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Review Article

REVIEW ON CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF GENUS JUNIPER

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ABSTRACT

Juniper species belonging to the family Cupressaceae are evergreen shrubs or trees that thrive in dry, rocky, or sandy soils. There are roughly 67 species in the genus, all indigenous to the northern hemisphere. Several species of this genus have been reported to have a variety of pharmacological activities, including diuretic, anti-inflammatory, anti-fungal, hepatoprotective, antidiabetic, and anti-hyperlipidemic properties. Additionally, some species have been shown to have antioxidant, antimicrobial, and neuroprotective properties in Parkinson's disease patients. The majority of these activities are caused by the phytochemical constituents found in these species. This article covers most of the constituents of plants of the genus juniper reported from 2010 to 2023. Furthermore, the biological activities of plants of the genus juniper are presented.

Keywords: Juniperus, Essential oils, Phenols, Sesquiterpenes, Antiproliferative, Antioxidant

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INTRODUCTION

For decades, academics, herbalists, and botanists have been fascinated by the genus juniper, which includes a vast and taxonomically varied group of evergreen plants. Renowned interest in this genus is due to its ecological flexibility, cultural relevance, and most importantly, its store of bioactive chemicals. This genus stands as a captivating subject of study within botany, pharmacognosy, and ethnobotany domains.

Juniper plants (*Cupressaceae)* are evergreen shrubs and trees that prefer dry, rocky, or sandy soils. The genus has roughly 67 species, all native to the northern hemisphere, except *juniper procerahochst*. growing southward along the rift mountains of East Africa into the southern hemisphere [1].

The genus juniper is widely dispersed across continents and has been used in traditional medicine, culinary traditions, and the production of aromatic essential oils.

Plants of this genus have been reported as diuretic, having anti-inflammatory properties [2], anti-fungal activity [3], analgesic activity [4], hepatoprotective activity [5], antidiabetic and antihyperlipidemic activity [6], antimicrobial activity [7], antioxidant activity [8], anti-hypercholesterolemic activity [9], antibacterial activity [10], anticataleptic activity, neuroprotective activity in Parkinson's disease [11], as well as a cure to treat asthma and dysmenorrhea [12].

This review employed a comprehensive search strategy, drawing from reputable academic databases such as PubMed, Google Scholar, and Web of Science. Keywords utilized included "essential oil of genus juniper," "biological activities," and "relation between chemical constituents and pharmaceutical activities of juniper," ensuring a broad scope of relevant literature. The search was confined to articles published within the last decade to capture the most current research findings and perspectives. Additionally, studies were selected based on their relevance to the primary focus of this review, prioritizing peer-reviewed articles and systematic reviews.

This literature review seeks to delve into the expansive body of research dedicated to unraveling the chemical complexity of juniper plants and elucidating the diverse biological activities attributed to these compounds. By synthesizing findings from botanical, chemical, and pharmacological studies. This study aims to provide a comprehensive overview of the phytochemical diversity within the genus Juniper and explore the multifaceted biological effects demonstrated by its constituents.

MATERIALS AND METHODS

The exploration begins with data collection from 2010 to 2023 about juniper species, using different resources, including journals, databases, and other trustable sources. Genus juniper accumulates a wide array of secondary metabolites, mainly terpenoids, phenolic compounds, and essential oils. Each class of compounds contributes to the distinctive chemical profiles, structures, and potential therapeutic properties.

The second facet of this review focuses on the biological activities exhibited by juniper constituents. From antimicrobial and antioxidant properties to anti-inflammatory and anticancer effects, the spectrum of pharmacological actions attributed to juniper compounds is broad and intriguing.

Table 1 shows the different main juniper species, a member of the *Cupressaceae family*, which includes more than sixty recognized species.

Juniperus phoenicia

Juniper phoenicia is widely used in traditional medicine. It can be found throughout the Mediterranean basin, from Portugal and the Atlas Mountains in the west to Jordan and Saudi Arabia along the Red Sea in the east. Although it occurs in small and scattered populations, it is considered important due to its therapeutic properties [21, 22].

The leaves of *Juniper phoenicia* are commonly used to treat diarrhea, rheumatism, and diabetes. A decoction made from the leaves is taken orally for these purposes. In addition, a mixture of leaves and berries is used as an oral hypoglycemic agent. The essential oils of this species have antimicrobial properties, which make them useful as natural antimicrobial agents for treating human and infectious diseases, as well as for food preservation [20].

Juniperus excelsa and foetidissima

Four species of Juniper are native to lebanon. Two of these species*, Juniperus excelsa* and *Juniperus foetidissima,* have similar distribution ranges and occupy the same habitats. In Mediterranean countries, *Juniperus excelsa* grows in the warmest and driest areas, while in lebanon, it is an important member of high mountain plant communities [15]. Both species have been mentioned in previous studies as having carminative, urinary antiseptic, diuretic, emmenagogue, digestive, and anti-inflammatory properties. Additionally, their berries have been used to treat acute and chronic cystitis, albuminuria, catarrh of the bladder, renal suppression, leucorrhoea, and amenorrhea [16, 17].

Table 1: Illustrations of different main species of *juniper*

Juniperus species	Illustration	Reference
J. chinensis		[13]
J. conferta (blue pacific)		[14]
J. excelsa		[15]
J. foetidissima		[16, 17]
J. communis		[18, 19]
J. phoenicea		[20]

Juniperus chinensis

Juniperus chinensis is native to eastern Asia, including China, Mongolia, Japan, and the Himalayas. There are numerous varieties of the plant, which can take different forms and heights, ranging from ground covers to tall trees.

Juniper berries are believed to aid digestion and alleviate gas and bloating due to their mild carminative properties. They also contain compounds that possess antioxidant properties, which can help eliminate free radicals in the body. Studies suggest that juniper extracts may have anti-inflammatory effects, which can be advantageous in conditions associated with inflammation [13].

Junipeus conferta (blue pacific)

Juniper conferta, ordinarily called shore juniper, is a decumbent evergreen bush distributed in specific sandy beachfront areas of Japan and Russia.

It has been said that the *Blue Pacific Juniper* has numerous health benefits. It is commonly used to alleviate digestive issues such as upset stomach, bloating, heartburn, intestinal gas (flatulence), loss of appetite, Gastrointestinal infections (GI), and intestinal worms. This plant is also known for treating urinary tract infections (UTIs), as well as kidney and bladder stones. Additionally, it has been used to treat snakebite, diabetes, and cancer. Some people also use it topically on wounds and painful joints and muscles. The essential oil is inhaled to treat bronchitis and to numb pain [14].

Juniperus communis

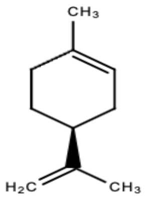
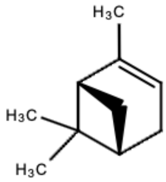
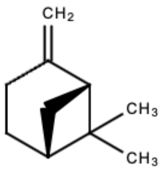
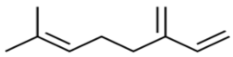
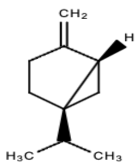
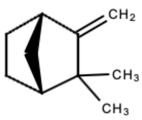
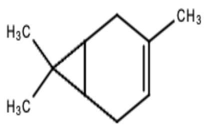
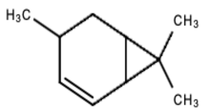
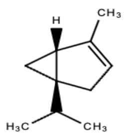
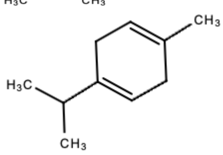
Juniperus communis l., commonly known as common juniper, is an evergreen shrub found in Himachal Pradesh at an altitude of 3000 m–4200 m. It is also distributed in Europe, southwestern Asia, and North America [11]. The plant is dioecious and aromatic, and has been traditionally used in many countries as a diuretic, antiseptic, and digestive aid. In Chamba, Manimahesh is the main area where this plant is found [18].

RESULTS

Chemical composition

The aromatic allure of juniper lies in its complex chemical profile, characterized by a rich assembly of secondary metabolites. Terpenoids, flavonoids, phenolic compounds, and essential oils constitute the chemical palette that imparts distinctive olfactory and therapeutic characteristics to juniper species. Delving into the nuances of chemical composition, this section dissects the structural diversity of these compounds:

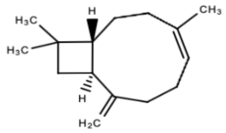
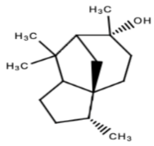
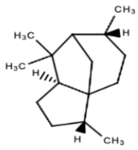
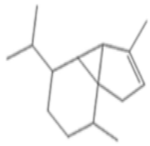
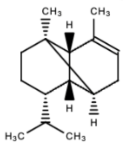
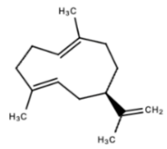
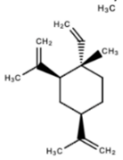
Table 2: Monoterpenes isolated from the genus juniper

Name	Structure	Source	References
limonene		*J. communis l* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa* *J. chinensis* *J. conferta*	[27] [20] [13]
Alpha – pinene		*J. communis l* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa* *J. chinensis* *J. conferta*	[27] [12]
Beta – pinene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa* *J. chinensis* *J. conferta*	[27] [26] [23]
Myrcene		*J. communis* *J. excelsa* *J. oxyderus* *J. phoenicia* *J. chinensis* *J. conferta*	[27] [13] [12]
Sabinene		*J. communis l* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa*	[27] [12]
camphene		*J. communis* *J. oxyderus* *J. phoenicia* *J. sabina* *J. communis* *J. excelsa*	[29] [27] [12]
3-carene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa* *J. conferta*	[12] [29]
4-carene		*J. communis* *J. oxyderus* *J. phoenicia* *J. sabina* *J. communis* *J. excelsa*	[27]
Alpha-thujene		*J. virginiana* *J. communis* *J. sabina* *J. oxyderus* *J. communis*	[27]
Gamma-terpinene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa* *J. chinensis* *J. conferta*	[29]

Essential oils/terpenoids

Juniper is particularly renowned for its abundance of terpenoids, including monoterpenes, sesquiterpenes, and diterpenes. Notable constituents such as α-pinene, β-pinene, and limonene contribute to the characteristic aroma and therapeutic potential of Juniper essential oils. Beyond terpenoids, juniper species harbor a diverse array of flavonoids and phenolic compounds, each with its unique chemical structure and potential bioactivity. The upcoming components shown in the following table 2 and table 3 are essential oils available in *J. chinensis, J. seravschinia, J. phoenicea, J. horizentalis, J. scopulorum, J. conferta, J. foetidissima, J. exselsa, J. communis*as well as *alpine*, *Sabina* and *Siberian juniper* [13-20, 23-26].

Table 3: Sesquiterpenes isolated from the genus Juniper

Name	Structure	Source	Reference
Caryophyllene		*J. communis* *J. oxyderus* *J. phoenicia* *J. sabina* *J. communis* *J. excelsa*	[30]
Cedrol		*J. communis* *J. oxyderus* *J. phoenicia* *J. sabina* *J. communis* *J. excelsa*	[30]
Cedrane		*J. communis* *J. oxyderus* *J. phoenicia* *J. sabina* *J. communis* *J. excelsa*	[30]
Cubebene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa*	[29]
Copaene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa*	[29]
Germacrene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa*	[29] [27]
Beta-Elemene		*J. communis* *J. oxyderus* *J. phoenicia* *J. turbinata* *J. communis* *J. excelsa*	[29] [27]

Phenols

Juniper species contain phenolic compounds. They are known for their antioxidant properties and play various roles in plant metabolism, defense mechanisms, and overall health. Juniper species contain phenolic compounds that include various classes of molecules such as flavonoids, tannins, and acids.

The presence of phenolic compounds in juniper species is of interest not only for their potential antioxidant properties but also for their possible contributions to the overall biological activities and health benefits associated with juniper extracts and essential oils. Table 4 below shows all the phenolic compounds recorded in different juniper species, including *J. communis*, *J. saxaliti, J. asheri, J. phoneicina, J. sibrina, J. excelsa and J. Sabina* [13, 23-26].

Pharmacological activity

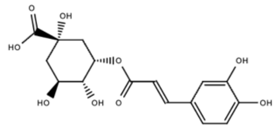
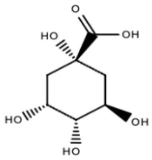
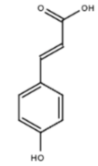
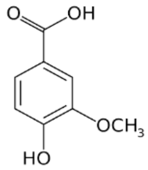
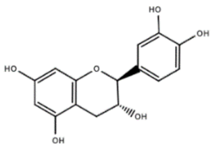
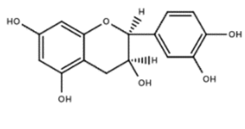
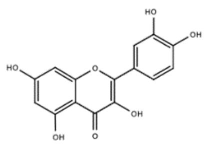
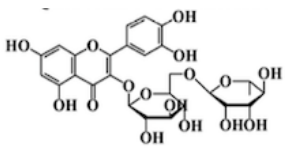
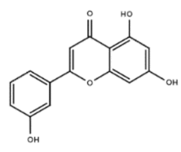
Anti-microbial, antifungal, anti-bacterial activity

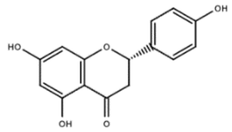
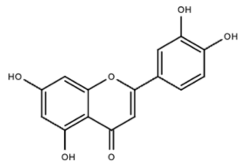
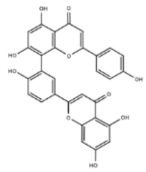
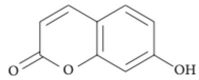
The antiviral activity of juniper species was reported in several articles. The researchers concluded that the extract had a more balanced composition in its components, such as α-pinene, β-pinene, p-cymene, or limonene, exhibited stronger antibiotic effects against multi-resistant hospital isolates belonging to species like *Staphylococcus aureus, Serratia marcescens, Enterobacter cloace, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumanii, and listeria monocytogenes*, as well as in *Candida albicans.* Peruc *et al.* [27], also confirmed that there was a synergistic effect between all the components of the oil.

In 2018, a research study indicated that various juniper species possess antimicrobial properties against certain microorganisms. The study revealed that the strongest antimicrobial activity was exhibited against *Gram-positive* bacteria and one yeast species. The essential oil (EO) of *J. communis* showed significant antimicrobial activity against *Candida glabrata*, while the EO of *J. excelsa* demonstrated even greater activity against the same microorganism. Additionally, the EO of *J. oxycedrus* showed significant antimicrobial activity against *Clostridium perfringens*, and the EOs of *Juniperus pygmaea* and *J. sabina* performed better than other EOs against *C. perfringens.* Furthermore, the EO of *J. sibirica* was found to be effective against *Staphylococcus aureus* [32].

Other reports showed that *J. alpine* has been shown to effectively inhibit the growth of various dermatophyte fungi, including *Epidermophyton floccosum, Microsporumcanis, M. gypseum, Trichophyton mentagrophytes,* *T. mentagrophytes var. interdigitale, T. rubrum, and T. verrucosum)* [31]. The methanolic extracts of *J. seravschanica* showed the strongest antibacterial activity against the six bacterial strains compared with the methanolic extracts of *J. chinensis,* according to Falasca *et al.* [19]. Several reports in the literature referred to the chemical composition of the essential oil from berries of juniper species and their antimicrobial activities [29, 30, 33]. Hexane and methanol extracts of *J. excelsa* were reported to demonstrate antimicrobial activity against microorganisms, including *Mycobacterium tuberculosis* [34] and the yeast *Saccharomyces cerevisiae* [35].

Table 4: Phenols isolated from the genus Juniper

Name		Structure	Source	References
Hydroxycinnamic acid	5-caffeoylquinic acid		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [31]
	Quinic acid		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
	p-coumaric acid		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
	Vannilic acid		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
Flavan-3-ols	Catechin		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
	Epicatechin		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
Flavonols	Quercetin		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
	Quercitin 3-o-rutinoside		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
Flavanones	Apigenin		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[7] [30] [25] [26] [27] [31]

Name	Structure	Source	References
Naringenin		*j. communis,* *j. saxaliti,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
Luteolin		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[27] [30] [25] [26] [27] [31]
Amentoflavone		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[30] [25] [26] [27] [31]
Umbillifenone (coumarins)		*j. communis,* *j. saxaliti,* *j. asheri,* *j. phoneicina,* *j. sibrina,* *j. excelsa* *j. Sabina*	[30] [25] [26] [27] [31]

Antioxidant activity

Many of the articles attributed the antioxidant activity of the genus juniper to the presence of many essential oils and other constituents [24].

The antioxidant activity of essential oils of juniper and its phenolic content was recorded in an article published in 2019. The results showed strong radical neutralization activity of phenolic content. *Communis* Berries ethanolic extract uncovers the ability to eradicate hydroxyl radicals, showing inhibitory percentages going from 65.59 to 88.12% for squashed berries and somewhere in the range of 15.52 and 32.85% for non-squashed berries [36]. Research conducted on the antioxidant properties of juniper essential oil has demonstrated the existence of multiple mechanisms that enable it to scavenge radicals, prevent radical formation, and protect against lipid peroxidation. Studies conducted in living organisms have confirmed these effects, indicating that the oil can prevent oxidation processes in yeast cells and enhance their adaptivity to reactive oxygen species [8].

On the other hand, the oil of *J. excelsa* has been found to have lower antioxidant capacity. The study also revealed that the antioxidant capacity of *J. communis galbuli* oil was lower than the oil of *J. sibirica*, but not significantly different from the oils of the other species. Moreover, the oil content in the galbuli of the six juniper species varied significantly, with *J. sabina* having the highest oil content at 1.59%, and *J. sibirica* having the lowest oil content at 0.47%. In general, the order of oil content was *J. sabina>J. communis>J. pygmaea>J. excelsa>J. oxycedrus>J. sibirica* [32].

Anti-cancer activity

Diana I. Ivanova and her team conducted a study on the antiproliferative activity of various species of juniper. They found that the leaf extracts from *J. virginiana, J. scopulorum'Moonlight', J. Sabina, and J. communis* exhibited high antiproliferative activity in K-562 human chronic myeloid leukemia (CML) and BV-173 human B cell precursor leukemia; T-24 human urinary bladder carcinoma; and HT-29 human colon adenocarcinoma cell lines [37]. In 2016, researchers tested extracts from juniper berries against two cancer cell lines, namely colorectal carcinoma cells and HeLa cervical cancer cells, to determine their inhibitory properties on cancer cell growth, where the methanol and water extracts both exhibited potent inhibitory activity and extracts exhibited substantially more potent inhibitory activity against cellular proliferation than cisplatin, according to the research [38].

Antidiabetic activity

Hydroethanolic extracts of some species of juniper displayed the ability to inhibit α-amylase and α-glucosidase activities. Moreover, the aqueous extracts of this genus at 50 g/l also showed the capacity to decrease glucose diffusion by 6% significantly [39, 40].

Juniper berries' decoction, when given orally at 250 and 500 mg/kg doses, have the potential to reduce hypoglycemia in normoglycemic rats, lower blood glucose levels, and prevent weight loss [41]. Gonçalves *et al.* have also found that the oral administration of *J. communis* methanolic extracts can effectively reduce blood glucose levels, total cholesterol, triglycerides, low-density lipoprotein, and very-low-density lipoprotein cholesterols while increasing high-density lipoprotein cholesterol. Other articles have also demonstrated the ability of this genus to reduce glucose and fructosamine levels in alloxan-induced non-obese diabetic mice after a 7 d treatment [42]. New research on Juniperus Phoenicia [43] showed that this plant possesses a hypoglycemic effect and insecticidal abilities.

Hepatoprotective activity

Leaves from *J. communis* have proactively been demonstrated to be promising hepatoprotective specialists. Rodents with hepatic harm who ingested juniper extricate parts north of about fourteen days showed lower levels of soluble phosphatase (−57.41%), direct bilirubin (−30.33%), and all-out bilirubin (−38.41%), serum alanine aminotransferase (−34.17%), and serum aspartate aminotransferase (−27.58%) than the untreated gathering [44]. Previous studies concerning *Juniperus phoenicia* growing in Egypt revealed antihepatotoxic effects of this plant which were related to its chemical constituents [28].

Neuronal activity

Juniper species of various parts showed incredible potential to work on memory and hinder the movement of certain catalysts related to the movement of neurological pathologies, for example, Alzheimer's and Parkinson's illness as indicated by a few articles [11, 45, 46]. Bais *et al.* [11] detailed that the day-to-day organization of 200 mg/kg of *J. Communis* methanolic separates for 21 d in rodents with actuated Parkin-child's sickness by chlorpromazine can diminish engine dysfunctions, including catalepsy and muscle unbending nature, and increment locomotor action when contrasted with the untreated gathering.

DISCUSSION

The collected data revealed the diversity of bioactive constituents of the genus in alignment with the corresponding biological activities. In terms of adsorbing and scavenging free radicals, they determine the antioxidant, and anti-inflammatory capacities that are linked to their volatile content, where most of these studies related these activities with the presence of essential oils, mainly alpha, beta-pinene, camphene, and 4-carene. The antimicrobial activity against many *Gram-positive and Gram-negative* bacteria was due to the essential oil's main compounds: α-pinene, β-pinene, c-elemene, sabinene, elemol, and 3-cyclohexen-1-ol. These findings generally agreed with those reported by other authors [47].

The chemical composition of the essential oil of six wild-growing junipers in Bulgaria varied significantly. The oil consisted mainly of monoterpenes such as α-Pinene, Sabinene, and β-Myrcene, as well as sesquiterpenes like β-caryophyllene, Germacrene-D, and α-Humulene. In the group of oxygen-containing monoterpenes, the most abundant was Terpinene-4-ol followed by α-Terpineol. The concentration of α-Pinene in galbuli EO of the six juniper species varied from 18.4% in *J. sabina* to 52.4% in J. excelsa, and was in the following order: *J. excelsa>J. pygmaea>J. communis>J. oxycedrus>J. Sabina*, thus explains the antioxidant and antimicrobial activity.

In 2014, a study revealed that the polar fractions of Juniper excelsa fruits, particularly the n-butanol fraction, displayed promising antioxidant potential. This suggests that the heartwood of juniper can eliminate free radicals and that the n-butanol fraction had the highest activity in scavenging radicals. Therefore, juniper can be used as an excellent source of antioxidant compounds [48].

Juniper also exhibited high antiproliferative activity in K-562 human chronic myeloid leukemia (CML) and BV-173 human B cell precursor leukemia T-24 human urinary bladder carcinoma; and HT-29 human colon adenocarcinoma cell lines. However, this activity was linked to the presence of podophyllotoxin, which is a secondary metabolite that mediates the antiviral, anthelmintic, anticancer, and other activities of junipers, where the anticancer activity precisely was associated with the high presence of the secondary metabolites, especially podophyllotoxin [37].

Both limonene and α-pinene have been found to inhibit NF-κB signaling, which is a major regulator of inflammatory diseases. However, according to the authors, the antiproliferative effect observed in the studied cells may be due to the inhibition of cellular receptor tyrosine kinases, specifically insulin-like growth factor receptor (IGF-1R) and c-erbB2/HER2/neu receptors. The antiproliferative effect reported for the aqueous *J. communis* berries extract may be due to inhibition of cell growth rather than inducing apoptosis [49-51].

Research conducted in 2015 showed that juniper oil and its constituents have antitumor activities, with good and moderate levels of tumor inhibition. Egyptian juniper oil, which contained 26.19% α-pinene, was more potent than the doxorubicin drug in HepG2, MCF-7, and another unnamed cell line [50]. Wang *et al.* [53] have mentioned that α-pinene demonstrated strong cytotoxicity towards human ovarian cancer cell lines (SK-OV-3 and HO-8910) and the human hepatocellular liver carcinoma cell line (Bel-7402). According to Matsuo *et al.* [52], α-pinene can induce apoptosis by disrupting the mitochondrial potential and producing reactive oxygen species.

Concerning the antidiabetic activity, which was shown clearly in the research, this higher anti-glycemic activity might be related to the relatively higher content of γ-terpinene [52].

Gamma-terpinene has recently gained attention due to its remarkable antioxidant properties. Another important finding from the hemoglobin glycation assay was the inverse association between essential oil concentration and anti-glycation effects. This might be explained by the fact that at higher concentrations, essential oil may act as an oxygen-carrying agent and elicit pro-oxidant effects [52].

The leaves and fruits of *J. communis var. saxatilis* contain high levels of monoterpene hydrocarbons, such as α-pinene, limonene, and β-myrcene [53]. Among these, α-pinene is the major component. According to Başak and Candan, α-pinene found in l*aurus nobilis* essential oil can inhibit α-glucosidase [54]. Additionally, the hydroalcoholic extract of *J. communis* var. saxatilis leaves has been found to significantly inhibit α-amylase. This effect may be due to the presence of certain secondary metabolites, such as lignans, coumarins, sterols, aliphatic compounds, and other terpenes in the extract [54].

The hepatoprotective activity of *Junipers communis* shown above was related mainly that the hepatoprotective potential may be due to their anti-oxidant potential against reactive oxygen and nitrogen species, which prevents lipid peroxidation that ultimately results in the prevention of necrosis or apoptosis of the liver cells [44].

A study published in 2019, reported the hepatoprotective activity of the total extract of *Juniperus sabina* l. against CCl4-induced liver toxicity in experimental animals, whereupon the chromatographic purification of this plant extract, nine compounds resulted, namely trans-calamenene, cadalene (cadalin), epi-cubenol, manool, calamenene-10b-ol, calamenene-10x-ol, 4-epi-abietic acid, sandaracopimaric acid, and isopimaric acid. Trans-calamine, epi-cubenol calamine-10b-ol, and epi-abietic acid belonged to cadinene sesquiterpenes while manool sandaracopimaric acids and iso-pimaric acid belonged to diterpenes. After being tested for their hepatoprotective activity, the third compound showed marked improvement in the levels of AST and ALT, manool was effective in improving the levels of AST, ALT, GGT, ALP, and bilirubin, while 4-epi-abietic acid showed significant improvement in GGT, ALP and bilirubin levels [55].

In research published in 2015, the neuronal activity was proven to be due to the anti-oxidant activity proven before. After injecting chlorpromazine model rats with methanolic extract of *J. communis* there was found a significant decrease in catalepsy episodes, an increase in locomotor activity, and an increase in muscle activity. The antioxidative properties of *J. communis* reduced the duration of the catalepsy, which decreased the elevated levels of lipid peroxidation in the chlorpromazine-treated animals. In other words, *Juniperus communis* has antioxidant properties and has shown promise in treating Parkinson's disease in animals. It may provide a safer therapeutic approach for the disease [56].

CONCLUSION

This review of the genus juniper highlights the diversity of the bioactive compounds present in its plants and provides scientific evidence for its various medicinal uses.

Based on the present result it could be concluded that juniper species possibly being considered an important natural antioxidant, anti-diabetic, and effective anti-microbial candidates for the pharmaceutical industry to produce a wide array of beneficial pharmaceutical products. It is recommended that further research should be carried out to identify new and more biologically active principles and discover their modes of action for maintaining a continuous supply of drugs and pharmaceutical products.

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AUTHORS CONTRIBUTIONS

GAM, MAH, AL, MA, made a significant contribution to the work reported, whether that is in the conception, the acquisition, analysis, or interpretation of data, or all the areas; took part in drafting, revising, or critically reviewing the article; and gave final approval of the version to be published. All have read and agreed to the published version of the manuscript.

CONFLICT OF INTERESTS

Declared none

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