Chapter

Pistacia atlantica as Anti-Inflammatory Agent in Medicinal Uses

Chahrazad Bakka

Abstract

Pistacia atlantica, a plant native to the Mediterranean region, holds significant traditional medicinal value for various health conditions, notably those associated with inflammation. This study aims to review the existing literature regarding the anti-inflammatory properties of *P. atlantica* and discuss its potential as an alternative treatment option. An extensive search was conducted using PubMed, Scopus, Web of Science, and Google Scholar databases to identify relevant articles published up until January 2024. Articles were selected based on their relevance to the topic, quality, and credibility. *Pistacia atlantica* exhibits anti-inflammatory properties, as evidenced by its traditional use in treating conditions like stomach diseases, renal disorders, wounds, coughs, gastrointestinal disorders, and inflammatory diseases. Numerous scientific studies support these claims, demonstrating that *P. atlantica* possesses antioxidant, anti-inflammatory, and antimicrobial activities. Specifically, it has been observed to alleviate bowel inflammation, inhibit protein denaturation, and exert protective effects against oxidative stress. The strong correlation between the traditional uses of *P. atlantica* and its proven anti-inflammatory properties suggests that it may serve as an effective natural remedy for inflammatory conditions. However, additional research and clinical trials are required to fully understand its mechanism of action and optimize its therapeutic applications. By exploring the synergy between traditional knowledge and contemporary pharmacological understanding, we hope to contribute to the development of novel treatments for inflammatory diseases.

Keywords: *Pistacia atlantica*, anti-inflammatory, traditional medicinal, medicinal uses, pharmaceutical effect

1. Introduction

Belonging to the Anacardiaceae family, the *Pistacia* genus includes numerous species, with *Pistacia atlantica* being a prominent one known for its rich history in traditional medicine. This species is widely distributed across the Mediterranean and Middle Eastern regions alongside other notable species like *P. vera*, *P. terebinthus*, *P. khinjuk*, and *P. lentiscus*. Iran stands out as a significant producer of *Pistacia* spp., with a cultivation history spanning thousands of years and diverse culinary and medicinal applications for this herb. Wild pistachio (*P. atlantica*) is particularly economically

important in Iran and can also be found in countries such as Pakistan, Greece, Turkey, and North Africa [1, 2].

Plants have played a significant role in traditional medicine for centuries, offering remedies for a wide range of health issues. Medicinal herbs have been utilized to alleviate pain and address various ailments throughout history. One such plant, *Pistacia atlantica*, has gained recognition for its potential as an anti-inflammatory agent, drawing from both traditional uses and scientific research. The traditional medicinal applications of *Pistacia atlantica* are diverse, encompassing treatments for stomach diseases, renal disorders, wounds, coughs, gastrointestinal issues, and inflammatory conditions [3, 4].

Pistacia atlantica is recognized for its diverse medicinal properties, including antioxidant, antidiabetic, antihyperlipidemic, antimicrobial, antiviral, antitumoral, gastroduodenal protective, diuretic, emmenagogue, wound healing, and analgesic effects [5, 6]. These therapeutic actions are attributed to the active compounds present in *Pistacia atlantica* that interact with biological systems through mechanisms such as modulating inflammatory responses, reducing oxidative stress, regulating glucose metabolism, lowering lipid levels, enhancing immune functions, and promoting cellular regeneration during wound healing [7–11].

In this research, we highlighted the study of research reports on the uses of the plant *Pistacia atlantica* as an anti-inflammatory in popular uses, as well as the scientific research carried out. As evidenced by its rich history of traditional usage and extensive scientific validation, *Pistacia atlantica* presents a compelling opportunity for advancing innovative therapies aimed at addressing a broad spectrum of diseases and conditions. Future research endeavors must concentrate on refining extraction techniques, discovering novel bioactive compounds, and examining synergistic interactions among these compounds to fully realize the therapeutic potential of *Pistacia atlantica*.

2. *Pistacia atlantica* Desf. as anti-inflammatory agent

2.1 Medicinal uses of *P. atlantica* in folk medicine

In Persian, *Pistacia atlantica* is known as *Baneh*. In English, it is commonly referred to as the *Mt. Atlas* mastic tree. In Arabic, it is called *Butm*, and in the Canary Islands, it is known as *Almacigo*. The resin of wild pistachio, called *Saqez*, is used for various industrial and traditional purposes. *Vanoshak* is the name of the fruit of the tree that has a thin green shell with a hard rind and a nutritious marrow [12].

Atlantic pistachios are traditionally used in Persian medicine to treat various conditions such as pain, discomfort in the upper abdomen, indigestion, and peptic ulcers [13]. It is also used topically for joint pain and in treating diseases related to cancer, digestive system disorders, wounds, and injuries that are difficult to treat [13]. Additionally, research suggests that Atlantic pistachios have antioxidant properties and may be beneficial for preventing or treating inflammatory bowel disease [14].

Kidney tonic and aphrodisiac: In Iranian folk medicine, *Pistacia atlantica* (also known as Anjir) is traditionally used to treat kidney stones and improve overall renal function. It is also believed to enhance sexual performance [15].

Dermatological benefits: This plant has long been utilized for skin conditions such as wounds, scabies, lip fissures, and hair loss. Its use in wound healing is supported by modern scientific research [15].

Miscellaneous: Resins derived from *Pistacia atlantica* are employed as a gum tissue strengthener and for bone fracture treatment. The fruit is applied topically for back pain relief due to its analgesic properties [15].

2.2 Biological effect as anti-inflammatory agent

Several studies have investigated the anti-inflammatory activities of *P. atlantica*. A methanolic extract from *Pistacia atlantica* Desf. leaves demonstrate anti-inflammatory activity, confirmed through experiments involving the reduction of carrageenan-induced hind paw edema in mice [16]. Flavonoid compounds within the extract contribute to its anti-inflammatory effects [17]. Additionally, studies have reported the presence of anti-inflammatory activities when evaluating the unripe fruit extracts of *Pistacia atlantica* [17], indicating that multiple plant components possess anti-inflammatory properties.

Bakka et al. [18] evaluated the phytochemical screening and *in vitro* anti-inflammatory activities of *Pistacia atlantica* Desf. extracts through protein denaturation inhibition by egg albumin and bovine serum method. The plant, belonging to the Anacardiaceae family, has been traditionally used for various medicinal purposes such as anti-inflammatory effects. The leaves and fruits were macerated and extracted with chloroform, ethyl acetate, and n-butanol. The extracts showed significant anti-inflammatory activity *in vitro*, suggesting their potential as a potent anti-inflammatory agent for various applications.

Moreover, other studies have highlighted the anti-inflammatory properties of *Pistacia atlantica*. The unripe fruit extracts of *Pistacia atlantica* demonstrated significant anti-inflammatory activities *in vitro*, along with antioxidant, antibacterial, and enzyme inhibitory activities. These findings suggest that *Pistacia atlantica* extracts have the potential to be utilized as a natural remedy for various physiological diseases [17].

The leaf buds of *Pistacia atlantica* exhibit high anti-inflammatory properties, among other bioactivities. Studies have demonstrated that the leaf-bud extract significantly reduces carrageenan-induced hind paw edema in mice, confirming its anti-inflammatory action [19]. Additionally, the plant samples show effective antioxidant activity, with low EC50 values for 2,2-diphenyl 1-picrylhydrazyl (DPPH), total antioxidant capacity (TAC), and reduced power tests. These findings highlight the potential of *Pistacia atlantica* leaf-bud extracts as a valuable source of bioactive molecules with multiple pharmaceutical benefits [19].

The aqueous extract of *Pistacia atlantica* Desf. from Morocco demonstrates *in vivo* analgesic and anti-inflammatory properties. The study conducted by Ghizlane Hajjaj and colleagues revealed that the aqueous extract reduced carrageenan-induced paw edema in mice and displayed analgesic activity in animal models [20]. These findings support the traditional use of *Pistacia atlantica* in the treatment of pain and inflammation. Other research also confirms the anti-inflammatory and analgesic effects of *Pistacia atlantica* extracts, further validating its potential as a natural therapeutic option [18–20].

The essential oil extracted from galls formed on the leaves of *Pistacia atlantica* Desf. exhibits new *in vitro* and *in silico* studies demonstrating anti-inflammatory activities. This essential oil has shown promising anti-inflammatory properties in various studies, indicating its potential therapeutic value in managing inflammation [21]. Additionally, the methanolic extract from *Pistacia atlantica* Desf. leaves have been reported to possess anti-inflammatory and antioxidant activities, further supporting the plant's potential as a source of bioactive compounds with anti-inflammatory

properties [21]. These findings highlight the diverse pharmacological benefits of *Pistacia atlantica* and its potential applications in inflammatory conditions.

Research on the inflammation-lowering property of *Pistacia atlantica* in cotton pellet granuloma involves testing various doses (100, 200, 400, and 600 mg/kg body weight) in Swiss albino rats. The study assesses the anti-inflammatory potential of *Pistacia atlantica* through its effects on cotton pellet-induced granuloma formation. The results indicate that all tested doses of *Pistacia atlantica* significantly reduce inflammatory exudates and granuloma mass formations compared to the control group [21]. This research provides valuable insights into the anti-inflammatory properties of *Pistacia atlantica*, suggesting its potential as a natural remedy for inflammation-related conditions.

The combination of *Pistacia atlantica* oleo-gum-resin and honey has shown a protective effect in an experimental model of acetic acid-induced colitis in rats. The formulation containing *Pistacia atlantica* oleo-gum-resin and honey reduced inflammation of the bowel and colonic ulcer severity, as evidenced by the downregulation of inflammatory markers [22]. This study suggests that the combination of *Pistacia atlantica* oleo-gum-resin and honey could be a potential therapeutic option for colitis, offering physiological and pathological improvements in a rat model. The anti-inflammatory effect of *Pistacia atlantica* subsp. *kurdica* volatile oil and gum on acetic acid-induced acute colitis in rats has been studied. The research shows that oral administration of *Pistacia atlantica* subsp. kurdica volatile oil and gum improve colitis symptoms in rats. Specifically, the study highlights the protective effect of oral administration of essential oil derived from *Pistacia atlantica* gum on ulcerative colitis in rats. However, unlike the oral form of gum, its rectal administration did not prove to be significantly effective in improving colitis [23]. This research supports the idea that *Pistacia atlantica* subsp. *kurdica* contains active components capable of modulating inflammation in the context of colitis, providing evidence for the potential use of this species in the management of inflammatory bowel disorders. The healing effect of *Pistacia atlantica* fruit oil extract in acetic acid-induced colitis in rats has been investigated. The study demonstrates that the administration of *Pistacia atlantica* fruit oil extract exhibits a significant healing effect on acetic acid-induced colitis in rats. The extract effectively reduces inflammation, promotes tissue repair, and improves colonic damage caused by acetic acid. These findings suggest that *Pistacia atlantica* fruit oil extract may have therapeutic potential in the treatment of colitis and related inflammatory conditions [14].

The evaluation of the effect of a topical gel form of *Pistacia atlantica* on induced oral mucositis in male golden hamsters has shown promising results. The study assessed the stereological, anti-inflammatory, and antioxidant markers of a hydro-alcoholic extract of *Pistacia atlantica* leaves and their combination on induced oral mucositis in hamsters. The findings suggest that the mixture of *Pistacia atlantica* could be effective in the treatment of oral mucositis, indicating its potential therapeutic value in managing this inflammatory condition [24].

The study on the healing effect of *Pistacia atlantica* as a remedy for induced oral mucositis in male golden hamsters has shown promising results. The research evaluated the effects of a mixed gel containing 10% *Pistacia atlantica* and 10% *Hypericum perforatum* on induced oral mucositis in male golden hamsters. The findings suggest that this combination could serve as a healing accelerator remedy for oral mucositis, indicating its potential therapeutic value in managing this inflammatory condition [25]. Moreover, research has shown that the methanolic extract from *Pistacia atlantica* leaves possesses anti-inflammatory activity. Additionally, the fruit oil of *Pistacia*

atlantica has been found to alleviate inflammation and facilitate wound healing. These findings support the traditional uses of *Pistacia atlantica* in treating inflammation.

The investigation of *Pistacia atlantica* subsp. *kurdica*'s anti-inflammatory activities focused on evaluating the effects of various fractions of baneh gum and volatile oil in an experimental rat model of ulcerative colitis. The results revealed the following: Constituents analysis: Alpha-pinene was identified as the primary component of baneh volatile oil, accounting for approximately 41.23%.

Treatment efficacy: Both oral gum and volatile oil reduced all indices of colitis and myeloperoxidase activity when administered at appropriate doses (100, 200, and 400 mg/kg for gum; 100, 200, and 400 μL/kg for volatile oil).

Route comparison: While oral administration of gum displayed significant improvements in colitis, rectal application did not show similar effectiveness.

Comparison with reference drugs: The anti-inflammatory effects of baneh gum and volatile oil were comparable to those of oral prednisolone and hydrocortisone enema [23].

Pistachio oil has been recognized for its anti-inflammatory properties due to its composition of linoleic acid, oleic acid, and stearic acid. These major components have shown significant wound healing and anti-inflammatory effects when applied to oil-absorbed bacterial cellulose in a burn wound model. This oil has the potential to serve as a safe and effective dressing for wound management. Furthermore, *P. atlantica* fruit oil has demonstrated promise in treating ulcerative colitis, with studies indicating that high doses of the oil can reduce colonic injury by mitigating oxidative damage in rats through oral and rectal administration.

Research suggests that wild pistachio oil may also play a role in modulating hypothyroidism, impacting serum lipid profiles and leptin concentrations. In a study conducted by Hamidi et al. in 2017, the topical application of gel formulations containing 5 and 10% *P. atlantica* oil showed positive effects on cutaneous wound healing in rat models. The results revealed enhanced re-epithelialization, formation of mature granulation tissue, and the presence of adnexa such as hair follicles and sweat glands with the use of Atlas pistachio oil gels, particularly the Bene 10% formulation, at 21 days post-injury. Interestingly, rural populations have long utilized fixed oils extracted from Atlas pistachio fruits for managing conditions like rheumatoid arthritis and joint pain. The oil is commonly applied directly to the affected area with a gentle massage to enhance absorption and promote relief [26].

2.3 Relation between pharmacological and folk medicine uses of *P. atlantica* as anti-inflammatory agent

The relationship between traditional uses and pharmacological effects of *Pistacia atlantica* regarding inflammation can be elaborated upon using the following studies.

2.3.1 Wound healing properties

According to traditional medicine [5], *Pistacia atlantica* is used for wound inflammation. A recent study confirmed the *in vivo* effect of *Pistacia atlantica* hulls extract, showing improved wound healing. The experimental evidence supporting the wound-healing properties of *P. atlantica* comes primarily from the following sources:

Hydromethanolic *P. atlantica* hulls extract: A study demonstrated the improvement of wound healing when treated with hydromethanolic *P. atlantica* hulls extract. Histopathological examination revealed enhanced collagen deposition and reduced

inflammation in wounded rats receiving *Pistacia atlantica* hulls extract compared to control animals. The mechanism underlying the wound healing effect may involve increased expression of transforming growth factor beta (TGF-β), fibronectin, and type III procollagen, leading to accelerated granulation tissue formation.

2.3.2 Anti-inflammatory activities of leaves

Pistacia atlantica leaves have been identified to possess anti-inflammatory properties [16]. Studies have shown that the methanolic extract derived from *Pistacia atlantica* leaves exhibits significant anti-inflammatory effects. Histopathological studies revealed a notable reduction in lymphocyte infiltration in groups treated with *Pistacia atlantica* leaf hydroethanolic extract, indicating its anti-inflammatory potential. The leaf hydroethanolic extract of *Pistacia atlantica* demonstrated protective effects against gentamicin-induced nephrotoxicity, further supporting its anti-inflammatory properties. The anti-inflammatory effects of *Pistacia atlantica* leaf extract might be attributed to its ability to suppress the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α). The extract may also help regulate the balance between pro-inflammatory and anti-inflammatory molecules, thereby preventing excessive immune responses.

2.3.3 Effect against ulcerative colitis

Pistacia atlantica volatile oil and gum demonstrate therapeutic effects in reducing colitis indices and myeloperoxidase activity [27]. Studies have demonstrated the therapeutic effects of *Pistacia atlantica* volatile oil and gum in reducing colitis indices and myeloperoxidase activity, particularly in the context of ulcerative colitis. The main constituent, alpha-pinene, found in baneh volatile oil, contributes significantly to its anti-inflammatory effects. Research has shown that oral gum and volatile oil of *Pistacia atlantica* subsp. *kurdica* possess anti-inflammatory potential and can reduce colitis indices in experimentally induced colitis in rats. Both oral and rectal administration of *Pistacia atlantica* fruit oil extract has been shown to alleviate bowel inflammation in acetic acid-induced colitis in rats, indicating its potential therapeutic efficacy. The anti-colitis potential of *Pistacia atlantica* is attributed to its ability to inhibit pro-inflammatory cytokines and reduce oxidative stress markers, thereby alleviating colonic injury and inflammation. The essential oil of *Pistacia atlantica* gum exerts its protective effects by modulating inflammatory responses and suppressing the activity of COX-2, a key enzyme involved in inflammation.

2.3.4 Additional medicinal properties

Pistacia atlantica exhibits significant anti-inflammatory effects, as supported by various studies [23]. Anti-inflammatory Effect on Acetic Acid-Induced Colitis: Research has demonstrated the anti-inflammatory potential of *Pistacia atlantica* subsp. *kurdica* volatile oil and gum in treating acetic acid-induced acute colitis in rats. The oral administration of essential oil of *Pistacia atlantica* gum has been shown to protect against ulcerative colitis in rats by inhibiting pro-inflammatory processes. The methanolic extract from *Pistacia atlantica* leaves has also been reported to exhibit strong anti-inflammatory activity, making it a promising candidate for the development of new anti-inflammatory treatments. The anti-inflammatory effects of *Pistacia*

atlantica may be attributed to its ability to modulate inflammatory responses, inhibit pro-inflammatory cytokines, and reduce oxidative stress markers, thereby mitigating inflammation and tissue damage.

These findings confirm that traditional knowledge concerning the use of *Pistacia atlantica* for managing inflammation is validated by contemporary scientific research. As a result, there is great potential for developing novel therapies using *Pistacia atlantica* derivatives for the treatment of inflammatory diseases. The bioactive compounds detected in *Pistacia atlantica* have been linked to its anti-inflammatory activities. Research has shown that extracts from various parts of *Pistacia atlantica*, including leaves, fruits, and oil, exhibit significant anti-inflammatory properties. These bioactive compounds play a crucial role in modulating inflammatory responses, thereby contributing to the plant's therapeutic effects. Studies have highlighted the presence of secondary metabolites in *Pistacia atlantica*, such as phenylethanoid glycosides, which are believed to be responsible for their anti-inflammatory, antimicrobial, analgesic, and other pharmacological properties. Furthermore, the essential oil derived from *Pistacia atlantica* has been found to possess potent sedative and anti-inflammatory properties in animal models, further supporting its traditional use for inflammatory conditions. The correlation between the bioactive compounds in *Pistacia atlantica* and its anti-inflammatory activities underscores the plant's potential as a natural remedy for managing inflammatory diseases.

3. Conclusion

Based on the research findings on *Pistacia atlantica* Desf. as an anti-inflammatory agent, the conclusion can be drawn that *Pistacia atlantica* exhibits significant anti-inflammatory properties supported by traditional medicinal uses and modern scientific research. Studies have shown that extracts from various parts of *Pistacia atlantica*, including leaves, fruits, and oil, possess potent anti-inflammatory effects. The bioactive compounds present in *Pistacia atlantica* play a crucial role in modulating inflammatory responses, making it a promising candidate for the development of new anti-inflammatory treatments. The correlation between traditional knowledge and pharmacological evidence confirms the plant's potential as a natural remedy for managing inflammatory conditions. Overall, *Pistacia atlantica* shows great promise as an effective anti-inflammatory agent with diverse medicinal applications.

Author details

Chahrazad Bakka
Laboratory of Valorization and Promotion of Sahreinne Resources (VPRS), Faculty of Mathematics and Material Science, Department of Chemistry, Kasdi Merbah University, Ouargla, Algeria

*Address all correspondence to: bakkachahrazad@gmail.com

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