Review Article

Five *Pistacia* species (*P. vera*, *P. atlantica*, *P. terebinthus*, *P. khinjuk*, and *P. lentiscus*): A Review of Their Traditional Uses, Phytochemistry, and Pharmacology

Mahbubeh Bozorgi, 1 Zahra Memariani, 1 Masumeh Mobli, 1 Mohammad Hossein Salehi Surmaghi, 1,2 Mohammad Reza Shams-Ardekani, 1,2 and Roja Rahimi 1

1 Department of Traditional Pharmacy, Faculty of Traditional Medicine, Tehran University of Medical Sciences, Tehran 1417653761, Iran
2 Department of Pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

Correspondence should be addressed to Roja Rahimi; rojarahimi@gmail.com

Received 1 August 2013; Accepted 21 August 2013

Academic Editors: U. Feller and T. Hatano

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*Pistacia*, a genus of flowering plants from the family Anacardiaceae, contains about twenty species, among them five are more popular including *P. vera*, *P. atlantica*, *P. terebinthus*, *P. khinjuk*, and *P. lentiscus*. Different parts of these species have been used in traditional medicine for various purposes like tonic, aphrodisiac, antiseptic, antihypertensive and management of dental, gastrointestinal, liver, urinary tract, and respiratory tract disorders. Scientific findings also revealed the wide pharmacological activities from various parts of these species, such as antioxidant, antimicrobial, antiviral, anticholinesterase, anti-inflammatory, antinociceptive, antiabetic, antitumor, anti-atherosclerotic, and hepatoprotective activities and also their beneficial effects in gastrointestinal disorders. Various types of phytochemical constituents like terpenoids, phenolic compounds, fatty acids, and sterols have also been isolated and identified from different parts of *Pistacia* species. The present review summarizes comprehensive information concerning ethnomedical uses, phytochemistry, and pharmacological activities of the five mentioned *Pistacia* species.

1. Introduction

The genus *Pistacia* belongs to the Anacardiaceae, a cosmopolitan family that comprise about 70 genera and over 600 species. The species of the genus *Pistacia* are evergreen or deciduous resin-bearing shrubs and trees which are characterized as xerophytic trees and growing to 8–10 m tall. *Pistacia lentiscus* L., *P. atlantica* Desf., *P. terebinthus* L., *P. vera* L., and *P. khinjuk* Stocks. are distributed from the Mediterranean basin to central Asia [1, 2]. Three *Pistacia* species naturally occur in Iran: *P. vera* L., *P. khinjuk* Stocks., and *P. atlantica* Desf.; *P. atlantica* has three subspecies or varieties which have been described as *cabulica*, *kurdisca*, and *mutica* [3]. *P. vera* is the only species of the genus cultivated commercially, and the rest of the species are mostly used as rootstocks for *P. vera* [1, 2].

Different parts of *Pistacia* species have been investigated for various pharmacological activities. Most of the papers are devoted to the resin of *P. lentiscus* that is known as mastic. In addition to their therapeutic effects, *Pistacia* species are used in food industry, for example, consumption of pistachio (*P. vera*) nut as food additive [4], *P. terebinthus* fruit as snack food or in making coffee-like drink [5, 6], and the anthocyanin composition of *P. lentiscus* fruit as food colorants [7].

Chemical studies on *Pistacia* genus have led to discovering diverse secondary metabolites in addition to high level of vitamins and minerals.

Our review presents a comprehensive report on phytochemical aspects, pharmacological activities, and toxicity of the genus *Pistacia* by focusing on the data reported since
the year 2000 via papers on databases including PubMed, Scopus, Google Scholar, and Web of Science.

2. Traditional Uses

Traditional uses, plant part used, and pharmacological activities of *Pistacia lentiscus*, *P. atlantica*, *P. terebinthus*, *P. vera*, and *P. khinjuk* from different regions are listed in Table 1.

Different parts of *Pistacia* species including resin, leaf, fruit, and aerial part have been traditionally used for a wide range of purposes. Among them, *P. lentiscus* is the most commonly used in different regions and resin of that has been utilized for as long as 5000 years. Resin of *P. lentiscus* has been used for variety of gastric ailments in the Mediterranean and Middle East countries for the last 3000 years [8]. It was used in ancient Egypt as incense; it has also been used as a preservative and breath sweetener [4] Most of the traditional uses reports for resin of *P. atlantica* are from Iran and have been used for the treatment of digestive, hepatic, and kidney diseases [9]. Fruit of *P. vera* (pistachio) is used all over the world. Records of the consumption of pistachio as a food date to 7000 BC [4]. Pistachio is cultivated in the Middle East, United States, and Mediterranean countries. Iran is one of the biggest producers and exporters of pistachio nuts [10]. In traditional Iranian medicine (TIM), different parts of *P. vera*, *P. atlantica*, *P. khinjuk*, *P. terebinthus*, and *P. lentiscus* have been used for a long time as useful remedies for different diseases, for example, the fruit kernel of *P. vera* as a cardiac, stomach, hepatic, and brain tonic; the fruits of *P. atlantica*, *P. khinjuk*, and *P. terebinthus* for their aphrodisiac activity and treatment of liver, kidney, heart, and respiratory system disorders, and the gum resin of *P. lentiscus*, *P. atlantica*, *P. khinjuk*, and *P. terebinthus* for their wound healing activity, and treatment of brain and gastrointestinal disorders [9, 11].

3. Phytochemical Studies

Various compounds from different phytochemical groups were identified in *Pistacia* species. These are summarized below and also in Table 2 based on the structure of finding components.

3.1. Terpenoids

3.1.1. Monoterpenoids, Sesquiterpenoids, and Volatile Oil. Essential oil is one of the main components reported from different parts of *Pistacia* species including leaves, resin, ripe and unripe fruits, galls, leaf-buds, twigs, and flowers. Analysis of essential oils is mostly performed by means of gas-chromatography (GC) based techniques. There are many qualitative and quantitative variations between the content of essential oils. These variations are related to several parameters like plant species and part, sex of cultivars, harvesting time, geographical origin, and climatic conditions [12, 13]. Hydrocarbon and oxygenated monoterpenes are the major chemical constituents in essential oil and among hydrocarbon monoterpenes, α-pinene (1) has been reported as the main compound of some samples like *P. vera* [12, 14, 15], *P. terebinthus* [16–18], *P. lentiscus* [19–24], and *P. atlantica* [25–27]. In addition to α-pinene, other major components isolated from different parts of *Pistacia* species are as follows: limonene (2), α-terpinolene, and ocimene (3,4) from fruits and leaves of *P. vera* [28]; (E)-β-Ocimene (5) and limonene in fruits [18, 28, 29]; (E)-β-Ocimene and terpinen-4-ol (6) in leaves and p-cymen, (7) in young shoots of *P. terebinthus* [28–30]; bornyl acetate (8), terpinen-4-ol, sabine (9), and myrcene (10) in fruits, terpinen-4-ol, myrcene, p-menth-1(7),8 diene (11), and ocimene from leaves [27, 28, 31], sabine and p-mentha-1(7),8 diene in leaf buds, and δ3-carene (12) in unripe galls of *P. atlantica* [31, 32]. Monoterpenes are also detected in mastic water which was separated from the mastic oil during steam distillation. Verbenone (13), α-terpinolene (14), linalool (15), and trans-pinocarveol (16) are the main constituents of mastic water [33], β-pinene (17) in oleoresin, β-myrcene and sabine in fruits [28, 30, 34], terpinen-4-ol in aerial parts [22], and limonene, myrcene, sabine, and teroien-4-ol in leaves of *P. lentiscus* were determined as the main composition [28, 30, 35, 36].

Some of the other monoterpenes identified as effective antibacterial components of these essential oils are camphene (18), limonene, and carvacrol (19) from *P. vera* resin [12].

Sesquiterpenes isolated in lower amount compared with monoterpenes. Germacrene-D (20) and β-caryophyllene (21) were identified in *P. lentiscus* and *P. terebinthus* leaves with higher concentration in comparison with other sesquiterpenes [28]. Spathulenol (22), an azulenic sesquiterpene, alcohol, is the predominant component of leaves of *P. atlantica* and *P. khinjuk* [37, 38]. Congiu et. al. [34] recovered Caryophyllene with the highest amount from *P. lentiscus* leaves by means of supercritical CO2 extraction. Germacrene-D in *P. terebinthus* flowers, β-caryophyllene in *P. lentiscus* galls, and Longifolene (23) in aerial parts of *P. lentiscus* are dominant [24, 29, 39].

3.1.2. Diterpenoids. Trace amounts of Diterpenoids were isolated from the essential oil of these species. Abietadiene (24) and abietatriene (25) were detected in essential oil of *P. vera* resin [12].

3.1.3. Triterpenoids. Resin of these species has been characterized by penta and tetracyclic triterpenes. Triterpenes such as masticadienonic acid (26), masticadienolic acid (27), morolic acid (28), oleanolic acid (29), urosonic acid (30) and their derivatives have been detected in acidic fractions of *P. lentiscus*, *P. terebinthus*, and *P. atlantica* resins [40–42]. Several triterpenoid compounds were isolated from neutral fraction of *P. lentiscus* and *P. terebinthus* resins like tircalcalor (31), dammaradiene (32), β-Amyrin (33), lupeol (34), oleanolic aldehyde, and 28-norolean-12-en-3-one. Quantitative and qualitative variations in chemical composition of resins according to the method of collection were reported [40, 41].

Anti-inflammatory properties have been reported from masticadienonic acid, masticadienolic acid, and morolic acid isolated from *P. terebinthus* [43]. Among triterpenes isolated from the resin of three sub-species of *P. atlantica* (kurdica,
| Species          | Regions | Plant part(s) used | Traditional uses and ethnobotanical reports                                                                 | Reference(s) |
|------------------|---------|-------------------|------------------------------------------------------------------------------------------------------------|--------------|
| *Pistacia atlantica*  | Algeria  | Fruit             | Stomach ache, cough, stress, tonic, and antidiarrheal                                                  | [20, 63]     |
|                   | Greek    | Fruit             | Mouth flavouring, tanning, and as fodder                                                              | [31]         |
|                   | Iran     | Resin             | Peptic ulcer, mouth freshener, antiseptic, gum tissue strengthener, as chewing gum, appetizer, phlegm dissolver, astringent, laxative, demulcent, diuretic, emmenagogue, carminative, visceral inflammation, scabies, stomach, liver and kidneys tonic, gastrointestinal disorders, and motion sickness | [9]          |
|                   | Jordan   | Fruit             | Stomach ache                                                                                           | [137]        |
|                   | Morocco  | Leaf              | Antidiabetic                                                                                           | [109]        |
|                   |          | Leaf              | Eye infection                                                                                          | [134]        |
|                   | Turkey   | Leaf              | Gum tissue strengthener, breath deodorizer, cough, chill, and stomach disease                           | [27]         |
|                   |          | Resin             | Mouth disease                                                                                          | [138]        |
|                   |          | Leaf              | As vegetables and food                                                                                 | [127]        |
|                   |          | Resin             | Wound healing                                                                                         | [138]        |

**Table 1:** Ethnomedicinal uses of selected *Pistacia* species.
Table 1: Continued.

| Species       | Regions | Plant part(s) used | Traditional uses and ethnobotanical reports                                                                 | Reference(s) |
|---------------|---------|-------------------|------------------------------------------------------------------------------------------------------------|--------------|
| Pistacia vera | Iran    | Nut shell         | Tonic, sedative, and anti diarrheic                                                                        | [11]         |
|               | Jordan  | Oil               | Food                                                                                                          | [10]         |
|               | Turkey  | Resin             | Asthma, stomach ache, and hemorrhoids                                                                        | [146]        |
| Pistacia khinjuk | Iran  | Aerial part        | Veterinary use                                                                                               | [147]        |
|               |         | Resin             | Stomach discomfort, nausea, vomiting, and motion sickness                                                  |              |

3.2. Phenolic Compounds. Gallic acid (36), catechin (37), epicatechin (38), and gallic acid methyl ester were identified in *P. vera* seed and skin, leaves of *P. lentiscus* and leaves and galls of *P. atlantica* [44–46]. Bhouri et al. [47] demonstrated that digallic acid (39) from fruits of *P. lentiscus* has antimutagenic properties. Monounsaturated, diunsaturated, and saturated cardanols have been detected in *P. vera* kernel. 3-(8-Pentadecenyl)-phenol (40) was the dominating cardanol in *P. vera* [48]. Trans and cis isomers of phytoalexin, resveratrol (3,5,4′-trihydroxy stilbene) (41–42), and trans-resveratrol-3-O-β-glucoside (trans-piceid) were quantified in *P. vera* kernel [49–51]. *P. lentiscus* leaf is a rich source of polyphenol compounds (75% of leaf dry weight) especially galloyl derivatives like mono, di, and tri-O-galloyl quinic acid (43) and monogalloyl glucose (44) [45].

1,2,3,4,6-Pentagalloyl glucose (45) and gallic acid from fruits of *P. lentiscus* were introduced as antioxidant and anti-mutagenic compounds [52].

Flavonoid compounds have been detected in different parts of these species. Naringenin (46), eriodictyol (47), daizein (48), genistein (49), quercetin (50), kaempferol (51), apigenin (52), and luteolin (53) were isolated from *P. vera* fruit, and quercetin-3-O-rutinoside (54) is the main constituent of seed [44]. Decrease in flavonoid content of *P. vera* has been reported during the fruit ripening [51]. In addition to some known flavonoids isolated from *P. terebinthus* and *P. atlantica* fruits, 6′-hydroxyhypolaetin 3′-methyl ether (55) has been identified in fruits of *P. terebinthus* [46, 53]. Flavonoids were also isolated from aerial parts of *P. atlantica* and *P. lentiscus*, and quercetin-3-glucoside (56) was reported as the most abundant one [54]. 3-Methoxycarpachromene (57), a flavone with anti-plasmodial activity, was isolated from aerial parts of *P. atlantica* [55].

Myricetin-3-glucoside (58), myricetin-3-galactoside (59), and myricetin-3-rutinoside (60) are the major flavonoid glycosides from *P. khinjuk* [54]. Myricetin derivatives also were determined as 20% of the total polyphenol amount of *P. lentiscus* leaves [45].

Anthocyanins have been reported from some *Pistacia* species. Cyanidin-3-O-glucoside (61), cyanidin-3-galactoside (62), and quercetin-3-O-rutinoside are the main anthocyanins of *P. vera* fruit [44, 56, 57]. Cyanidin-3-O-glucoside and delphinidin-3-O-glucoside (63) have been detected in *P. lentiscus* berries and leaves [7, 45].

3.3. Fatty Acids and Sterols. *Pistacia* species have oleaginous fruits considered by several researchers. The oil content in *P. vera* kernel and seed is about 50–60% [58, 59] and in ripe fruits of *P. lentiscus*, *P. terebinthus*, and *P. atlantica* is 32.8–45% [60–63]. The main fatty acid in seed and kernel of *P. vera* is oleic acid [58, 64, 65]. Oleic acid has been also determined
Table 2: Chemical compounds isolated from selected *Pistacia* species.

| Name of compound | Structure | Species                | Plant part                  | References |
|------------------|-----------|------------------------|-----------------------------|------------|
| Monoterpenoids, sesquiterpenoids, and volatile oil | | | | |
| 1 α-pinene | ![α-pinene](image) | *P. vera* | Leaf and unripe fruit, Resin | [14] |
| | | *P. terebinthus* | Fruit | [12, 15] |
| | | *P. terebinthus* var. *palaestina* | Leaf and gall | [18] |
| | | *P. lentiscus* var. *chia* | Resin | [19] |
| | | *P. lentiscus* | Fruit | [20] |
| | | *P. lentiscus* Aerial part | Aerial part | [22–24] |
| | | *P. atlantica* | Leaf, fruit, and gall, Resin | [25] |
| 2 Limonene | ![Limonene](image) | *P. vera* | Leaf | [28] |
| | | *P. terebinthus* | Unripe and ripe fruits | [29] |
| | | *P. lentiscus* | Fruit | [28] |
| 3 Terpinolene | ![Terpinolene](image) | *P. vera* | Leaf | [28] |
| | | *P. atlantica* | Leaf | [28] |
| 4 α-Ocimene | ![α-Ocimene](image) | *P. vera* | Leaf | [28] |
| | | *P. terebinthus* | Unripe and ripe fruits | [18] |
| 5 β-Ocimene | ![β-Ocimene](image) | *P. vera* | Leaf | [28] |
| | | *P. terebinthus* | Unripe and ripe fruits, Leaf | [28] |
| Name of compound         | Structure | Species      | Plant part | References |
|--------------------------|-----------|--------------|------------|------------|
| 6 Terpinen-4-ol          | ![Structure](image) | *P. terebinthus* | Leaf [30]  |            |
|                          |           | *P. atlantica* | Unripe fruits [31] |          |
|                          |           | *P. lentiscus* | Aerial parts [22] |          |
|                          |           |              | Leaf [27, 31] |            |
| 7 p-Cymene               | ![Structure](image) | *P. terebinthus* | Young shoots [29] |          |
| 8 Bornyl acetate         | ![Structure](image) | *P. atlantica* | Fruits [27] |            |
| 9 Sabinene               | ![Structure](image) | *P. atlantica* | Unripe fruits [28] | Fruits [31] |
|                          |           | *P. lentiscus* | Leaf buds [31] | Fruits [28] |
| 10 Myrcene               | ![Structure](image) | *P. atlantica* | Unripe fruits [31] | Leaf [31] |
|                          |           | *P. lentiscus* | Fruits [34, 36] | Leaf [31] |
| 11 p-Mentha-1 (7),8 diene | ![Structure](image) | *P. atlantica* | Leaf [31] | Leaf buds [31] |
| 12 Δ3-carene             | ![Structure](image) | *P. atlantica* | Unripe galls [32] |          |
| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| 13 Verbenone     | ![Structure](image1) | *P. lentiscus* | Mastic water Mastic oil | [33] [19] |
| 14 α-terpineol   | ![Structure](image2) | *P. lentiscus* | Mastic water Mastic oil | [33] [19] |
| 15 Linalool      | ![Structure](image3) | *P. lentiscus* | Mastic water | [33] |
| 16 *Trans*-pinocarveol | ![Structure](image4) | *P. lentiscus* | Mastic water | [33] |
| 17 β-pinene      | ![Structure](image5) | *P. lentiscus* | Resin | [30] |
| 18 Camphene      | ![Structure](image6) | *P. vera* | Resin | [12] |
| 19 Carvacrol     | ![Structure](image7) | *P. vera* | Resin | [12] |
| 20 Germacrene-D  | ![Structure](image8) | *P. lentiscus* *P. terebinthus* | Leaf Flowers | [28] [29] |
| 21 β-caryophyllene | ![Structure](image9) | *P. terebinthus* | Leaf | [28] |
|                  |           | *P. lentiscus* | Leaf Galls | [34] [24] |
| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| **22 Spathulenol** | ![Structure](image1) | *P. atlantica* | Leaf | [37] |
|                  |           | *P. khinjuk* | Leaf | [38] |
| **23 Longifolene** | ![Structure](image2) | *P. lentiscus* | Aerial parts | [39] |

**Diterpenoids**

| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| **24 Abietadiene** | ![Structure](image3) | *P. vera* | Resin | [12] |
| **25 Abietatriene** | ![Structure](image4) | *P. vera* | Resin | [12] |

**Triterpenoids**

| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| **26 Masticadienonic acid** | ![Structure](image5) | *P. lentiscus* | Resin | [40] |
|                  |           | *P. terebinthus* | Resin | [41] |
|                  |           | *P. atlantica* | Resin | [42] |
| **27 Masticadienolic acid** | ![Structure](image6) | *P. lentiscus* | Resin | [40] |
|                  |           | *P. terebinthus* | Resin | [41] |
|                  |           | *P. atlantica* | Resin | [42] |
| Name of compound | Structure | Species | Plant part | References |
|-----------------|-----------|---------|------------|------------|
| 28 Morolic acid | ![Structure](image1.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| | | P. atlantica | Resin | [42] |
| 29 Oleanolic acid | ![Structure](image2.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| | | P. atlantica | Resin | [42] |
| 30 Ursonic acid | ![Structure](image3.png) | P. atlantica | Resin | [42] |
| 31 Tirucallol | ![Structure](image4.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| 32 Dammaradienone | ![Structure](image5.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| 33 β-Amyrin | ![Structure](image6.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| 34 Lupeol | ![Structure](image7.png) | P. lentiscus | Resin | [40] |
| | | P. terebinthus | Resin | [41] |
| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| 3-O-acetyl-3-35 episomasticadienolic acid | ![Structure](image1) | *P. atlantica* | Resin | [42] |
| Phenolic compounds | ![Structure](image2) | *P. vera* | Seed and skin | [44] |
| 36 Gallic acid | ![Structure](image3) | *P. vera*, *P. lentiscus*, *P. atlantica* | Seed and skin, Leaf, Fruit, Gall and Leaf | [44], [45], [52], [46] |
| 37 Catechin | ![Structure](image4) | *P. vera*, *P. lentiscus* | Seed and skin | [44], [45] |
| 38 Epicatechin | ![Structure](image5) | *P. vera* | Seed and skin | [44] |
| 39 Digallic acid | ![Structure](image6) | *P. lentiscus* | Fruits | [47] |
| 40 3-(8-Pentadecenyl)-phenol | ![Structure](image7) | *P. vera* | Kernel | [48] |
| Name of compound                  | Structure | Species | Plant part | References |
|----------------------------------|-----------|---------|------------|------------|
| Trans-resveratrol                | ![Structure](image1.png) | *P. vera* | Kernel     | [49–51]    |
| Cis-resveratrol                  | ![Structure](image2.png) | *P. vera* | Kernel     | [49]       |
| 3,4,5-Tri-O-galloyl quinic acid  | ![Structure](image3.png) | *P. lentiscus* | Leaf     | [45]       |
| Monogalloyl glucose              | ![Structure](image4.png) | *P. lentiscus* | Leaf     | [45]       |
| 1,2,3,4,6-Pentagalloyl glucose   | ![Structure](image5.png) | *P. lentiscus* | Fruit    | [52]       |
| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| 46 Naringenin    | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 47 Eriodictyol   | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 48 Daidzein      | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 49 Genistein     | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 50 Quercetin     | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 51 Kaempferol    | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| 52 Apigenin      | ![Structure](image) | *P. vera* | Seed and skin | [44]       |
| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| 53 Luteolin      | ![Luteolin Structure](image) | *P. vera* | Seed and skin | [44] |
| 54 Quercetin-3-O-| ![Quercetin-3-O-rutinoside Structure](image) | *P. vera* | Seed and skin | [44] |
| 55 6'-Hydroxyhypolaetin 3'-methyl ether | ![6'-Hydroxyhypolaetin 3'-methyl ether Structure](image) | *P. terebinthus* | Fruits | [53] |
| 56 Quercetin-3-glucoside | ![Quercetin-3-glucoside Structure](image) | *P. atlantica* | Aerial parts | [54] |
| 57 3'-Methoxycarpachromene | ![3'-Methoxycarpachromene Structure](image) | *P. atlantica* | Aerial parts | [55] |
| Name of compound         | Structure | Species   | Plant part | References |
|--------------------------|-----------|-----------|------------|------------|
| 58 Myricetin-3-glucoside | ![Structure](image1.png) | *P. khinjuk* | Aerial parts | [54]       |
| 59 Myricetin-3-galactoside | ![Structure](image2.png) | *P. khinjuk* | Aerial parts | [54]       |
| 60 Myricetin-3-rutinoside | ![Structure](image3.png) | *P. khinjuk* | Aerial parts | [54]       |
| 61 Cyanidin-3-O-glucoside | ![Structure](image4.png) | *P. vera* | Skin | [44] |
|                           |           | *P. vera* | Nuts | [56] |
|                           |           | *P. lentiscus* | Berries leaves | [7] |
|                           |           | *P. lentiscus* | leaves | [45] |
Table 2: Continued.

| Name of compound | Structure | Species | Plant part | References |
|------------------|-----------|---------|------------|------------|
| 62 Cyanidin-3-galactoside | ![Structure](image1) | P. vera | Skin | [44, 56] |
|                   |           |         | Nuts      | [57]       |
| 63 Delphinidin-3-O-glucoside | ![Structure](image2) | P. lentiscus | Berries | [7] |
|                   |           |         | Leaves    | [45]       |

as the most abundant fatty acid in oil of *P. atlantica* and *P. terebinthus* fruits [62, 66, 67]. Increase of oleic acid and decrease of linoleic acid have been recorded during ripening of *P. lentiscus* fruits [60]. Other fatty acids identified in these species are linolenic, palmitic, palmitoleic, stearic, myristic, eicosanoic, behenic, lignoceric, arachidonic, pentadecanoic, hexadecanoic, octadecanoic, and margaric acid [58, 66, 68].

The most abundant sterol reported in fruits of *P. vera*, *P. atlantica*, *P. lentiscus*, and *P. terebinthus* is β-sitosterol followed by campesterol, Δ^5^-avenasterol, stigmasterol, brassicasterol, and cholesterol [59, 60, 69, 70].

The oil from fruits of *P. atlantica*, *P. lentiscus*, and *P. terebinthus*, in addition to its desirable odor and taste, has been recommended as a new source for production of vegetable oils concerning the high amount of mono-unsaturated and omega-3 fatty acids like oleic acid and linolenic acid and high quantity of phytosterols like β-sitosterol [60, 68].

3.4. Miscellaneous. Chlorophylls *a* and *b* and lutein are the major colored components of *P. vera* nuts [56]. Pheophytin, β-carotene, neoxanthin, luteoxanthin, and violaxanthin were also determined in different samples of *P. vera* nuts [71]. α-tocopherol was determined in leaves of *P. lentiscus, P. lentiscus* var. *chia*, and *P. terebinthus* [72]. Tocopherols and tocotrienols are the most abundant constituents of unsaponifiable matter of *P. atlantica* hull oil [73]. Different isomers of tocopherol, tocotrienol, and plastochromanol-8 have been identified in seed oil of *P. terebinthus* [70]. Evaluating the nutritional composition of *P. terebinthus* fruits illustrates the richness of this fruit in protein, oil, minerals, and fiber [62, 68].

4. Pharmacological Aspects

Different pharmacological activities of five mentioned *Pistacia* species have been described in detail in Table 3.

4.1. Antioxidant Activity. Different parts and constituents from *P. lentiscus* have been shown in vitro radical scavenging properties [23, 47, 52, 74–76]. *Pistacia lentiscus* var. *chia* and *P. terebinthus* var. *chia* resins were effective in protecting human LDL from oxidation in vitro [77]. *P. atlantica* leaf and fruit have shown antioxidant activity similar to or significantly higher than those of standard antioxidant compounds in different in vitro antioxidant assays [78–80]. However, the essential oil from *P. atlantica* leaf showed weak antioxidant activity in DPPH test compared to synthetic antioxidants.
| Pharmacological activity | Plant          | Plant part | Assay                        | Extract/essential oil/isolated component | Dose or concentration | Observations                                                                 | Ref. |
|--------------------------|---------------|------------|------------------------------|------------------------------------------|----------------------|-----------------------------------------------------------------------------|------|
| Antioxidant              | P. lentiscus  | Fruits     | Invitro DPPH method         | Polyphenols: gallic acid (GA) and 1,2,3,4,6 pentagalloyl-glucose (PGA) | 1, 3, 10, 30, and 100 μg/mL | Dose dependent radical scavenging activity of GA (IC50: 2 μg/mL) and PGA (IC50: 1 μg/mL) | [52] |
|                          |               |            | Xanthine oxidase inhibition |                           | 100, 200, and 300 μg/mL | Formation of uric acid and superoxide anions (O2-) by increasing concentrations of both GA and PGA |      |
|                          |               |            | Inhibition of lipid peroxidation induced by H2O2 in K562 cell line |                           | 200, 400, and 800 μg/mL | Dose dependent inhibition by GA (IC50: 220 μg/mL) and PGA (IC50: 200 μg/mL) |      |
|                          | P. lentiscus  | Leaf       | Reducing power               | Seven different extracts (1) Ethanol, (2) Ethyl acetate, (3) Aqueous/ethyl acetate, (4) Hexane, (5) Aqueous/hexane, (6) Chloroform, (7) Aqueous/chloroform | 10 μg/mL | Higher activity of aqueous fractions from hexane and chloroform than standards (BHA and α-tocopherol) |      |
|                          |               |            | DPPH method                  | Essential oil                  | 10 μg/mL | Inhibition of linoleic acid peroxidation by aqueous extracts from chloroform and hexane comparable to those of the standard (BHA) |      |
|                          |               |            | Scavenging activity against hydrogen peroxide | Essential oil                  | 10–100 μg/mL | High scavenging activity (90%) equivalent to that of the standard BHA (BHA) |      |
|                          |               |            | DPPH method                  | Methanolic extracts             | 100 μg/mL | High scavenging capacity against H2O2 comparable to standards (α-tocopherol and BHA) |      |
|                          | P. lentiscus var. chia | Resin | FRAP assay                   | Resin solution in dichloromethane | 0.05, 0.1, and 0.15% w/w | Antioxidant activity ranged between 0.52 and 4.61 mmol/L |      |
|                          |               |            | Oil oxidation assay by the oven test |                           | 0.05, 0.1, and 0.15% w/w | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          |               | Aerial parts | DPPH method                  | Methanolic extracts             | 0.2, 0.4, 1.0, 2.0, and 4.0 mM | IC50 ranged between 5.09 and 11.0 mg/L | [23] |
|                          |               |            | DPPH method                  | Methanolic extracts             | 100, 80, 50, 30, 20, 10, and 5 mg/L | Higher activity of aqueous fractions from hexane and chloroform than standards (BHA and α-tocopherol) | [75] |
|                          | P. lentiscus var. chia | Resin | FRAP assay                   | Resin solution in dichloromethane | 5000 mg/L | Antioxidant activity ranged between 0.52 and 4.61 mmol/L |      |
|                          |               |            | Oil oxidation assay by the oven test |                           | 0.05, 0.1, and 0.15% w/w | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          |               |            | Oil oxidation assay by the oven test |                           | 0.05, 0.1, 0.15, and 0.2 mg/mL | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          |               |            | ABTS                        |                           | 0.05, 0.1, and 0.15% w/w | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          |               |            | Oil oxidation assay by the oven test |                           | 0.05, 0.1, and 0.15% w/w | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          |               |            | Oil oxidation assay by the oven test |                           | 0.05, 0.1, 0.15, and 0.2 mg/mL | Activity ranged between 0.4 and 13.4 mmol Fe2+/L plant extract; IC50: 5.09–11.0 (mg/L) |      |
|                          | P. lentiscus  | Fruit      | Xanthine oxidase (XO) inhibition and superoxide scavenging activity  | Digallic acid                  | 50, 100, and 150 μg/mL | 21% XO inhibitory activity at 150 μg/mL; 28% reduction of superoxide anion activity | [47] |
|                          |               |            | TBARs                        |                           | 200, 400, and 800 μg/mL | Lipid peroxidation (IC50: 178 μg/mL) |      |
|                          |               | Gum        | Spectroscopy for the determination of hydroxyl radical by Fenton reaction | Mastic in water | ND | Effectively scavenged hydroxyl radical generated by the Fenton reaction | [76] |
|                          |               |            | Nitrate/nitrite colorimetric assay |                           | 0–3 mg/mL | No nitric oxide scavenging activity |      |
Table 3: Continued.

| Pharmacological activity | Plant          | Plant part | Assay                                      | Extract/essential oil/isolated component | Dose or concentration | Observations                                                                 | Ref. |
|--------------------------|----------------|------------|--------------------------------------------|------------------------------------------|-----------------------|-------------------------------------------------------------------------------|------|
|                          | *P. lentiscus* var. chia, *P. terebinthus* var. chia | Gum        | Copper-induced LDL oxidation                | Hexane and methanol/water extracts       | 2.5, 5, 10, 25, and 50 mg/2 mL | LDL protective activity; methanol/water extract of *P. lentiscus* showed the most LDL protection | [77] |
|                          | *P. lentiscus* | Leaf       | Reduction power activity                    | Ethanolic extract                        | 0.25; 0.5; 0.75; 1; 2; 3 mg/mL | Reducing power comparable to ascorbic acid                                    | [88] |
|                          | *P. atlantica* | Leaf       | Reduction power activity                    | Ethanolic extracts                       | 0.25; 0.5; 0.75; 1; 2; 3 mg/mL | Reducing power close to values observed by ascorbic acid                      | [88] |
|                          | *P. atlantica* subsp. mutica | Hull      | FRAP test                                  | The unsaponifiable matter (USM) of fruit’s hull oil | ND                     | Significant reducing power; the highest reducing power amongst the USM fractions belonged to the tocopherols and tocotrienols and linear and triterpenic alcohols respectively | [80] |
|                          | *P. atlantica* | Leaf       | DPPH radical-scavenging assay               | Decoction                                 | (1) 20–100 μg/mL | (1) Reducing power of significantly higher than α-tocopherol and BHT and nearly similar to BHA | [78] |
|                          | *P. atlantica* subsp. mutica | Fruit hull | Rancimat test                              | *n*-Hexane extract                       | Different percentages (up to 15%) | (2) The chelating activity of 1.0 mg/mL was nearly fourfold less than EDTA at 0.037 mg/mL and has slightly effective capacity for iron binding | [79] |
|                          | *P. atlantica* | Leaf       | DPPH test                                  | Essential oil                            | 50 μL                  | Weak radical scavenging activity                                             | [32] |
|                          | *P. vera*      | Fruit hull | Oven test                                  | Water and methanol extracts              | 0.02%, 0.04%, and 0.06% in soybean oil | Higher antioxidant capacity relative to ascorbic acid                          | [81] |
|                          | *P. vera*      | Kernel     | ABTS radical cation decolorization assay   | Methanol/water or Dichloromethane         | ND                     | Effective in retarding oil deterioration at 60°C at concentration of 0.06%, similar to BHA and BHT added at 0.02% | [81] |
|                          | *P. vera*      | Seed and skin (hull) | Copper-mediated LDL oxidation | Radical scavenging activity | Extracts from 30, 60, or 100 μg of nut | The antioxidant activity of the lipophilic extract was much lower than hydrophilic one | [82] |
|                          | *P. vera*      | Seed and skin (hull) | DPPH assay                                | Trolox equivalent antioxidant capacity (TEAC) assay (ABTS radical) scavengeing activity against the superoxide anion | Methanol/water extract | Inhibition of LDL oxidation                                                  | [44] |

ND = not determined
### Table 3: Continued.

| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------|------------|-------|------------------------------------------|----------------------|--------------|------|
| Antimutagenic            | P. lentiscus | Leaf | (AFBI)-induced mutagenicity in S. typhimurium TA100 or TA98 | Essential oil | 0.3, 250, 500, 1000 μg/plate | In TA100: 76.8% and 96.5% mutagenic inhibition for 250, 500, and 1000 μg/plate, respectively; in TA98: 99% and 100% mutagenic inhibition rate with 250 and 500 μg/plate and 50 μg/plate; 23% inhibition in TA100 and 52.2% in TA98; 300 and 600 μg/plate: 67.7% and 87.8% for TA100 and 63.8% and 75.1% for TA98 | [87] |
| Antimutagenic            | P. lentiscus | Leaf | (AFBI)-induced mutagenicity in S. typhimurium TA100 | Aqueous extract | 0.3, 50, 300, 600 μg/plate | Mutagenic inhibition of 76.7% by 250, 82.8% by 500, and 96.3% by 1000 μg/plate | [86] |
| Antimutagenic            | P. lentiscus | Leaf | (AFBI)-induced mutagenicity in S. typhimurium TA100 | Flavonoid-enriched extract extracts | 50, 300, 600 μg/plate | In TA100: 75.6, 52.6, 82.5, and 75.6% inhibition by 50, 300, and 500 μg/plate, respectively | [87] |
| Pharmacological activity                                                                 | Plant                                               | Plant part | Assay                      | Extract/essential oil/isolated component | Dose or concentration | Observations                                                                                                                                                                                                 |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------|------------|----------------------------|------------------------------------------|-----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sodium azide-induced mutagenicity in *S. typhimurium* TA1535 and TA100                  |                                                     |            | Disc diffusion              | Essential oil                           | 1.5, 10, 15, 30 μg/Plate | TA100: 79, 83, and 94% inhibition by 10, 15, and 30 μg/plate, respectively; TA1535: 62, 76, and 93% inhibition by 10, 15, and 30 μg/plate, respectively. |
|                                                                                        |                                                     |            |                            | Aqueous extract                          | 1.5, 50, 300, 600 μg/plate | TA100: 92, 96, and 98% inhibition by 50, 300, and 600 μg, respectively; TA1535: 62, 80, and 94% for the same concentrations. |
|                                                                                        |                                                     |            |                            | Flavonoid-enriched extract extracts       | 50, 300, 600 μg/plate       | 50 and 300 μg/plate: from 54 to 68% inhibition in TA1535 and from 84 to 93% in TA100.                                                                                                                         |
|                                                                                       | *P. lentiscus*                                      | Leaf       | Disc diffusion              | Essential oil                           | 0.03, 0.15, 0.62, 2.5, 10.0, 40.0 mg/mL | Noticeable activity against *S. enteritidis* (MIC: 30 μg/mL) and *S. aureus* (30 μg/mL); less important activity against *S. typhimurium*, (MIC: 150 μg/mL); |
|                                                                                       |                                                     |            |                            | Ethanol extract                          | 5 and 10 μL              | No significant inhibitory activity towards *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*                                                                                          |
|                                                                                       |                                                     |            | Disc diffusion              | Ethanol extract                          | 50, 100, 500 μL, and 1 mL | Most active against *S. typhimurium*, (MIC: 4 μg/mL), significant inhibitory activity towards *P. aeruginosa* and *S. enteritidis* (MIC: 40 μg/mL), and no activity against *S. aureus*, *E. coli*, and *Ent. faecalis* up to 1000 μg/mL. |
|                                                                                       |                                                     |            | Disc diffusion              | Aqueous extract                          | ND                     | No effect on *Klebsiella pneumonieae* and *Escherichia coli*.                                                                                                                                               |
|                                                                                       |                                                     |            | Disc diffusion              | Total oligomer flavonoid-enriched extract | ND                     | Inhibiting activity on *Trichoderma sp* and *Pusarium sp*                                                                                                                                                 |
|                                                                                       |                                                     |            | Microdilution agar          | Essential oil                           | ND                     | Activity against *S. enteritidis*, *S. typhimurium*, and *S. aureus* (MICs between 30 and 620 μg/mL). No effect on *Ent. faecalis*, *P. aeruginosa*, and *E. coli* up to 1000 μg/mL. |
|                                                                                       | *P. lentiscus var. chia*                           | Gum        | Disc diffusion              | Essential oil and its fractions and components | ND                     | Escherichia coli, *Staphylococcus aureus*, and *Bacillus subtilis* were resistant to α-pinene. *E. coli* is resistant to β-myrcene, *S. aureus* showed an intermediate response, and *B. subtilis* is sensitive to p-Cymene, β-caryophyllene, methyl isoeugenol, limonene, γ-terpinene, and trans-anethole showed moderate antibacterial activity, and in some cases, the bacteria were resistant to them. *E. coli* and *S. aureus* were resistant to β-pinene, slightly inhibited *B. subtilis*. Verbenone, R-terpineol, and linalool showed higher antibacterial activity than other components. |
|                                                                                       |                                                     |            | Disc diffusion              | Mastic gum water and its major constituents | MW R (58 mg/mL), (−)-trans-pinocarveol (13 mg/mL), (−)-linalool (37.6 mg/mL), (±)-linalool (36.6 mg/mL), (−)-verbenone (29.3 mg/mL), and (+)-α-terpineol (29.2 mg/mL) | The broadest average inhibition zones were for *E. coli* and *S. aureus* by (+)-α-terpineol and (±)-linalool compared to the positive control (gentamicin in 10 μg); significant antifungal activity against *Candida albicans* by MW R. |
|                                                                                       |                                                     |            | Microdilution agar          | Essential oil                           | 4%, 2%, 1%, 0.5%, 0.25%, 0.125%, 0.063%, and 0.032% (v/v) | The most potent antimicrobial constituents were (±)-linalool and α-terpineol against *E. coli* and *S. aureus*. Significant antifungal activity of MW R, (±)-linalool, (−)-verbenone, and (+)-α-terpineol against *C. albicans*. |
| Pharmacological activity | Plant/ Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------------------|-------|---------------------------------------|----------------------|-------------|-----|
| **P. lentiscus** | Gum | ND | Liquid mastic | 2% liquid mastic | Activity against Porphyromonas gingivalis and Prevotella melaninogena | [76] |
| Human T-cell leukemia MT-4 cells infected with HIV-1; viable cell number determination by MTT assay | | | Solid mastic: 0–200 µg/mL; liquid mastic: 0–0.0006% | Neither solid nor liquid mastic had any anti-HIV activity compared to positive controls |
| **Pistacia lentiscus var. chia** | Gum | Microdilution | Total mastic extract without polymer (TMWEP), acidic and neutral fractions | MEWP: 0.049 to 1.560 mg/mL, fractions: 0.060 to 1.920 mg/mL | The acidic fraction exhibited the highest activity against Helicobacter pylori followed by the TMWEP and neutral fraction | [33] |
| In vivo administration of extract in infected mice with *H. pylori* | | | Total mastic extract without polymer (TMWEP) | 180 µg/mL | Moderately reduced *H. pylori* colonization in the antrum and corpus of the mice stomach. Visible reduction in *H. pylori* colonization observed in histopathology evaluations |
| **P. atlantica, P. atlantica (sp. cabulica, kurdica, and mutica)** | Gum | Broth microdilution | Isolated components of the acidic fractions of the gum | ND | Against all tested bacteria mentioned in previous row, MIC values for essential oil and pure α-pinene ranged 500–1000 mg/mL | [152] |
| **P. atlantica (sp. kurdica)** | Gum | ND | Essential oil, α-pinene | ND | Against all tested bacteria mentioned in previous row, MIC values for essential oil and pure α-pinene ranged 500–1000 mg/mL | [152] |
| Leaf and twig | Modified [*H]-hypoxanthine incorporation assay | Flavone 3-methoxycarpachromene from ethyl acetate extract | 0.8 and 4.9 µg/mL | IC50 of 3.4 µM against *P. falciparum* K1 strain where the positive controls artemisinin and chloroquine had IC50s of 3.6 and 89 nM, respectively |
| Leaf and fruit | Disk diffusion method | Methanol, ethanol, ethanol + water, and water extracts | 25, 50 and 75 mg/mL | Dose dependent activity against *E. coli*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*; less activity in comparison with gentamycin (10 µg/disk), tobramycin (10 µg/disk), and kanamycin (30 µg/disk) |
| **P. atlantica** | Leaf | Disk diffusion | Ethanolic extract | 5 and 10 µL | Kleruviella pneumoniae and *Escherichia coli* were not sensitive to the extract. *Candida albicans*, *Staphylococcus aureus*, and *Salmonella typhi* showed a sensitizing effect at the 5 µL and a very significant effect at 10 µL | [91] |
| | Disc diffusion | Ethanolic extract | (50, 100, 500 µL and 1 mL) of Ethanolic extract (0.338 g/mL) | No inhibiting activity was observed against *Aspergillus flavus*, *Rhizopus stolonifer*, *Trichoderma sp.*, *Pusarium sp.* and *Aspergillus flavus* |
| Gall | Disc diffusion | Aqueous extract | 4.9 mg | Activity against the *Bacillus* species and *Pseudomonas aeruginosa* Delayed not block fungal growth in *Fomitopsis pinicola* and *Penicillium sp*. by volatile constituents of gall, volatile constituents of leaf inhibited only the growth of *Penicillium sp*. |
| Leaf and gall | Disc diffusion | Essential oils | Final 0.1% v/v | | | [92] |
| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------|------------|-------|----------------------------------------|-----------------------|-------------|-----|
| Gum                      | Agar disc diffusion | Essential oil | 10^{-1}, 10^{-2}, 10^{-3}, and 10^{-4} μg/mL | Most active against *E. coli* followed by *S. aureus* and *S. pyogenes*. *S. aureus* and *S. pyogenes* were susceptible to 0.5 μg/mL, and *E. coli* was tolerant to this concentration. *E. coli*, *Staphylococcus aureus*, and *Streptococcus pyogenes* were sensitive to 10^{-1} μg/mL. | [90] |
| Gum                      | Disc diffusion, microdilution | Essential oil and gum smoke | ND | Activity of essential oil against all tested bacteria including *Bacillus subtilis*, *Salmonella typhi*, *Escherichia coli*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa*; activity of nonpolar smoke fraction on all of strains especially on *S. dysenteriae*, *E. coli*, *B. subtilis*, and *P. aeruginosa*. | [140] |
| Gum                      | Disc diffusion, microdilution | Ethanol extract and its fractions | ND | Active against Gram-positive and Gram-negative bacteria especially n-butanolic fraction | [153] |
| Gum                      | Microdilution | Chloroform, ethyl acetate, ethyl alcohol, and diethyl ether extracts | ND | Activity against bacteria including *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Klebsiella pneumoniae* (MIC = 0.02–0.5 mg/mL) and fungi including *Candida albicans* and *Saccharomyces cerevisiae* (MIC = 0.06–0.4 mg/mL). Chloroform extract inhibited growth of fungi more than others. | [38] |
| Gum                      | Microdilution | Methanolic extract | 25, 50, 75 mg/mL | Hydroalcoholic extract of fruits from *E. coli*, water extract on *S. epidermidis*, and methanolic extract on *S. aureus* (all in 75 mg/mL) had higher antibacterial activity than tobramycin and same as gentamicin and kanamycin. No inhibitory activity against *Trypanosoma brucei rhodesiense*. | [91] |
| Gum                      | Microdilution | Lipophilic extracts | 0.8 to 9.7 μg/mL | No significant inhibitory potential against *Trypanosoma cruzi*. Remarkable activity of branches extract at 4.8 μg/mL against *Leishmania donovani*. Dried leaf extract displayed notable activity against *Plasmodium falciparum* at 4.8 μg/mL. | [94] |
| Gum                      | Hole-plate, agar dilution | Essential oil | 1/10, 1/20, 1/40, 1/80, and 1/100 v/v | All isolates of *Helicobacter pylori* were sensitive to the essential oil (MIC: 1.55 μg/mL). Dose dependent activities against *Corynebacterium xerosis*, *Bacillus brevis*, *B. megaterium*, *Mycobacterium smegmatis*, *St. aureus*, *Klebsiella oxytoca*, *Enterococcus faecalis*, *Micrococcus luteus*, *Escherichia coli*, *Yersinia enterocolitica*, *Kluuyveromyces fragilis* *Rhodotorula rubra*, and *Candida albicans*. | [15] |
| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|------|------------|-------|------------------------------------------|----------------------|-------------|-----|
| Hull                     |      |            | Disk diffusion test | Aqueous | 1200 µg/plate 0.5 to 10 mg/mL | Gram positive bacteria were the most sensitive | [150] |
| Hull                     |      |            | Agar dilution method | Aqueous | 256 and 512 mg/mL | Greater activity against Gram positive bacteria than Gram-negative; remarkable antifungal activity against *C. albicans* and *C. parapsilosis* | [89] |
| Hull                     |      | Leaf, branch, stem, kernel, shell skins, and seeds | Microdilution | Lipophylic extracts | Extracts of shell skin and fresh kernel had significant activity against *Parainfluenza virus* and *Herpes simplex virus* same as the acyclovir | [95] |
| Anti-inflammatory P. terebinthus | Gall |            | In vitro antiviral assay | Methanolic extract | 1 mg/ear | 31% and 38% nonsignificant inhibition of edema by masticadienolic acid and morolic acid, whereas masticadienolic acid was inactive | [95] |
|                          |      |            | Mouse ear edema induced by multiple topical applications of TPA | Methanolic extract | 1 mg/ear | 58% inhibition of chronic inflammatory swelling | |
|                          |      |            | In vitro phospholipase A2 activity assay | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Myeloperoxidase assay | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Phospholipase A2 (PLA2)-induced mouse ear edema | Methanolic extract | 1 mg/ear | Non significant effect | |
|                          |      |            | Ethyl phenylpropionate (EPP) induced mouse ear edema | Methanolic extract | 1 mg/ear | | |
|                          |      |            | 12-O-Tetradecanoylphorbol-13-acetate (TPA)-induced mouse ear edema | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Inhibiton of the production of LTB4 from rat polymorphonuclear leukocytes (PMNL) | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Ethyl phenylpropionate-induced mouse ear oedema | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Mouse ear edema induced by TPA | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Mouse ear edema induced by DPP | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Delayed type hypersensitivity induced by fluorobenzene in mouse ear | Methanolic extract | 1 mg/ear | | |
|                          |      |            | Mouse ear inflammation induced by multiple topical applications of TPA | Methanolic extract | 1 mg/ear | | |
### Table 3: Continued.

| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------|------------|-------|-----------------------------------------|-----------------------|--------------|------|
| Gastrointestinal disorders | P. lentiscus | Resin | Pyloric ligation-, Aspirin-, phenylbutazone- and reserpine-induced and cold-restraint stress ulcer in rat | Powder finely suspended in corn oil | An oral dose of 500 mg/kg | Intensity of gastric mucosal damage in all models | [103] |
| | P. lentiscus | Resin | TNBS-induced colitis in rats | Powder in polyherbal formulation | 50,100, and 200 mg/kg of formula with 4% *P. lentiscus* resin | Macroscopic and microscopic colonic damage; | [106] |
| | P. lentiscus var. chia | Resin | 3-week double-blind randomised placebo controlled study on patients with functional dyspepsia | Powder | 350 mg TID | Improved the feeling of symptoms significantly | [104] |
| | P. lentiscus var. chia | Resin | Dextran-sulfate sodium (DSS) model of colitis in mice | Powder | 0.20 g/kg chow (0.02%) 2.0 g/kg chow (0.20%) | Delayed the onset and progression of acute colitis and weight loss caused by the disease | [105] |
| | P. lentiscus var. chia | Resin | 4-week pilot study on 10 patients with Crohn's disease and 8 controls | Capsules of fine powder | 2.22 g/day (6 capsules, 0.37 g/cap) | Crohn's disease activity index and plasma inflammatory mediators such as C-reactive protein, interleukin-6 (IL-6) without any side effects; immunomodulatory effect by tumor necrosis factor-alpha (TNF-α) and macrophage migration inhibitory factor | [107] |

### P. vera

| Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|------------|-------|-----------------------------------------|-----------------------|--------------|------|
| Fruits, leaf, branches, peduncles, and oleoresin | Myeloperoxidase assay | ND | Inhibition of neutrophil infiltration by oleanonic and oleanolic 84% and 67%, respectively | | |
| | Phospholipase A2-induced hind paw mouse edema | 30 mg/kg | ↓edema by both compounds | | |
| | Bradykinin-induced mouse paw edema | 30 mg/kg | ↓edema by 61% | | |
| | Carragenan-induced hind paw edema | Oleanonic acid | ND | ↓leukotriene B4 (IC50: 17 μM) | [146] |
| | p-Benzquinone-induced abdominal constriction test in mice | Ethanolic and aqueous extracts | 250,500 mg/kg | Among all extracts, only the oleoresin exhibited a dose-dependent anti-inflammatory activity | [97] |
| | Hot plate test | Aqueous extract, ethanolic extract | 0.4 and 0.5 g/Kg | Dose-dependent antinociceptive activity after 30–60 min of treatment | Significant anti-inflammatory activities | |
| | | Aqueous extract | 0.4, 0.16, 0.28 g/Kg | | Significant and dose-dependent anti-inflammatory activity | |
| | | Aqueous extract, ethanolic extract | 0.4 g/Kg 0.35, 0.5 g/Kg | | | |
| | | Aqueous extract, ethanolic extract | 0.4, 0.28 g/Kg 0.35, 0.5 g/Kg | | | |
| | | Modification of VCAM-1 and ICAM1 expression by ELISA | Neutral extract and isolated phytosterol tirucallol | Extract: 25, 50, 100, 200 μg/mL  Tirucallol: 0.1, 1, 10, 100 μM | Significant dose-dependent ↓in vascular adhesion molecule 1 (VCAM-1) and intracellular adhesion molecule 1 (ICAM-1) expression | [98] |

### P. lentiscus var. chia

| Gum | \( P. lentiscus \) | Resin | TNBS-induced colitis in rats | Powder in polyherbal formulation | 50,100, and 200 mg/kg of formula with 4% *P. lentiscus* resin | Macroscopic and microscopic colonic damage; ↓TNF-α, IL-1β, MPO, and lipid peroxidation; not significantly increase in antioxidant power of colon | [106] |
| | 3-week double-blind randomised placebo controlled study on patients with functional dyspepsia | Powder | 350 mg TID | Improved the feeling of symptoms significantly | | [104] |
| | Dextran-sulfate sodium (DSS) model of colitis in mice | Powder | 0.20 g/kg chow (0.02%) 2.0 g/kg chow (0.20%) | Delayed the onset and progression of acute colitis and weight loss caused by the disease | | [105] |
| | 4-week pilot study on 10 patients with Crohn's disease and 8 controls | Capsules of fine powder | 2.22 g/day (6 capsules, 0.37 g/cap) | Crohn's disease activity index and plasma inflammatory mediators such as C-reactive protein, interleukin-6 (IL-6) without any side effects; immunomodulatory effect by tumor necrosis factor-alpha (TNF-α) and macrophage migration inhibitory factor | | [107] |
| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------|------------|-------|------------------------------------------|----------------------|-------------|------|
| Antidiabetic | *P. lentiscus var. chia* Resin | 4-week pilot study on 10 patients with Crohn’s disease and 8 controls | Capsules of fine powder | 2.22 g/day (6 caps/d, 0.37 g/cap) | Immunomodulatory activity ↓ TNF-α and ↑ macrophage migration inhibitory factor (MIF) in these patients | [108] |
| | *P. atlantica* Leaf | In vitro and in vivo (normoglycemic and streptozocin-induced hyperglycemic rats) | Aqueous extract | 2 mL plant extract equivalent to 200 mg of starting material | Significant inhibitory effect on α-amylase in vitro; no significant hypoglycemic activity in normoglycemic and hyperglycemic rats | [109] |
| | *P. lentiscus var. chia* Resin | In vitro enzymatic starch digestion and rat model | Aqueous extract | 1, 5, 10, 12.5, 25, 50, and 100 mg/mL, 125, 250, and 500 mg/kg | In vitro: significant dose dependent dual inhibition of α-amylase and α-glucosidase comparable to acarbose In vivo: significant acute postprandial antihyperglycemic activity comparable to metformin and glipizide and improved glucose intolerance in oral starch tolerance test | [110] |
| | *P. lentiscus var. chia* Resin | Human study | Powder diluted in 250 mL of water | 0.7 g per day | Significantly decrease (3.1 mg/dL per month, *P* = 0.003) in serum glucose level among male subjects | [111] |
| | *P. lentiscus var. chia* Resin | In vitro study on human colon cancer cells (HCT116) | Ethanol extract | ND | Inhibited proliferation and induced apoptosis of human colorectal tumor cells | [112] |
| | | In vitro study on human leukemic cell line | Liquid and solid resin | 0–200 μg/mL (solid mastic) or 0–2 (v/v)% of liquid mastic | The most cytotoxic effect against promyelocytic leukemia HL-60 among 13 human cell types; inhibition of natural apoptosis of oral polymorphonuclear leukocytes | [76] |
| | | In vivo human colon cancer/immunodeficient mouse model | Hexane extract | 200 mg/kg administered daily for 4 consecutive days (followed by 3 days without treatment) | Anticancer activity via its delay effect on the growth of colorectal tumors developed from HCT116 xenografted into mice | [8] |
| | *P. lentiscus* Resin | Human cell line (androgen-responsive prostate cancer cell line) Human prostate cancer cell lines (LNCaP and DU-145), RT-PCR, and Western blotting were used to detect maspin expression | ND | 2, 4, 6, 8, 10, and 12 μg/mL | Remarkable potency to decrease the expression and function of the androgen receptor in androgen-responsive prostate cancer cell line (LNCaP) | [154] |
| | | The human prostate cancer cell lines (PC-3), MTT assay, gene assay, RT-PCR, and Western blotting | ND | 2, 4, 6, and 8 μg/mL | Increased maspin expression in LNCaP cells | [113] |
| Antitumor | *P. lentiscus* Resin | | Ethanol extract | ND | Inhibited proliferation and blocked the cell cycle progression in androgen-independent prostate cancer PC-3 cells by suppressing NF-κB activity and the NF-κB signal pathway A time-dependent modification in the expression of 925 genes and phenomena in Lewis lung carcinoma cells by its antiproliferative, proapoptotic, and anti-inflammatory activities | [114] |
| | | Lewis lung carcinoma cells | Essential oil | 0.01% v/v | Significant inhibition on tumor growth without signs of toxicity related to apoptosis induction, reduced neovascularization, and inhibiting chemokine expression | [115] |
| | | Immune competent mice | Essential oil | 45 mg/kg intraperitoneally, 3 times a week for 3 weeks | Antiproliferative and proapoptotic effect on K562 human leukemia cells; inhibited the release of vascular endothelial growth factor from K562 and B16 mouse melanoma cell; concentration-dependent inhibition of endothelial cell proliferation without affecting cell survival; significant decrease of microvessel formation | [116] |
| | *P. atlantica sub. kurdica* Fruit | Cells line and the in vivo chicken embryo CAM angiogenesis model | Essential oil | 0.01–0.1% v/v | | | |
| Pharmacological activity | Plant | Plant part | Assay | Extract/essential oil/isolated component | Dose or concentration | Observations | Ref. |
|--------------------------|-------|------------|-------|------------------------------------------|----------------------|-------------|-----|
| Rat liver medium-term carcinogenesis bioassay (Ito-test) human colon carcinoma HT29 cells | P. vera | Resin | In vitro cytotoxic activity against human cell lines | Powder in diet | 0, 0.01, 0.1 and 1% | Promoted the preneoplastic lesions development in rat liver with increasing liver relative weight | [117] |
| P. lentiscus | Leaf | Rat model using Carbon tetrachloride | Aqueous extract | 4 mL/kg (contained 1.946 g of solid matter) | [bilirubin and activity of 3 enzymes including alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST)] | Hepatic fibrosis, an inflammatory response, mild cholestasis, and depletion of reduced glutathione associated with an increase in its oxidized form for five weeks administration in healthy rats; in thioacetamide-induced rat liver lesions, it aggravated the inflammatory, fibrotic, and glutathione depleting responses without affecting the extent of lipid peroxidation | [121] |
| P. lentiscus var. chia | Resin | Human model | Powder diluted in one glass (250 mL) of water | 5 g | Serum total cholesterol, LDL, total cholesterol/HDL ratio, lipoprotein, apolipoprotein A-I, apolipoprotein B, AST, ALP, and gamma-GT were reduced in human subjects | [111] |
| P. lentiscus | Seeds oil | Rabbit model, mercury induced toxicity | Pistacia oil | 5% | Mercury induced toxicity in rabbits caused increase in the level of ALP, AST, and urea serum, while it was reported that P. lentiscus oil-treated rabbits showed none of those changes | [156] |
| P. vera | Fruit (roasted, unsalted pistachio nuts) | Human model (10 patients with moderate hypercholesterolemia) | Nut | 20% in diet | [total cholesterol, total cholesterol/HDL ratio, and LDL/HDL ratio and ↑HDL after 3 weeks use] | Inhibited the development of hydroptic degeneration and fatty changes in the liver and demonstrated hypopolipectic effect | [124] |
| P. terebinthus | Fruit | Rabbit model | Fruit | 1 g/kg | | | [125] |
| P. verum | Fruit | Rabbit model | Methanolic and cyclohexane extracts | Methanolic extract (1% v/v), cyclohexane extract (5% v/v) | Beneficial effects on HDL, LDL, and aortic intimal thickness. The methanolic extract additionally showed an antioxidant activity and remarkable decrease in aortic surface lesions | [123] |
| P. terebinthus | Fruit | Rabbit model | Cell culture (peripheral blood mononuclear cell, PBMC); cell viability assessed via MTT assay | Fruit | Inhibited the development of the atherosclerotic lesions in the thoracic artery | [125] |
| P. lentiscus | Resin | Total polar extract | 2.7, 27, and 270 μg/mL | | Restored intracellular antioxidant glutathione (GSH) levels and downregulated CD36 mRNA expression resulted in antioxidant and antiatherogenic effects | [126] |
| P. atlantica | Leaf | TLC bioautography assay, Ellman’s colorimetric method | Aqueous extract | 5, 10, 15, 20, and 25 μg/mL | Strong acetylcholinesterase (AChE) inhibition | [13] |
| P. atlantica | Leaf | Ellman’s colorimetric method | Methanol and ethyl acetate extracts | 0.1 mg/mL | Relatively weak AChE inhibitory activity | [127] |
| P. terebinthus | Fruit | Ellman’s colorimetric method and the modified dopachrome method | Ethyl acetate and methanol extracts | 25, 50, 100, and 200 μg/mL | No inhibitory activity against AChE and tyrosinase while selectively inhibited butyrylcholinesterase (BChE) at moderate levels (below 50%) at the tested concentrations | [85] |
and essential oil of Helicobacter pylori [47, 52].

In one study, the extract from P. terebinthus leaf had nearly 12-fold higher antioxidant capacity than those of BHA and ascorbic acid [84]. P. terebinthus fruits showed noticeable metal-chelation properties as compared to EDTA and high radical scavenging activity similar to the standards. Antioxidant activity of the fruits may be elevated by roasting process [85].

4.2. Antimutagenic Activity. Essential oil and different extracts from P. lentiscus leaves indicated significant inhibitory effect on mutagenicity in vitro [86, 87]. Gallic acid, digallic acid, and 1,2,3,4,6-pentagalloylglucose, polyphenols isolated from the fruits of P. lentiscus, induced an inhibitory activity against mutagenicity and genotoxicity in in vitro assays [47, 52].

4.3. Antimicrobial and Antiviral Activities. Pistacia species have demonstrated significant antibacterial activity against various Gram positive and Gram negative bacteria as shown in Table 3. Antimicrobial activity of Pistacia lentiscus resin, the essential oil and gum from P. atlantica var. kurdica and its major constituent α-pinene and P. vera gum against Helicobacter pylori were recorded [15, 33]. A study indicated that antibacterial activity of P. lentiscus gum oil can be attributed to combination of several components rather than to one particular compound. Verbenone, R-terpineol, and linalool showed high antibacterial activity against Escherichia coli, Staphylococcus aureus, and Bacillus subtilis which is comparable to that of mastic oil itself [19]. P. lentiscus gum revealed selective antibacterial activity against Porphyromonas gingivalis and Prevotella melaninogenica and had antiplaque activity on teeth by inhibiting bacterial growth in saliva [76].

Significant antimicrobial activity was seen from essential oil of P. lentiscus leaf and gum, different extracts of P. khinjuk leaf, and essential oil of P. vera gum [15, 19, 38, 88]. Evaluating the effect of P. vera gum essential oil on growth of 13 bacteria and 3 yeasts demonstrated inhibitory effect on all of them except Bacillus cereus, Pseudomonas aeruginosa, and Klebsiella pneumonia and more effective yeasticide than nystatin. Carvacrol was found to be the most effective constituent [12, 15]. Lipophilic extracts from different parts of P. vera showed a little antibacterial activity and noticeable antifungal one against C. albicans and C. parapsilosis. Kernel and seed extracts showed significant antiviral activity [89].

Some active constituents of essential oil from the aerial parts of P. khinjuk responsible for its antibacterial and antifungal activity are α-pinene, β-pinene, myrcene, beta-caryophyllene, Germacrene B, and Spathulenol [38].

Organic fraction of mastic water obtained during the steam distillation of resin from Pistacia lentiscus var. chia indicated acceptable antifungal activity but moderate antibacterial effect. Among some of its major compounds, (±)-linalool and α-terpineol had the highest antimicrobial effect [33].

Essential oil from leaf and gum of P. atlantica showed acceptable antibacterial and antifungal activities [90–92]. However, leaf ethanolic extract had no distinct antimicrobial activity [88].

A remarkable inhibitory activity of different extracts and essential oil from P. lentiscus leaves was observed against Salmonella typhimurium; additionally, essential oil showed significant inhibitory effects against S. enteritidis and Staphylococcus aureus [86, 87].

As reported by Adams et al. [55], the leaves and twigs of P. atlantica and its active substance 3-methoxycarpachromene showed antiprotozoal activity against Plasmodium falciparum. P. atlantica var. kurdica gum controlled cutaneous leishmaniasis in mice infected with Leishmania major [93]. Extract from P. vera branch had significant inhibitory activity against Leishmania donovani and leaf extract inhibited Plasmodium falciparum without cytotoxicity on mammalian cells [94].

4.4. Anti-Inflammatory and Antinociceptive Activity. Anti-inflammatory and antinociceptive activity of five mentioned Pistacia species have been shown in Table 3. P. terebinthus gall showed anti-inflammatory activity in different in vivo models of acute and chronic inflammation [95]. Masticadienonic acid (26), masticadienolic acid (27), and morolic acid (28), three triterpene isolated from P. terebinthus gall, seem to be responsible for its anti-inflammatory activity [43]. Additionally, oleanonic acid (29) from the galls of P. terebinthus, reduced the production of leukotriene B4 from rat peritoneal leukocytes and showed antiedematous activity in mice [96]. Oleoresin and leaf extract from P. vera showed significant anti-inflammatory and antinociceptive activity [97].

Extract of the resin of P. lentiscus var. Chia and its isolated phytosterol tirucallol (31) showed anti-inflammatory activity on human aortic endothelial cells and had significant inhibitory activity on adhesion molecules expression in TNF-α-stimulated human aortic endothelial cells [98]. It was proposed that the anti-inflammatory effect of P. lentiscus var. chia gum may be related to inhibition of protein kinase C which leads to decrease in superoxide and H2O2 production by NADPH oxidase [99].

4.5. Effects on Gastrointestinal Disorders. One of the most important traditional uses of gums from Pistacia species is for management of gastrointestinal disorders. Moreover, there are several scientific studies that confirm this property [100–102]. Resin of P. lentiscus significantly reduced the intensity of gastric mucosal damage induced by pyloric ligation, aspirin, phenylbutazone, reserpine, and restraint with cold stress via its antisecretory and cytoprotective activities [103]. In one double-blind placebo controlled trial, P. lentiscus gum improved the feeling of symptoms significantly in patients with functional dyspepsia [104]. Moreover, Pistacia species exerted significant antibacterial activity on Helicobacter pylori

[32]. P. vera fruit revealed significant antioxidant activity similar to the synthetic antioxidant [81]. Lipophilic extract from P. vera nuts showed lower antioxidant potential than of hydrophilic extract [82]. One survey showed P. vera skins had a better antioxidant activity compared to seeds by means of four different assays because of higher content of antioxidant phenolic compounds in skins [44]. Antioxidant activity has been also reported from other parts of P. vera [83].
Supplementation with *P. lentiscus* oil in experimental model of colitis delayed the onset and progression of acute colitis and led to decrease weight loss caused by the disease [105]. A polyherbal formula that contains *P. lentiscus* gum caused significant decrease in colonic damage and biochemical markers related to pathophysiology of IBS in rat model of colitis [106]. Administration of *P. lentiscus* var. *chia* resin to patients with established mild to moderate active crohn’s disease (CD) for 4 weeks caused significant reduction in CD activity index and plasma inflammatory mediators without any side effects and also as an immunomodulator resulted in significantly reduction in tumor necrosis factor-alpha (TNF-\(\alpha\)) and enhanced macrophage migration inhibitory factor in these patients [107, 108].

### 4.6. Antidiabetic Activity

Aqueous leaf extract from *P. atlantica* showed significant inhibitory effect on \(\alpha\)-amylase and \(\alpha\)-glucosidase in vitro [109, 110]. It demonstrated significant acute postprandial antihyperglycemic activity comparable to metformin and glipizide in starch-fed rats. It also improved glucose intolerance [110]. However, another study on this extract did not show significant hypoglycemic activity when tested in normoglycemic and streptozocin-induced hyperglycemic rats [109]. Administration of *P. lentiscus* var. *chia* gum to human subjects for 12 months caused significantly decrease in serum glucose level among male subjects. Serum glucose in women was not affected [111].

### 4.7. Antitumor Activity

Among mentioned species of *Pistacia, P. lentiscus* is the most investigated for antitumor activity (Table 3). *P. lentiscus* var. *chia* gum inhibited proliferation and induced apoptosis of human colorectal tumor cells in vitro [112]. The resin exerted the most cytotoxic effect against promyelocytic leukemia among I3 human cell types and also inhibited the natural apoptosis of polymorphonuclear leukocytes [76]. The gum demonstrated anticancer activity via delaying the growth of colorectal tumors developed from human colon cancer cells xenografted into mice [8]. It also increased maspin (a mammary serine protease inhibitor with tumor suppressive activity for prostate cancers) expression in responsive prostate cancer cells and inhibited cell proliferation and blocked the cell cycle progression [113, 114]. Essential oil of *P. lentiscus* demonstrated significant inhibition on tumor growth in immunocompetent mice without signs of toxicity, related to apoptosis induction, reduced neovascularization, and inhibiting chemokine expression [115]. In addition, it had antiproliferative and proapoptotic effect on human leukemia cells and inhibited the release of vascular endothelial growth factor from these cells [116]. Despite many reports on antitumor activities of *P. lentiscus*, one in vivo study showed that the high dose of *P. lentiscus* gum promoted the preneoplastic lesions development in rat liver with increasing liver relative weight which proposed that desirable anticarcinogenic effects of mastic could be obtained at relatively low doses [117]. In one recent study, the current data on the anticancer activities of gum, oil, and extracts of *P. lentiscus* L. and its major constituent, have been reviewed comprehensively with special attention to the probable anticancer mechanisms [118].

The fruit extract of *P. atlantica* sub. *kurdica* showed growth inhibition in human colon carcinoma cells similar to Doxorubicin [119]. *P. vera* oleoresin demonstrated moderate cytotoxic effect against breast cancer cell line, hepatocellular carcinoma cell line, cervix cancer cell line, and normal melanocytes [120].

### 4.8. Effects on Liver and Serum Biochemical Parameters

*P. lentiscus* leaf demonstrated significant hepatoprotective activity against carbon tetrachloride induced hepatotoxicity in rats by reducing the level of bilirubin and activity of liver enzymes [121]. However, another study reported hepatic fibrosis, mild cholestasis, and depletion of reduced glutathione by long-term administration of aqueous leaf extract in healthy rats [122]. Administration of *P. lentiscus* var. *chia* gum for 18 months in healthy volunteers caused reduction in liver enzymes and exerted hypolipidemic effect [111]. Extracts from *P. vera* fruits have shown beneficial effects on HDL and LDL level in rabbit model of atherosclerosis [123]. Positive changes in lipid profile were recorded after three-week use of *P. vera* nuts in patients with moderate hypercholesterolemia. The decrease in triglyceride and LDL levels was not significant [124]. *P. terebinthus* fruit demonstrated hypolipidemic effect in hypercholesterolemic rabbits [125].

### 4.9. Effects on Atherosclerosis

More over than the antihyperlipidemic activity that described above, *Pistacia* species exerts their antiatherosclerotic effects by direct activity on atherosclerotic lesions moreover than their antihyperlipidemic activity. Both methanolic and cyclohexane extracts from *P. vera* fruits have shown beneficial effects on HDL, LDL, and aortic intimal thickness in rabbit model of atherosclerosis. The methanolic extract additionally showed an antioxidant activity and remarkable decrease in aortic surface lesions [123]. *P. terebinthus* fruits inhibited the development of the atherosclerotic lesions in the thoracic artery [125]. *P. lentiscus* resin that downregulated CD36 mRNA expression (as the oxLDL receptor in macrophages that play a pivotal role in atherosclerotic foam cell formation) resulted in antiatherogenic effects [126].

### 4.10. Anticholinesterase Activity

Aqueous extracts from *P. atlantica* and *P. lentiscus* leaves showed strong acetylcholinesterase (AChE) inhibition [13]; additionally, both the methanol and ethyl acetate extracts of *P. atlantica* leaf showed relatively weak AchE inhibitory activity [127]. However, one study showed that ethyl acetate and methanol extracts of various commercially terebinth coffee brands (an oily brown-coloured powder produced from the dried and roasted fruits of *P. terebinthus*) and the unprocessed fruits of *P. terebinthus* did not have inhibitory activity against AChE and tyrosinase, while they selectively inhibited butyrylcholinesterase (BChE) at moderate levels [85].
5. Conclusion

In traditional Iranian medicine textbooks and papers, five species of *Pistacia* genus including *P. vera*, *P. lentiscus*, *P. terebinthus*, *P. atlantica*, and *P. khinjuk* had been introduced for treating the wide range of ailments. These species until now have been utilized in Iran by people for different nutritional and medicinal proposes. This review considered findings about phyichochemical and pharmacological properties of these five species and presents comprehensive analysis of papers published since the year 2000. Ethnopharmacological data about these species may help us to know that many pharmacological aspects proposed nowadays for these species have been derived from traditional uses like antiseptic and antimicrobial, anti-inflammatory and anti-nociceptive, antihepatotoxic, and anticancer activities and their beneficial effects in gastrointestinal disorders. Furthermore, there are several pharmacological activities discussed in traditional medicine such as diuretic, lithotritypic, anti-tussive, antiirritable, antiasthmatic, antihypertensive, and aphrodisiac activities which are not supported by any current scientific documents, and so, they could be considered for investigation by researchers.

Phytochemical studies provided evidence for traditional applications of these species. With respect to traditional assays, triterpenes found in the resin and monoterpens are the most abundant composition of the essential oil from different parts of these species. Essential oil constituents might be valuable chemotaxonomic marker to ascertain different *Pistacia* chemotypes. Considering the therapeutic effect of isolated components, it can be concluded that terpenoids including mono, di-, and triterpenoids are associated with anti-inflammatory and antimicrobial effects. High amount of natural phenos and flavonoids is related to potent antioxidant and anticancer activities.

Review on current researches about the genus *Pistacia* L. highlighting pharmacological studies on crude plant parts, extracts, and some pure metabolites has provided scientific evidence for traditional uses and has revealed this genus to be a valuable source for medicinally important molecules.

So many studies were carried out on antioxidant activity of this genus considering their flavonoids, anthocyanins, and other phenolic compounds as preventive factors against cancer and cardiovascular diseases. *P. lentiscus* is the most studied species for antioxidant effects followed by *P. atlantica*, *P. vera*, *P. terebinthus* and *P. khinjuk*.

Most of the studies showed antimicrobial activity of these species especially *P. lentiscus* on a wide range of microorganisms including Gram-positive and -negative, aerobic and aerobic bacteria, viruses and fungi. The findings indicated that α-pinene, verbenone, R-terpineol, linalool, carvacrol and flavones are major compounds related to antibacterial activity.

### Abbreviations

| Abbreviation | Full Form |
|--------------|-----------|
| AST          | Aspartate aminotransferase |
| B(a)p        | Benzo(a)pyrene |
| BHA          | Butylated hydroxyanisole |
| BHT          | Butylated hydroxytoluene |
| DMDP         | N,N-dimethyl-p-phenylenediamine |
| DPPH         | 2,2-Diphenyl-1-picrylhydrazyl |
| EC50         | Half maximal effective concentration |
| EDTA         | Ethylenediaminetetraacetic acid |
| EPP          | Ethyl phenylpropiolate |
| FRAP         | Ferric reducing antioxidant power |
| Gamma-GT     | Gamma-glytamyl transpeptidase |
| IC50         | The half maximal inhibitory concentration |
| LOX          | Lipoxygenase |
| MBC          | Minimum Bactericidal Concentration |
| MDA          | Malonaldehyde |
| MIC          | Minimum inhibitory Concentration |
| NF-kB        | Nuclear factor kappa-light-chain-enhancer of activated B cells |
| OxLDL        | Oxidized low density lipoprotein |
| PL2A         | Phospholipase A2 |
| SGOT         | Serum glutamic oxaloacetic transaminase |
| SGPT         | Serum lumatic-pyruvic transaminase |
| SOD          | Superoxide dismutase |
| TBARS        | Thiobarbituric acid active substances |
| TBHQ         | Tertiary Butyl hydroquinone |
| TPA          | 12-O-Tetradecanoylphorphol-13-acetate. |

### Conflict of Interests

The authors declare that they have no conflict of interests.

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