flavonoids, phenolic compounds, and other bioactive compounds, which exhibit numerous pharmacological properties [7,9,37]. In term of medicinal use, parts of *Juniperus phoenicea* including tar, leaves, and fruits are used to treat wounds, abdominal pain, digestive issues, and microbial infections. Numerous studies worldwide have investigated the chemical composition of *Juniperus phoenicea* which is characterized by an abundance of secondary metabolites such as terpenoids including monoterpenes, sesquiterpenes, and diterpenes, flavonoids, phenolic compounds and essential oils [45] each with its unique chemical structure and potential bioactivity. Many studies were reported from different countries which are Algeria, France, Morocco, Greece, Jordan, Egypt, and Tunisia detected the chemical composition of essential oils of *Juniperus phoenicea* where these studies have exploited *Juniper* essential oil as antimicrobial potential [17,27,29]. The essential oil of *Juniperus phoenicea* contains a variety of bioactive compounds such as monoterpene hydrocarbons and oxygenated monoterpenes, and

mono and sesquiterpenoids with their derivatives are the main classes found in nearly all *Juniperus* [49,52,75]. In term of medical use, the leaves of *Juniperus phoenicea* are used to treat bronchopulmonary diseases and act as a diuretic while the berries are used to treat cough [9]. As well as, both leaves and berries of *Juniperus phoenicea* were used as an oral hypoglycemic agent [16]. By the time the acceptance of folk medicine as an alternative form of health care is increased because of microbial resistance to the available antibiotics [57]. Therefore, this review highlights the need for improving our understanding of *Juniperus phoenicea* in term of its bioactive compounds that explore the antimicrobial activity.

## Methodology

To evaluate plant bioactive compounds and their microbial activities, this review compiled information from the literature and was conducted utilizing several electronic databases including the Semantic scholar, Wiley online library and Google Scholar databases. Search terms such as bioactive, microbial activities, bioactive properties, were used to perform the literature search.

## Plant distribution

*Junipers sp.* is resistant to dry environmental conditions, and can adapt to challenging environments [21,51]. In general, *Junipers sp.* grows successfully in areas characterized by drought and high temperature ranges [66]. It is well known that *Juniperus phoenicea* grows natively in specific regions of the Mediterranean, of North African countries, reaching the Arabian coast of the Red Sea to the east, and extending westward to the Canary Islands and Madeira. This species is widely distributed, that allows for a tremendous amount of genetic variability [17]. *Juniperus phoenicea*, has a significant presence in Libya, particularly in the east part of Libya at El-Gabel El-Akhdar (Cyrenica) along approximately 250 kilometers and coastal regions where constitutes about 80% of the total vegetation of this area [53]. This species is adapted to the Mediterranean climate and thrives in arid and semi-arid environments. El-Gabel El-Akhdar region in northeastern Libya; that characterized by rocky limestone formations, moderate rainfall, and cooler temperatures compared to other parts of Libya, providing a suitable environment for the species.

## Bioactive compounds content of *Juniperus phoenicea*

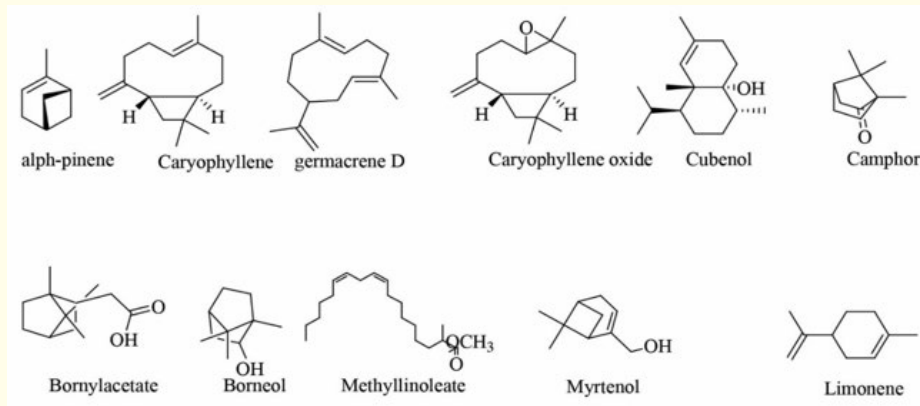
*Juniperus phoenicea* is well known for its rich content of tannins, flavonoids, mono- diterpenoid, saponins, glycosides, steroids, reducing agents, alkaloids, and catechins compounds, which contributed to its various medicinal properties [37,44,64] These bioactive compounds were shown in table 1.

Position	Part	Extract or fraction	Compounds	References
Egypt	leaves	Methanol fraction	Myricitrin, quercetin, cosmosin, quercitrin $\rho$ -coumaric acid caffeic acid	[12]
Saudi Arabia	Aerial parts	Petroleum ether, chloroform and methanol fractions	4-epi-abietol, ferruginol, hinokiol, sugiol, Z-communic acid and hinokiol-1-one $3\beta$ , 12- dihydroxyabieta-8,11,13-triene-1-one)	[15]
Kursistan-Iraq	Barks	Ethanol extract	1-[2,4-dihydroxy-3-(2-hydroxy-3-methyl-3-butenyl)-6-methoxyphenyl]-3-(4-hydroxyphenyl)2-propen-1-one.	[14]
Egypt	fruits	Chloroform fraction	Ferruginol, 7-dehydroabietanone, sugiol 6- $\alpha$ -hydroxy-7-oxoferruginol, totarolone and a labdane	[31]

Egypt	Berries & leaves	Ethyl acetate	Isoetin-7-O- $\beta$ -glucoside Amentoflavone Agathisflavone Isoscutellariin	[50]
Tunisian	leaves	methanol	Quercetin 3-O-glucoside, isoscutellarein 7-O-pentoside quercetin 3-O-pentoside	[43]
Egypt	Aerial parts	70% methanol	Catechin, 3,4-dihydroxybenzoic acid, naringenin, gallic acid myricetin, quercetin, catechin, gallic acid and p-Coumaric acid	[2]

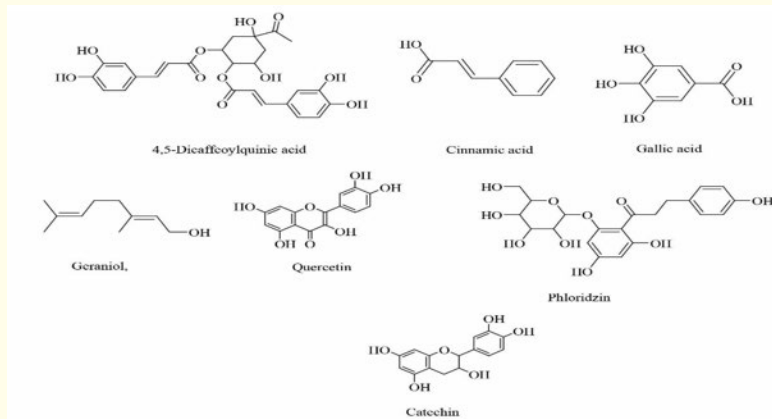
**Table 1:** Bioactive compounds in *Juniperus phoenicea*.

Several studies have been conducted to identify the bioactive compounds found in essential oils of *Juniperus phoenicea* such as  $\alpha$ -pinene, caryophyllene, germacrene D, caryophyllene oxide, cubenol, hydrocarbon monoterpenes, camphor, bornylacetate, borneol, methylillinoleate, myrtenol, limonene, and bornyl acetate using GC-MASS [18,32,80]. Bioactive active compounds of essential oils in *Juniperus phoenicea* are shown in figure 2.



**Figure 2:** Bioactive active compounds of essential oils in *Juniperus phoenicea* identified by GC-MASS.

The phenolic compounds are considered one of the main bioactive compounds of *Juniperus phoenicea* and have been investigated in several studies in the last decay (2010 to 2024). A variety of analytical techniques including high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), and liquid chromatography-mass spectrometry (LC-MS) were used to identify and quantify the phenolic compounds in *Juniperus phoenicea* which are 4,5-Dicaffeoylquinic acid Cinnamic acid, Gallic acid, Geraniol, Phloridzin, Quercetin and Catechin (Figure 3) [36,39,63,72]. These phenolic compounds are found in both the leaves and fruits of *Juniperus phoenicea*, and the specific content of each compound can vary depending on the location and growing conditions of the plant.



**Figure 3:** Phenolic compounds content of *Juniperus phoenicea* identified using GC-MS and LC-MS.

## Antimicrobial activity

### Antibacterial activities of *Juniperus phoenicea*

Discovering new antimicrobial agents is very important in order to control the pathogenic microbes, especially for treating the infections caused by resistant microorganisms. Medicinal plants with antimicrobial activities are considered a great source of new drugs. *Juniper sp.* are one of the most important source of bioactive compounds with antibacterial properties [28]. Many studies have showed that *Juniper sp.* extracts exhibited strong antibiotic effects against resistant pathogenic bacteria like *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* [37]. In addition, Juniperus's essential oils showed antimicrobial activity against Gram-positive bacteria such as *Bacillus cereus*, *Bacillus subtilis*, *Micrococcus flavus*, *Micrococcus luteus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Clostridium perfringens*, and *Enterococcus faecalis* [5,10,18,41,79].

In 2016, a study was conducted in Eastern Morocco to evaluate the antibacterial activity of essential oil of the leaves and ripe berries and unripe berries of *Juniperus phoenicea L.*, the results demonstrated a strong potential effect of essential oils against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, and *Micrococcus luteus* [13]. In addition, a study was conducted in Algeria indicated that the essential oils obtained from the leaves by steam-distillation of *Juniperus phoenicea L.* showed moderate antimicrobial effect on the growth of three Gram-positive such as *Staphylococcus aureus*, *Enterococcus faecalis*, and *Bacillus cereus* and two Gram-negative such as *Escherichia coli* and *Pseudomonas aeruginosa* [3,54,55]. Also, it was reported that the antimicrobial activity of essential oil extracted from fresh leaves, dried leaves and berries of *Juniperus phoenicea* had potential effect on the growth of *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, and *Staphylococcus aureus* [24]. The essential oil obtained from aerial parts of *Juniperus phoenicea* exhibited antibacterial activities where *Staphylococcus aureus* was more sensitive compared to the other tested bacteria [67]. Additionally, a moderate potential effect of hydroethanolic and infusion extracts of *Juniperus phoenicea* was recorded against Gram-positive bacteria [38]. A study conducted in Tunisia aimed to evaluate the antimicrobial activity of essential oil extracted from different species of *Juniper* including *Juniperus phoenicea* showed a strong inhibitory effect of the plant extract on the growth of *Shigella sonnei* [23]. In addition, the essential oil extracted from branches of Algerian *Juniperus phoenicea* using steam distillation demonstrated an inhibitory power against *Staphylococcus aureus*, *Enterococcus faecalis*, *Listeria monocytogenes*, *Pseudomonas aeruginosa* (yellow), *Bacillus cereus*, *Escherichia coli*, and *Pseudomonas aeruginosa* (green) [58]. Another study reported that the essential oil from the aerial parts of three species of *Juniper* including *Juniperus phoenicea* showed antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* [42,59]. In addition, a study showed the antibacterial activity of the essential oil of leaves plant against human pathogenic bacteria including *Listeria*



*monocytogenes* and *Salmonella enteritidis* [56]. In line with this, a study conducted in Libya in 2021 showed that methanol, acetone, and aqueous extracts from leaves of *Juniperus phoenicea* had antibacterial effects against *Staphylococcus aureus*, *Staphylococcus haemolyticus*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* [11]. Addition study in Libya showed that the bark and leaf extracts of Libyan *Juniperus phoenicea* extracts had antimicrobial activity against the growth of *Rhizobium radiobacter*, *Erwinia carotovora*, *Rhodococcus fascians* and *Ralstonia solanacearum* [60]. Similarly, a study reported strong antibacterial activity of Libyan *Juniperus phoenicea* leaf extracts, prepared using three solvents (70% methanol, 70% ethanol, and 70% acetone), against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter sp.* [30]. In general, almost all parts of *Juniperus phoenicea* exhibited antibacterial effect against wild variety of bacteria.

### Antifungal activity of *Juniperus phoenicea*

Many studies have reported that both extracts and essential oil of *Juniper sp.* represent potential activity against species of *Candida* such as *Candida glabrata* and *Candida albicans* [74,78,79]. The oil extracted from the leaves of *Juniperus phoenicea* showed good antimicrobial activities against *Candida albicans* [19]. In addition, *Junipers spp.* have demonstrated potential to inhibit the growth of several dermatophyte fungi like *Trametes versicolor*, *Gloeophyllum trabeum*, *Microsporium canis gypseum*, *Epidermophyton floccosum*, *Trichophyton mentagrophytes var. interdigitale*, *Trichophyton mentagrophytes*, *Trichophyton verrucosum*, and *Trichophyton rubrum* [34,62]. Moreover, *Juniperus phoenicea L* essential oil had the potential to prevent and control fungi by interfering and disrupting the permeability of cell membranes (leading to the leakage of cell contents and an increase in extracellular conductivity and total lipid content), causing oxidative damage, changing mycelial morphology, and inhibiting pathogenesis-related enzyme activity [76]. In 2023, research was conducted to evaluate the chemical composition and antifungal activity of *Juniperus phoenicea* essential oils, the study indicated that the main compositions *Juniperus phoenicea* oil were  $\alpha$ -Pinene and  $\delta$ -3-Carene and the antifungal activity test was showed great effect against *Aspergillus sp.* and *Penicillium sp.* [65]. The essential oil of *Juniperus phoenicea* had strong effect on the growth of *Candida glabrata* [23]. In addition, the essential oil from the leaves, berries ripe and unripe berries of *Juniperus phoenicea L.* demonstrated antifungal activity against *Aspergillus niger*, *Penicillium digitatum*, *Penicillium expansum*, *Gloeophyllum trabeum*, *Coniophora puteana*, *Poria placenta* and *Coriolus versicolor*; the result indicated that the essential oil obtained from ripe berries was the most effective against the applied mycelial fungi [13]. As well as, a study conducted in Algeria 2010, indicated that the essential oils obtained from the leaves of *Juniperus phoenicea L.* showed a moderate antimicrobial effect against three species of fungi including *Aspergillus flavus*, *Fusarium oxysporum*, and *Rhizopus stolonifera* [54]. Also related to this, the antifungal activity of essential oil from the seeds of *Juniperus phoenicea* was reported against *Candida albicans*, *Aspergillus niger*, *Aspergillus flavus*, and *Fusarium oxysporum* [26]. A study conducted in 2022 showed that both communic acid extracted from the cones of *Juniperus phoenicea* and Metrazol (antifungal) had potential effect on *Candida albicans* [6]. As well as, a study reported that the essential oil extracted from twigs and leaves of *Juniperus phoenicea* collected from the central region of Morocco exhibited strong antifungal activity against *Fusarium oxysporum*, *Alternaria alternata*, and *Candida albicans* [46]. In Jordan, a 2013 study was conducted to evaluate the antimicrobial activity of the essential oils extracted from *Juniperus phoenicea* berries, the tests demonstrated high antifungal activity against dermatophytes and *Cryptococcus neoformans* [5]. Another study investigated the effectiveness of plant organ, season, and drying method on the antimicrobial activities of essential oils of *Juniperus phoenicea L.* and positive results were reported against bacteria and *Mucor ramannianus* [61]. Based on the prewise researches, *Juniperus phoenicea* is a great source of antifungal compounds that used to treat the infection caused by microorganisms especially bacteria and fungi.

### Conclusion

It is well known that *Juniperus phoenicea* produces a large variety of novel bioactive compounds and has been widely used in food and treatment for certain diseases through traditional medicine. Several studies have shown that extracts from different parts of *Juniperus phoenicea* exhibited antimicrobial activity against various pathogenic bacteria, fungi, and *Candida* that affect the health of humans. The bioactive phenolic compounds (flavonoids, chlorogenic acid, catechin, terpenoids and podophyllotoxin) of *Juniperus phoenicea* were

extracted and identified from cones, seeds, fruits, barriers and leaves of the plant. As well as other active compounds such as terpenes, including  $\alpha$ -pinene, limonene,  $\beta$ -pinene, and  $\beta$ -laurene were found in the essential oil of this medically important plant. *Juniperus phoenicea* is highly recommended for treating and controlling the infection of pathogenic microbes. However, it is essential to evaluate the safety and toxicity of antimicrobial agents from *Juniperus phoenicea* before it would be used in folk medicine. In the past 10 years, researchers pay more attention to the essential oil of *Juniperus phoenicea* because of its positive effect on a wide variety of human pathogens with respect to its toxicity. Finally, this mini-review provides valuable insights on *Juniperus phoenicea* in terms of its antimicrobial activity and potential applications.

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### Conflicts of Interest

The authors declare no conflict of interest.

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