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The therapeutic effects of *Pistacia Atlantica* used in foods: A review

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ABSTRACT

The present study investigates the potential medicinal and health benefits of the Middle Eastern and North African herb *Pistacia atlantica*. Research shows that its compounds, such as flavonoids, phenolic compounds, and oils, could be beneficial. It can help with heart disease, sugar sickness, and brain illness because of its antioxidant and anti-inflammatory attributes. Also, *P. atlantica* can kill bacteria and help heal cuts. It might help fight cancer too. But we need to study more to know all its uses, enhance extraction techniques, and make sure it's safe and works well in tests with people. The review will focus on the pharmacological properties, constituents, and mechanisms of action of *P. atlantica*, discussing its traditional use in medicine, effects on inflammatory diseases, antibacterial properties, promise in cancer treatment, and potential for treating diabetes and other metabolic issues. The review aims to comprehensively understand *P. atlantica*'s potential as a therapeutic agent and identify areas for further research.

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1. Introduction

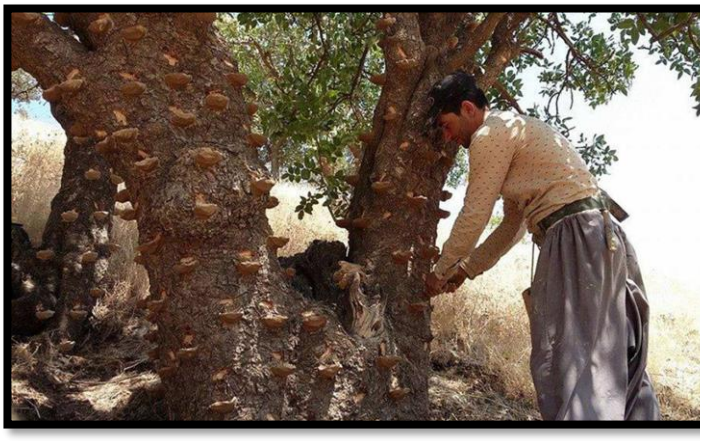
Medicinal plants have long been the main source of bioactive phytochemicals utilized in the treatment and prevention of diseases since ancient times. Their safety, availability, and affordability make them valuable for reaping benefits. Around 60% of the global population relies on medicinal plants as a primary healthcare solution. These plants not only provide essential human needs like food, clothing, and shelter but also serve as sources for transportation, fragrances, flavors, and medicinal components. Natural compounds have garnered significant attention due to their low toxicity levels and potential in managing various chronic ailments. These resources hold immense value and were traditionally gathered from the natural surroundings [1–8].

Among these traditional medicine plants is *Pistacia***.** One of these traditional medicinal plants is Pistacia. *Pistacia*, a genus of plants, has a wide distribution from the Mediterranean to Central Asia. Some notable species within this genus are *Pistacia lentiscus* L., *P. khinjuk*., *P. terebinthus* L., *P. vera* L., and *P. atlantica* Desf [9].

Pistacia atlantica (wild pistachio) is one of more than 600 species in the family Anacardiaceae, a genus of the order Sapindales. It is widely used in traditional medicine for a variety of conditions, including relief of upper abdominal pain and discomfort, dyspepsia and peptic ulcers, and has significant ethnopharmacological relevance. It grows from the Mediterranean to Central Asia [10].

P. atlantica is classified as a thermophilus xerophyte, with a preference for arid environments characterized by dry, stony or rocky slopes. It can also be found near fields, roadsides, at the foot of dry-stone walls and other similar habitats [11].

The range of *Pistacia atlantica* subspecies Kurdica includes Iraq (specifically the Kurdistan Region or Southern Kurdistan), Turkey (Northern Kurdistan), Syria, Armenia, Lebanon (specifically the Anti-Lebanon region), Afghanistan, Pakistan and Iran (Eastern Kurdistan and other areas). This species of *Pistacia atlantica* subsp. kurdica was found in Ranya, Sulaymaniyah province, in Iraqi Kurdistan, and is a deciduous tree that reaches a maximum height of 7 m. Its branches spread out and grow upright, forming a thick crown. The trunk is sturdy and covered with fissured bark. A trained and experienced person makes Kurdish chewing gum. The tree is wounded with a sharp adze tool and then the clay is prepared for resin extraction [12] (Figure 1).



a

b

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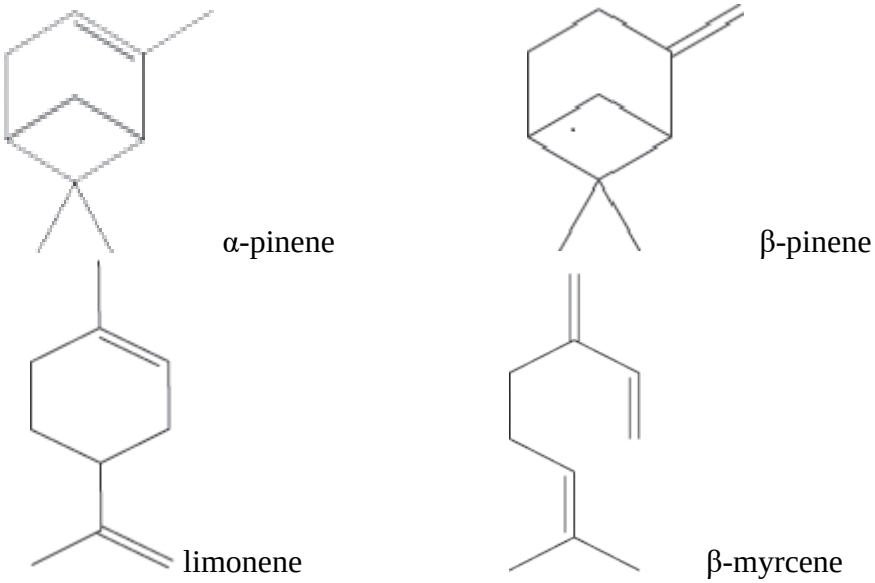
Figure 1: Kurdish man creating clay for tree resin collection (a), Collecting trunk exudate (b) [12]

Pistacia atlantica is endemic to the Kurdistan region of western Iran and can be found throughout the Zagros Mountains [13]. It comes in many different varieties, such as cabulica, kurdica and mutica, and has small, round, acidic fruits that are dark green in color. It looks like a pistachio, but the seed is smaller. *Pistacia atlantica* is dried to reduce the amount of water it contains so that it can be stored for a long time and retain its qualities [14]. *Pistacia* resins have antibacterial and antioxidant properties, and there is growing evidence that they may help reduce and prevent many chronic diseases, including cardiovascular disease, gastrointestinal problems and many malignant tumors [15].

This review aims to examine the potential health impacts of the herb *Pistacia Atlantica*, offering a thorough comprehension of its advantages, antioxidant, antimicrobial, and anti-inflammatory characteristics, as well as its potential for treating various ailments, including cancer, diabetes, hyperlipidemia.

1. Chemical composition of *Pistacia atlantica*

Analysis of phytochemicals has shown the existence of a wide range of useful molecules such as volatile compounds, phenolic compounds, fatty acids and flavonoids [16]. An essential oil is a type of organic compound derived from various parts of *P. atlantica*, such as resin, fruits, twigs, flowers, leaf buds, leaves and galls. It is classified as a metabolite [17]. Essential oil makes up about 20% of the crude gum [18]. It consisted mainly of monoterpene and sesquiterpene hydrocarbons, which accounted for about 93.50% and 5.45% of the total detected constituents, respectively, α-pinene, α-myrcene, a-limonene. α-Pinene and α-terpineol were the major constituents in *Pistacia atlantica* [19]. β-Pinene, trans-Verbenol, trans-Pinocarveol, α-Phellandrene [20]. The resin of P. atlantica contains triterpenes such as oleanolic acid, ursonic acid, masticadienonic acid, morolic acid and 3-O-acetyl-3-epiisomasticadienolic acid, [17] as mentioned in Figure 2.



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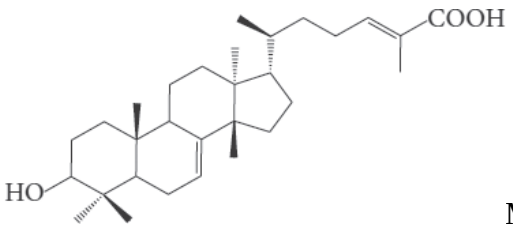
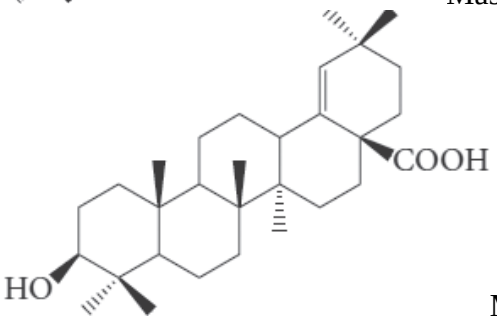


Masticadienolic acid



Morolic acid

Figure 2. The chemical of isolated structure from *Pistacia atlantica* [17]

Some studies have been undertaken on several components of the tree, as seen in Figure 3, revealing the existence of active compounds isolated from the leaves, gum, roots, fruits, and hulls.

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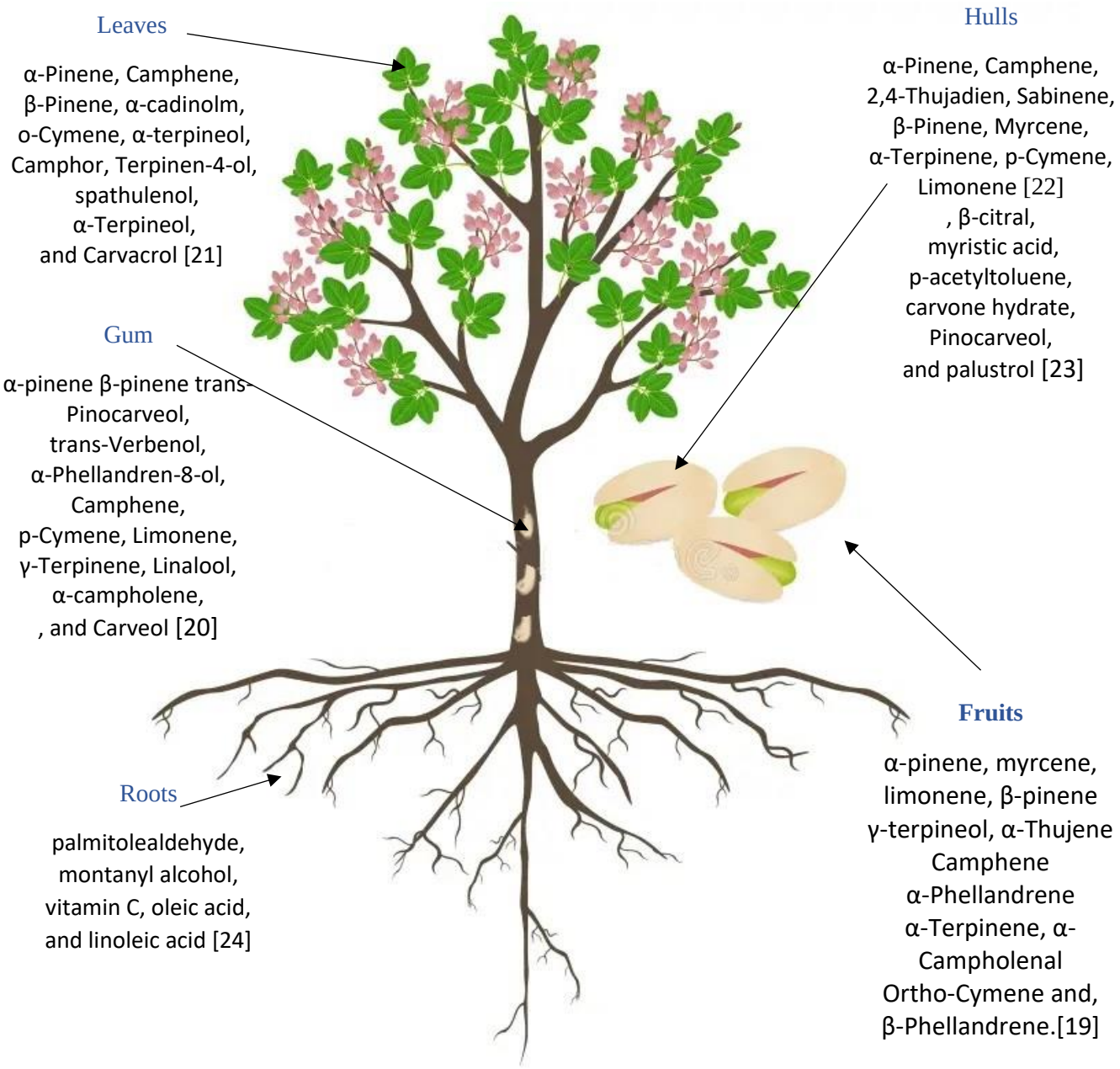

Figure 3. The active compounds of tree parts of *Pistacia atlantica* essential oil by GC-mass analysis according to researches [19–24]

2. The applications of *Pistacia atlantica* in foods products and other applications

The unripe fruits of *Pistacia atlantica* are often eaten as a snack, but both ripe and unripe fruits are used as ingredients in the preparation of various culinary dishes. The aesthetically pleasing dried fruits are used in the production of a pearl [12]. In Iran it is used to flavor yoghurt drinks, ghee, pickles and jams [14]. Extraction of gum resin from *Pistacia atlantica* Desf. is used in various industries including paper glue, shoe polish, soap and sealing wax. It is also used as a component in varnishes and paints, as a flavoring or for its gum-forming properties in chewing gum, and as a key ingredient in the manufacture of cosmetics such as toothpaste, hair and skin lotions, and perfumes [25].

The gum-like resin and fruit of the Atlas Pistachio, rich in essential and fixed oils, have been used in traditional medicine, cosmetics and health and beauty products since ancient times. Atlas Pistachio Solid

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Oil is now used in soaps, lotions and shampoos for its therapeutic benefits. Plant extracts are used in food preservation, medicines, and cosmetics because of their functional qualities, such as their antioxidant and antibacterial activity, which are caused by a variety of biologically active chemicals. Atlas Pistachio oils consist of bioactive compounds such as alpha-pinene and beta-pinene in the resin, terpinen-4-ol in the leaves and oxygenated monoterpenes in the fruit. The main constituents of oil fruits are unsaturated fatty acids (oleic, linoleic, palmitic and stearic acid), sterols and tocopherols. Each of these chemicals has medicinal and cosmetic benefits [26,27]. Figure 4 illustrates the numerous uses for *Pistacia atlantica*

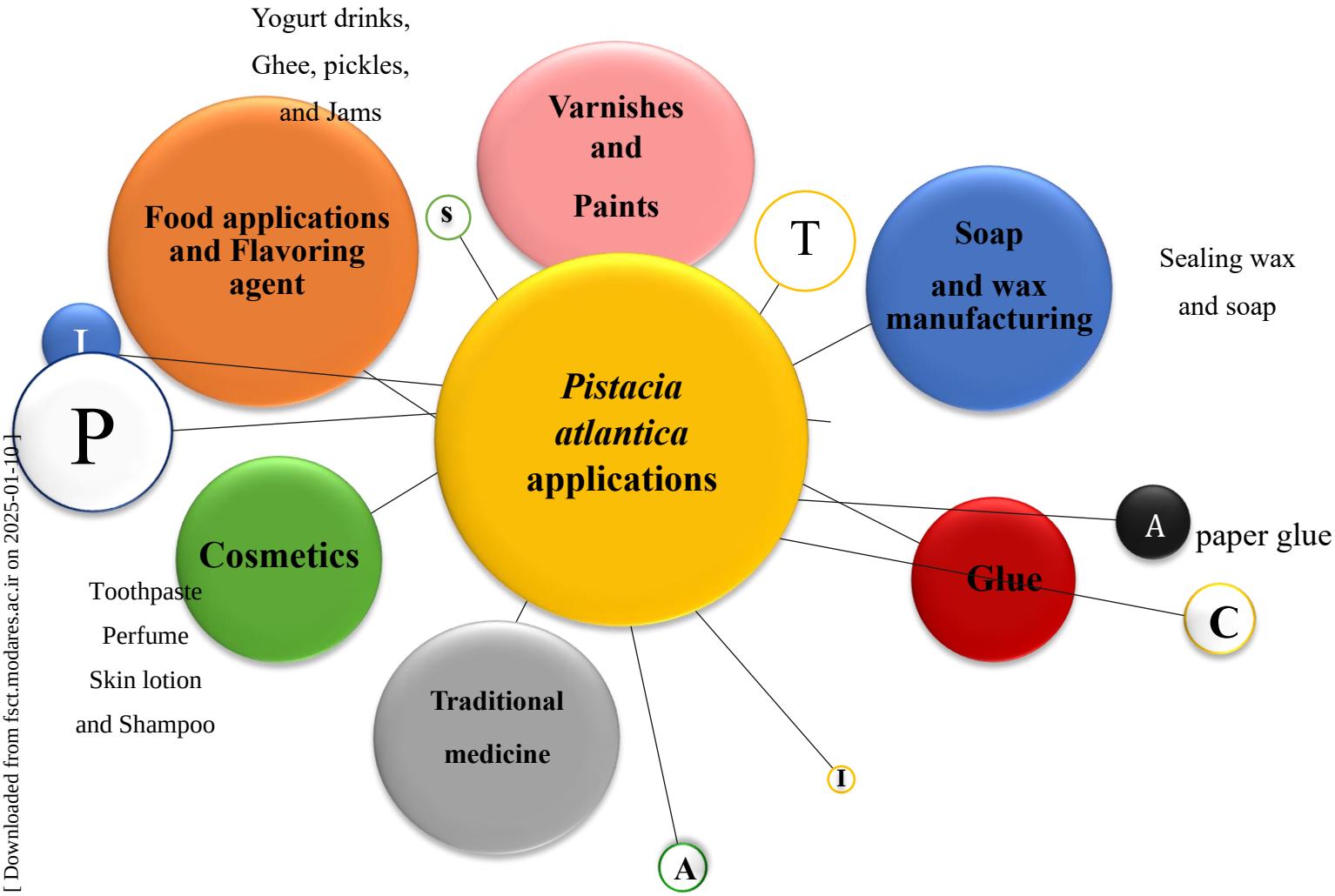

Figure 4. The numerous uses for *Pistacia atlantica*

3. The health and therapeutic effects of *Pistacia atlantica* on Diseases

Today, herbal drugs are used by most people around the world to take care of their health [28]. Because plant medicine can help with healing, it has been used to treat a wide range of illnesses, including gastrointestinal problems like indigestion, diarrhea, gastralgia, and peptic ulcer disease. [18,29,30]. According to the results, the *Pistacia atlantica* tree has been used as medicine for a long time to treat 20

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different diseases and conditions in humans. This particular wild tree has been studied and found to be an important species that has grown naturally in the Kurdistan area for a long time. Over the course of history, it has been very important for the region's health and economic growth. Since ancient times, people have known how important it is because of its economic and ethnopharmacological effects [12]. The essential oil from *P. atlantica* has been observed to be good for health in many ways, such as fighting bacteria, free radicals, and diabetes [31]. It has been proven that high doses (2000 mg/kg) of the essential oil of *P. atlantica* oleoresin are safe to take by mouth, so it can be used in the food industry [31].

Pistacia atlantica has been used as medicine to treat a number of conditions, such as stomach problems, wounds, and breathing problems. Researchers have found that *P. atlantica* has a number of health benefits, such as the ability to lower cholesterol and fight diabetes. Besides that, it might help with digestive problems [17]. Figure 5 illustrates the therapeutic effects of *Pistacia atlantica* on diseases.

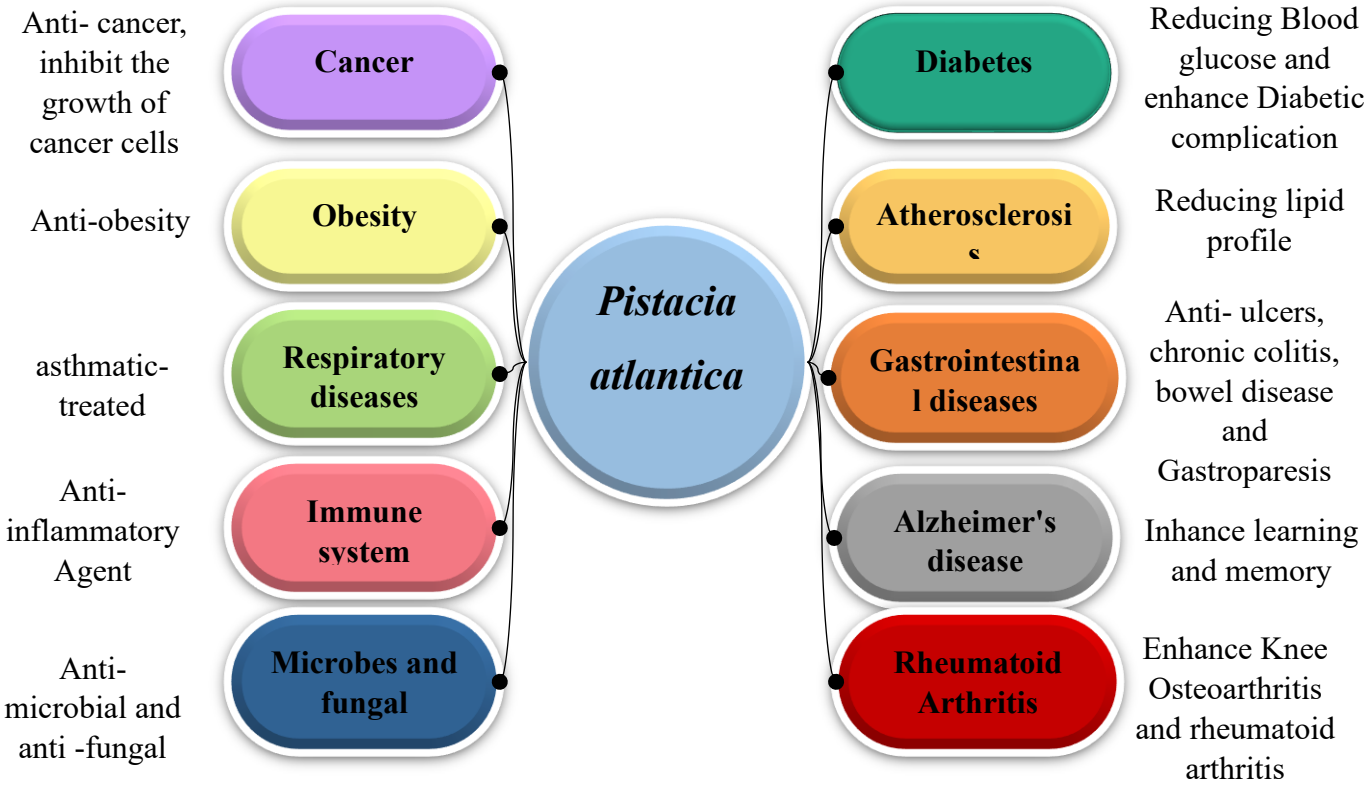

Figure 5. The therapeutic effects of *Pistacia atlantica* on diseases

3.1. Respiratory diseases

Asthma, COPD and pneumonia are just some of the lung diseases that contribute to a wide range of health problems around the world. As a result of the widespread use of COVID-19, scientists have shifted their focus to discovering and testing new treatments for lung disease [32]. Researchers studied how the aqueous extract of *P. atlantica* gum affected the pathological and cellular aspects of asthma in BALB/c mice, which are used as a model for asthma. They were given different doses of the extract for 48 days. Aqueous *P. atlantica* gum extract reduced eosinophils, anti-ovalbumin cytokines and lung tissue pathology, regardless of the dose. The extract-treated animals were significantly more anti-inflammatory than the dexamethasone and asthma-treated groups. In addition, the IFN-γ/IL-4 ratio increased

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significantly in a dose-dependent manner compared to the untreated asthmatic group [33].

3.2. Anti- obesity

Obesity is becoming a major health problem around the world, but it's still not curable and leads to a lot of illness and death [34]. Research was conducted to evaluate the inhibitory effect of *Pistacia atlantica* root extract on porcine pancreatic lipase. The results indicated a significant reduction in lipase activity with the administration of this extract. The inhibition of lipase activity was found to be maximal (100%) at a dose of 1 mg/ml during a 30-minute incubation period [35].

3.3. Anti-cancer

Cancer is the second leading cause of death in the United States and a serious public health problem worldwide. In 2022, there are expected to be 1,918,030 new cases of cancer and 609,360 deaths from cancer in the US [36]. Plants can produce a variety of bioactive chemicals, including high levels of phytochemicals that may protect against damage caused by free radicals [37–39]. *Pistacia atlantica* has been studied and shown to have anti-cancer properties; in particular, the extract has been shown to inhibit the growth of cervical and gastric cancer cells. A potential source of anti-cancer drugs, the plant has a high concentration of phytochemicals. Its relatively strong antioxidant activity may be due to the phenolic and flavonoid components contained in this extract [40]. Mastic gum resin was tested for its effects on cancer cell growth, morphology and apoptosis using the MTT assay. It was discovered that mastic gum resin, at concentrations between 0.01 and 100 µM, effectively eradicated cancer cells in a manner influenced by dosage and duration. The efficacy of the resin in halting cell proliferation is directly linked to its polyphenol content, indicating a correlation between phenolic acid, flavonoids, and their impact upon the bloodstream. Because of its high polyphenol content, mastic gum resin could be used as an antioxidant and anticancer agent [29].

3.4. Anti-fungal and anti-Microbial Agent

Many plants have antifungal and antimicrobial qualities that support their historical usage as herbal remedies [8,41]. *Pistacia atlantica* (subsp. kurdica) was tested for antibacterial activity against six bacterial strains: *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Bacillus subtilis*, *Escherichia coli*, *Micrococcus luteus* and *Klebsiella pneumonia*. Different oil gum concentrations (100, 50 and 25 µl/ml) were tested for antifungal activity against *Aspergillus brasiliensis*. Bacteria and fungi could not grow in any concentration of the oil gum extract, and it stopped growing of *Aspergillus brasiliensis* very well, with a 19-mm inhibition zone [30]. It works best against microbes like *E. coli*, *Staphylococcus aureus*, and *Streptococcus pyogenes* [29]. It has been found that *Pistacia atlantica* essential oil works better against gram-positive bacteria than gram-negative bacteria when it comes to antibiotics. Professionals in the food industry strive to develop innovative, environmentally friendly packaging solutions, such as edible coatings and films, to preserve food quality during storage. Modern packaging techniques that inhibit or postpone microbiological development can extend the shelf life of a packed product. One of the most effective essential oils to use to keep food safe and lower the chance of germs is this one [19,42–44]. Pistacia essential oils may be able to help control the main germs that make bread go bad, according to studies. People suggest using *Pistacia atlantica* resin essential oil as a natural preservative in bread and other baked goods that can withstand high temperatures due to its limited effectiveness in killing *B. subtilis* [45].

One study investigated the antibacterial activity of essential oil (EO) against *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*,

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Streptococcus faecalis, *Bacillus cereus*, *Staphylococcus aureus* and *Candida albicans*. The EO had a minimum dose of 0.13 mg/mL for *C. albicans* and 0.42 mg/mL for *E. coli* that stopped the growth of those bacteria. Also, the EO had the lowest minimum concentration needed to kill bacteria (0.16 mg/mL) when tested against *C. albicans* and the highest concentration needed when tested against *E. coli* at 0.52 mg/ml. Also, the inhibition zone that was the biggest when tested against *C. albicans* was 24.2 mm, and the inhibition zone that was the smallest when tested against *E. coli* was 20.8 mm [23]. Researchers looked at how well organic and water-based extracts *of P. atlantica* killed Gram-negative (*E. coli*, *S. typhimurium*, *A. hydrophila*, and *P. aeruginosa*) and Gram-positive (*S. aureus*, *L. monocytogenes*, and *B. cereus*) bacteria by checking to see if there were any inhibitory zones. Antimicrobial activity of *P. atlantica* extracts (6.25-50 mg mL-1) against gram-negative and gram-positive bacterial strains. The ethanolic extracts of *P. atlantica* showed significant antibacterial activity, it had inhibition zones that were 14±0.6 to 16±0.3 mm wide for the bacteria that were tested. This confirmed that they could be used in traditional ways to treat infections and urged their use as alternatives to antibiotics [46]. In a recent study on *Pistacia atlantica*, standard strains of *Pseudomonas aeruginosa* which is considered an exploitative human pathogen [47], *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* and *Aspergillus flavus* were tested for antifungal and antibacterial activities. *Klebsiella pneumonia* and *P. aeruginosa* were the most sensitive bacteria to *P. atlantica*. *Aspergillus flavus* was the most sensitive fungal strain to *P. atlantica*. These results suggest that *P. atlantica* is antibacterial and antifungal. According to the research [48], these plant extracts may make antibacterial and antifungal drugs work better.

Anti-Oxidant properties

Antioxidants are very important for stopping and getting rid of free radicals, which protects people from inflammation illnesses. These days, researchers are mostly interested in "natural antioxidants" that come from plants, mostly because they are safe to use as medicine [49,50]. *P. atlantica* may be useful as an antioxidant in medicine and food, according to earlier studies [22]. Researchers found a strong link between bioactive phytochemicals and the antioxidant activity of tocopherols, carotenoids, and omega-3 fatty acids found in *Pistacia atlantica*. This result shows that crude oils from *P. atlantica* Desf. have a lot of promise as a natural source of antioxidants that could be used in the food and drug industries [51]. The resin's DPPH and ABTS+ free radical scavenging abilities served as a measure of its antioxidant activity. At 1-100 µg/ml, the resin's DPPH scavenging ability increased from 26.44% to 95.56%. An IC50 value of 2.5 µg/mL was established. Conversely, the resin demonstrated conspicuous ABTS+ radical scavenging activity. The scavenging activity ranged between 25.11% and 89.9% at concentrations of 150–2,400 µg/ml. The IC50 value, which represents the concentration required to scavenge 50% of the radicals, was determined to be 500 µg/mL [29].

The fruits of *Pistacia atlantica* (subsp. mutica) provide antioxidant vegetable oils. Gel forms from *P. atlantica* (subsp. mutica) oil extraction was tested for antioxidant efficacy on enzymatic antioxidants in rat wounds. The study showed that wound excision induced oxidative stress. Topical application of *P. atlantica* (subsp. mutica) gels, particularly gel 10%, increased antioxidant activity and reduced oxidative stress during wound closure [52]. Previous research suggests that bene extract contains phenolic compounds such as gallic acid and quercetin, which have antioxidant and

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radical scavenging properties. Research has found a favourable correlation between phenolic chemicals and antioxidant activity. At doses between 0.1 and 4 mg/ml, bene gum extract is much better at scavenging DPPH and has a higher antioxidant activity than BHT (86.54±0.24%) [53].

3.5. Anti-inflammatory Agent

Inflammatory disorders arise as a result of atypical immune responses manifested by an imbalance of both cells and inflammatory mediators [54]. One study found that mice given *Pistacia atlantica* at various doses for 52 consecutive days showed a dose-dependent reduction in delayed-type hypersensitivity responses that was statistically significant compared to the control group, a large decrease in IL-17 cytokine levels and a significant increase in IL-10 cytokine levels compared to the control group, and significant reductions in respiratory burst and *splenocyte* proliferation, but not phagocytic capacity. One way in which *Pistacia atlantica* may help the immune system is by switching the immune response from the pro-inflammatory cytokine IL-17 to the anti-inflammatory cytokine IL-10 [55].

3.6. Rheumatoid Arthritis

Both internal and external factors contribute to the development of rheumatoid arthritis (RA), a chronic inflammatory autoimmune disease. Deterioration of bone and cartilage is a hallmark of the disease [56]. In a recent study, a cream containing *P. atlantica* was used to reduce pain, inflammation and complications in people with osteoarthritis of the knee. In addition, this treatment demonstrated a reduction in the side effects often associated with traditional medications over a three-month period, with diclofenac gel administered as a control at the same dose and for the same duration. The use of *P. atlantica* cream resulted in a significant reduction in both pain and stiffness experienced by patients during the performance of activities of daily living. The primary factors contributing to the remarkable anti-inflammatory effect of *P. atlantica* are the potent analgesic properties of α-pinene and the anti-inflammatory properties of the plant itself [41].

3.7. Gastrointestinal diseases

Anti- ulcers

Ulcers, a condition of the digestive system, affect many people. It is essentially an irritated break in the skin or mucous membrane lining the digestive system. Ulceration occurs when there is an imbalance, such as increased aggressiveness or decreased mucosal resistance. Peptic ulcers are any ulcer of the duodenum or stomach. Possible causes include medication, poor diet, stress and related problems [57]. A study was conducted to evaluate the efficacy of essential oil derived from *Pistacia atlantica* Desf. oleoresin in the treatment of peptic ulcers (PU) and its ability to inhibit the growth of Helicobacter pylori bacteria. The standardized essential oil of *Pistacia atlantica* had a protective effect against ethanol-induced gastric ulcers and showed antibacterial activity against Helicobacter pylori. α-Pinene may be the causative agent [58]. Research was conducted to investigate the protective properties of *P. atlantica* extract against ethanol-induced ulcers, and the research found that pre-treatment with *P. atlantica* extract at doses of 200 and 400 mg/kg reduced gastric MDA levels, indicating decreased peroxidation, and increased gastric NO levels, acting as an antioxidant. *Pistacia atlantica* extract has been shown to be effective in preventing ethanol-induced gastric ulcers in rats [59].

Chronic colitis

Inflammatory bowel disease (IBD) is a chronic condition characterized by recurrent inflammation of the gastrointestinal tract. Iranian folk medicine prescribes *Pistacia* oleo-gum resin for a wide range of ailments, including gastrointestinal problems. A study was carried out to see what happened when *Pistacia atlantica* sub. kurdica oleoresin was mixed with honey and given to rats

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suffering from acetic acid-induced colitis. *Pistacia atlantica* oleo-resin (about 400 mg/kg) and honey (400 mg/kg) reduced intestinal inflammation and the intensity of colonic ulcers. This was achieved by reducing inflammatory cytokines, neutrophil infiltration and TLR-4 expression [60].

In rats with ulcerative colitis, a persistent inflammatory bowel disease affecting the gastrointestinal tract, different fractions of Baneh gum were tested at different doses. Three doses of gum (100, 200 and 400 mg per kilogram) were administered orally and intrarectally, while the volatile oil was administered orally for four days. The volatile oil of baneh consists mainly of α-pinene (41.23%). Both chewing gum and essential oil reduced all signs and symptoms of colitis and myeloperoxidase activity. Oral gum was more effective than rectal gum in treating colitis. An experimentally induced colitis showed that *Pistacia atlantica* subsp. kurdica gum and volatile oil were good for inflammation [61]. Research has shown that administration of a significant dose of *Pistacia atlantica* fruit oil extracts, both orally and rectally, resulted in physiological and pathological improvements in a rat model of colitis. These findings suggest that this intervention may be effective in the treatment of ulcerative colitis [62].

Gastroparesis

Gastroparesis is common in people who have diabetes mellitus types 1 and 2. The *Pistacia atlantica* group had significantly lower postprandial fullness/early satiety, bloating, and gastroesophageal satiety index (GCSI) scores compared to the placebo group. In one study, symptoms that improved overall in those who suffered from gastroparesis included: nausea reduction; vomiting reduction; postprandial fullness; and an early satiety decrease. At the end of the intervention period, systolic blood pressure dropped markedly as did BMI and HbA1c levels, which also decreased significantly in the *Pistacia atlantica* group [63].

Alzheimer's disease

Alzheimer's disease (AD) is the most common neurodegenerative disease, but therapeutic options are few and not very effective. The scientific community and pharmaceutical industry are interested in natural products with neuroprotective effects that can be used to develop new treatments for AD. These substances act on various pathological processes associated with the disease [64]. The study of several extracts from Pistacia leaves revealed significant anti-inflammatory properties and anti-cholinesterase activity. These findings support the potential use of these extracts in the prevention and treatment of Alzheimer's disease [65]. Table 1 shows the therapeutic effects of *Pistacia atlantica* on a variety of disorders and diseases according to the results of numerous studies.

Table 1: The therapeutic effects of *Pistacia atlantica* on Diseases

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The therapeutic effects of *Pistacia atlantica* on diseases

Type of gum	Disease	on	Country	Dosage type	Health benefits	Reference
Pistacia atlantica subsp. kurdica	diabetic gastroparesis	Humans	Iran	Chewing gum	↓ diabetic gastroparesis symptoms.	[63]
Pistacia atlantica subsp. kurdica	Chronic colitis	Rats	Iran	Orally and intrarectally Aqueous gum (Volatile oil)	(Orally)↓ Indices of colitis (Intrarectally) not significantly effective	[61]
Pistacia atlantica	Immune system	Mice	Iran	Aqueous extract	↓(anti-inflammatory)	[55]
Pistacia atlantica	the Knee Osteoarthritis	Humans	Iran	Topical Cream (oleoresins)	↓ pain of joint and stiffness	[57]
Pistacia atlantica	Inflammatory bowel disease	Rats	Iran	Orally (Oleo-Gum -Resin and Honey)	↓ Inflammation of the bowel and colonic ulcer severity	[60]
Pistacia atlantica	asthma	Mice	Iran	Orally (Aqueous extract)	↑anti-inflammatory and immunomodulatory	[33]
Pistacia atlantica + butyrate + *Lactobacillus casei*	ulcerative colitis	Rats	Iran	Orally	↓ colitis Improvement in Visible appearance)	[66]
Pistacia atlantica mutica	metabolic syndrome	Rats	Iran	Orally	↓blood sugar ↓triglycerides ↓cholesterol, ↓inflammation, and problems with pancreatic secretions.	[67]
Pistacia atlantica	peptic ulcer	Rats	Iran	Orally essential oil	↓ Helicobacter pylori ↓ peptic ulcer	[58]

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Diabetes

Diabetes mellitus is a common chronic disease with several contributing factors, including poor diet and physical inactivity. Insufficient secretion of insulin by the pancreas or inefficient use of insulin both contribute to the development and progression of the disease. Hyperglycemia, often known as high blood sugar, is the result of uncontrolled diabetes. Over time, the disease causes extensive damage to the human body, particularly to the neurological and cardiovascular systems. At a time when humanity is working to eliminate the diseases that have plagued the world's population, their achievement of physical and mental health represents a positive step forward for our species [68]. Diabetes causes 175 amputations and 530 heart attacks every week. At least £10 billion, or 10% of the annual NHS budget, is spent on diabetes care in the UK, 80% of which is spent on treating complications. Diabetes affects 1 in 6 people who are hospitalized [69].

The International Diabetes Federation (IDF) reports that by 2021, 10.5% of the world's population will have diabetes. By 2024, the total number of people with diabetes is expected to reach 783 million. Type 1 diabetes is an autoimmune disease in which the pancreas stops producing insulin. Over 90% of diabetes cases are type 2, which is linked to an unhealthy lifestyle, including lack of exercise and a high-fat, high-carbohydrate diet [70]. The number of people diagnosed with diabetes in Iraq is estimated to be around 1.4 million. The prevalence of type 2 diabetes (T2D) in Iraq ranges from 8.5% to 13.9% [71]. Type 2 diabetes and obesity are on the rise and are strongly associated with cardiovascular disease, which has become a serious public health problem worldwide [70]. Unfortunately, diabetes is still not solved by today's medical science. Insulin and oral diabetes medicines, for example, have a lot of side effects. Meanwhile, natural remedies pose no danger to the user. Medicinal plant extracts have been shown in several clinical trials to have anti-diabetic effects and to restore the function of pancreatic beta cells [72].

The effect of *Pistacia atlantica* on diabetes

In an Iranian study, diabetic mice were given different doses of an essential oil and hydroalcoholic extract of *P. atlantica* subsp. kurdica for three weeks. The results showed that it has properties that lower blood lipids and fight free radicals, making it a promising supplement for reducing complications caused by diabetes [73]. Research in diabetic rat models has shown that *Pistacia atlantica* reduces oxidative stress. These findings, obtained by controlling gene expression and antioxidant markers in diabetic rat models, imply that essential oils from *Pistacia atlantica* may have some protective effect against oxidative stress-related illnesses [74]. A recent trial gave diabetics 10 cc of *P. atlantica* extract twice a day for three months, or a placebo. The experimental group's fasting blood glucose was lower three months later than that of the control group on a diabetic diet. The average HbA1c after the procedure was 5.8 ± 1.0. Higher BMI patients saw a bigger drop than did those with normal BMIs. Its significance in controlling blood glucose levels in T2D patients is shown by a three-month trial [71]. Studies have found that *P. atlantica* leaf methanol extract may be a source of bioactive compounds with anti-diabetic effects. This is so because it may inhibit alpha-amylase and alpha-glucosidase, two enzymes involved in the breakdown of carbohydrates [75]. One research found that giving STZ-induced diabetic mice 200 mg/kg of *P. atlantica* extract orally every day for 15 days significantly lowered their blood sugar levels. These findings confirm the anti-hyperglycemic properties of *P. atlantica* and back up its conventional usage in the management of diabetes mellitus [76]. The month of harvest, sex, and growing site of *Pistacia atlantica* were examined in

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connection to the potential of the leaves to inhibit enzymes linked to type 2 diabetes (α-amylase and α-glucosidase) and hypertension (angiotensin-converting enzyme-I). Among the phenolic substances found in *P. atlantica* leaf extract are Gallotannin and hydroxybenzoic acids. These chemicals are believed to have antidiabetic and/or antihypertensive properties. This study revealed that the isolation and development of antidiabetic and hypertension medications have a rational foundation in P. atlantica leaf extract [77].

Diabetes wound healing

Among the complications of diabetes mellitus include metabolic syndrome and delayed healing of wounds. One frequent side effect of diabetes, diabetic foot ulcers afflict 2.5% of those with the condition annually [78,79]. In one study, the antioxidant properties of *Pistacia atlantica* resin oil significantly benefited diabetes rats. Also, higher levels of wound hydroxyproline and vascular endothelium growth factor (VEGF) showed that diabetic wounds had better collagen turnover and angiogenesis. Oil resin has been shown to be a safe, effective, and reasonably priced treatment for a range of wounds and skin disorders, including those brought on by diabetes [79]. *Pistacia atlantica* mastic's ability to promote wound healing and its impact on blood biochemical markers and oxidative stress were investigated. For twenty-one days, the treatment groups received daily applications of an oral solution and a topical cream made of mastic from *P. atlantica*. The results demonstrate that the *P. atlantica* mastic extract aids in the healing process of wounds [80]. Research on the back subcutaneous tissue of Wistar rats using a gel prepared from the essential oil of *Pistacia atlantica* Kurdica gum has shown its ability to eliminate bacteria, speed up the healing of skin wounds, and lower the quantity and levels of inflammatory cells. The experimental gel has excellent wound healing properties, making it suitable [81].

Cholesterol and Atherosclerosis

In recent years, human civilizations have moved away from cultivated foods and active lifestyles towards fast food and sedentary lifestyles as a result of widespread changes in people's behavior around the world [82]. An increase in smoking has led to an increase in cardiovascular disease. The rise in smoking associated with these diets has led to an increase in cardiovascular disease. The leading causes of death worldwide are heart disease and stroke, both of which are largely due to atherosclerosis [82]. Hyperlipidemia, particularly high levels of LDL in the blood, is the most common and significant contributor to the development of this condition [83].

As one of the five leading causes of death worldwide, hyperlipidemia is a major public health problem affecting people all over the world. The World Health Organization (WHO) estimates that 23.6 million people worldwide will suffer from cardiovascular disease by 2030 due to the increasing prevalence of hyperlipidemia [84]. Free radicals, hypertension, diabetes, genetic changes, hypercholesterolemia and even certain microbes such as herpes viruses and chlamydia all play a role in the development and progression of atherosclerosis, an inflammatory disease. Compounds that may be beneficial in more than one of these situations may be promising therapeutic agents for the treatment of atherosclerosis [82]. Medicinal plants continue to be used for the treatment of many diseases, including CVD. In modern medicine, herbal medicines are used to an unprecedented extent. The idea that they are safe and less expensive than modern drugs motivate this desire. Laboratory studies have shown that medicinal plants may interact with various CVD risk factors, making them potentially therapeutic [85]. One such plant is *Pistacia atlantica*.

The effects of *Pistacia atlantica* on Cholesterol and Atherosclerosis

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One study found that *Pistacia atlantica* extract dramatically increased HDL-C and decreased cholesterol, triglycerides and low-density lipoprotein (LDL-C) in a concentration-dependent manner [82]. In addition to lowering total lipid levels and triglycerides, natural mastic gum (*Pistacia lentiscus* var. chia) has been shown to absorb cholesterol, thereby reducing the risk of myocardial infarction and blood pressure [86]. Histological observations in a research study showed that *Pistacia terebinthus* L. effectively inhibited the progression of atherosclerosis in the thoracic artery and the occurrence of degenerative hydropic and fatty changes in the liver. The analysis of the biochemical data did not reveal any harmful effects associated with *P. terebinthus* L. The results of this research show that *P. terebinthus* L. has a hypolipidemic effect in rabbits with hypercholesterolemia [87]. Table 2 shows the therapeutic effects of *Pistacia atlantica* on diabetes and cholesterol.

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Table2: The therapeutic effects of *Pistacia atlantica* on Diabetes and cholesterol

The therapeutic effects of *Pistacia atlantica* on Diabetes and Cholesterol

Type of gum	Disease	on	Country	Dosage type	Health benefits	Reference
Pistacia atlantica subsp. kurdica	Diabetic and cholesterol	Mice	Iran	Orally	↓ Lipid profile ↓Inflammation process ↓Oxidative stress ↓ Lipid peroxidation ↑ Total antioxidant capacity	[73]
istacia atlantica	Oxidative Stress in Diabetic	Rats	Iran	Orally	↓ oxidative stress	[74]
Pistacia atlantica	wound healing (Diabetic)	Rats	Iran	topically (ointment) (Resin oil)	↑ wound healing	[79]
Pistacia atlantica	(Diabetic)	Mice	Iran	Orally (N-hexane extracts)	↓ blood glucose levels	[76]
Pistacia atlantica **Kurdica**	Wound healing	Rats	Iraq	implanted in tissue (Essential Oil extract)	↑ wound healing	[81]
Pistacia atlantica	Atherosclerosis	Rats	Iran	Orally (Aqueous Extract)	↓ Cholesterol ↓ TG ↓ LDL-C	[82]
Pistacia atlantica	Diabetes- Type2	Humans	Iraq/ Kurdistan	Orally Water-extract	↓ HbA1c ↓ FBS fasting blood sugar	[71]
Pistacia terebinthus L.	Atherosclerosis	Rabbit	Turkey	Orally	↓ TC ↓ TG ↓ VLDL ↓ LDL ↑HDL	[87]
Pistacia atlantica	ovary damage with diabetes	Rats	Iran	Orally (Hexane extract)	↓Ovarian problems caused by diabetes mellitus. ↓ Blood glucose	[88]

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Conclusion

Based on the aforementioned studies, it can be concluded that *Pistacia atlantica*, also known as wild pistachio or atlas mastic tree, has considerable potential in treating and managing various diseases that pose a threat to individuals' health in different countries worldwide. This is due to its notable antioxidant, antimicrobial, anti-inflammatory, and anticancer properties. Because *Pistacia atlantica* herb extracts have antioxidant properties, we suggest using them in the future to make nutritional supplements that improve overall health and strengthen the immune system. Also, we believe that the active chemicals in the plant *Pistacia atlantica* could serve as the foundation for developing new medicines to combat oxidative stress-related diseases such as cancer, heart disease, and neurological issues. Additionally, we believe that incorporating Pistacia atlantica herb extracts into the production process of wholesome and functional foods could enhance their nutritional value and health benefits. Nevertheless, more investigation is required to fully exploit its whole capabilities and define its definitive position in contemporary medicine

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Conflict interest

The author(s) declares no conflict of interest.

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اثرات سلامتی بخش گیاه *Pistacia Atlantica* مورد استفاده در موادغذایی: مروری

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چکیده

مطالعه حاضر مزایای بالقوه سلامتی و خواص درمانی *Pistacia atlantica*، گیاهی بومی شمال آفریقا و خاورمیانه را مورد بحث قرار می دهد. تحقیقات نشان می‌دهد که ترکیبات فیتوشیمیایی آن، از جمله فلاونوئیدها، ترکیبات فنلی و اسانس‌ها، دارای خواص آنتی‌اکسیدانی و ضدالتهابی است و به طور موثر شرایطی مانند بیماری‌های قلبی عروقی، دیابت و تخریب عصبی را درمان می‌کند. علاوه بر این، *P. atlantica* دارای خواص ضد باکتریایی قوی است که می تواند برای درمان بیماری های عفونی و بهبود زخم مورد استفاده قرار گیرد. مطالعات پیش بالینی همچنین فعالیت ضد توموری بالقوه را در انواع مختلف سلول های سرطانی نشان می دهد. با این حال، تحقیقات بیشتری برای درک کامل مزایای درمانی آن، بهبود روش‌های استخراج و اطمینان از ایمنی و اثربخشی آن در آزمایش‌های بالینی مورد نیاز است. این بررسی بر روی خواص دارویی، ترکیبات و مکانیسم‌های عمل *P. atlantica* تمرکز خواهد کرد، استفاده سنتی آن در پزشکی، اثرات آن بر بیماری‌های التهابی، خواص ضد باکتریایی، نویدبخش درمان سرطان، و پتانسیل برای درمان دیابت و سایر مسائل متابولیک است. هدف این بررسی درک جامع پتانسیل *P. atlantica* به عنوان یک عامل درمانی و شناسایی مناطق برای تحقیقات بیشتر است.

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