

# *Pistacia atlantica* as an Alternative Source for Anti-Inflammatory Drugs

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## Executive Summary

Inflammation is a natural immune system response characterized by increased blood flow and vascular permeability. In this study, 50 mice were divided into 5 groups, and after inducing inflammation, the levels of inflammatory and anti-inflammatory cytokines, antioxidant enzymes, and oxidative stress were measured. The results showed that the gum extract of the *Pistacia atlantica* significantly reduced the levels of inflammatory cytokines and oxidative stress while increasing the levels of antioxidant enzymes and anti-inflammatory cytokines. Therefore, the gum extract of the *Pistacia atlantica* plant may be considered as a natural compound with anti-inflammatory properties for the treatment of immunological disorders caused by inflammation.

**Keywords:** Inflammation, Cytokines, Antioxidant enzymes, Oxidative stress, *Pistacia atlantica*

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## Introduction

Inflammation is a natural immune response that occurs to combat pathogens and is characterized by increased blood flow and vascular permeability, leading to the accumulation of fluid, leukocytes, and inflammatory mediators like cytokines.<sup>1</sup> Inflammatory triggers can be microbial (bacteria, viruses, fungi), chemical (allergens, etc.), or physical (heat, ionizing radiation, ultraviolet rays, etc.). Inflammation may also arise from autoimmune reactions in the body, such as in rheumatoid arthritis. The body attempts to eliminate harmful agents and repair damage through inflammation.<sup>2</sup> The plant known as "Saquez," scientifically named *Pistacia atlantica kurdica*, is one of these plants. It has 11 species and is widely found in the mountainous regions of Zagros, particularly in the northwest and western parts of Iran.<sup>3</sup> In one study, a chemical analysis of the essential oil from the subspecies *kurdica* revealed that the resin oil contains compounds such as alpha-pinene, alpha-terpineol, sabinene, limonene, and beta-pinene.<sup>4</sup> Pharmacologically, the plant has antioxidant effects, antimicrobial activity, and effects on digestive

disorders, among others. The aerial parts of the plant are used in veterinary medicine, while the resin and gum of the plant are used to treat gastrointestinal ulcers, in mouthwashes to freshen breath, as an appetite stimulant, laxative, disinfectant, diuretic, for inflammation and disorders related to the kidneys and digestive system, and in the treatment of motion sickness.<sup>5</sup> The aim of the present study is to investigate the effects of the oil extract of the gum of the *Pistacia atlantica* plant on inflammation induced by carrageenan in the Balb/c mouse model.

## Materials and Methods

In this study, the extraction of the resin from the Benneh plant was conducted from the Benneh trees in the Kurdistan region. To investigate the effects of this extract, male Balb/c mice were kept under standard conditions of water, food, temperature, and adequate light. These mice were divided into several groups: The first group, as a positive control, received a solution injected into their paw, while another solution was injected into the opposite paw. The

second group received the oil extract of the Benneh resin orally for a period prior to inducing inflammation. The third group received the extract via intraperitoneal injection during the same time period. The fourth and fifth groups received the extract orally and via intraperitoneal injection, respectively, simultaneously with the induction of inflammation. To induce inflammation, a solution was injected into the paws of the mice, and another solution was injected into the opposite paw. After some time, the mice were anesthetized, and the weights of their paws were measured to calculate the percentage increase in weight of the injected paw compared to the opposite paw. Blood samples were then collected from the heart and sent to the laboratory for biochemical analysis. Additionally, the spleens of the mice were removed under sterile conditions to prepare a cell suspension, which was combined with a culture medium. Finally, the levels of cytokines and liver enzymes were assessed using commercial kits. These procedures were designed to evaluate the effects of the Benneh resin extract on inflammation induced by carrageenan.

## Results

In this study, the compounds present in the resin extract of the Bene plant were analyzed, identifying alpha-pinene as the main component. The toxic dose of the extract was determined. The results showed that the extract significantly reduced paw inflammation and inflammatory cytokines such as IL-1, TNF- $\alpha$ , and IL-17, while having no effect on IL-6 and IFN- $\gamma$ . Additionally, the extract increased the anti-inflammatory cytokines IL-4 and IL-10 and was effective in reducing oxidative stress biomarkers and increasing antioxidant enzymes. However, the extract had a negative impact on liver enzymes in the peritoneal groups prior to inflammation induction.

## Discussion and Conclusion

Bene resin is a traditional medicinal source used for relieving abdominal pain, stomach pain, indigestion, and gastric ulcers, as well as for treating asthma, eczema, throat infections, kidney stones, diarrhea, and as an astringent. It is also known for its antipyretic, antibacterial, and antiviral properties.<sup>6</sup> The essential oil of Bene resin contains important compounds such as alpha-pinene, beta-pinene, and trans-verbenol. Studies have been conducted to determine the antioxidant and antimicrobial activities of some Bene species. Given recent concerns about environmental pollution from synthetic packaging waste and the consumption of food containing natural compounds, the significance of producing and using films made from renewable biopolymers containing active compounds has been highlighted.<sup>7</sup> The aim of the present

study was to investigate the effects of the oil extract of Bene resin on inflammation induced by carrageenan in the Balb/c mouse model. The results of this study indicated that the Bene resin extract could significantly reduce the levels of inflammatory cytokines and oxidative stress compared to the control group. Additionally, the results showed that the Bene extract increased the levels of antioxidant enzymes and anti-inflammatory cytokines.

In 2020, Esmaili and colleagues conducted a study titled Investigating the Effects of Bene Resin on Immune Response Levels. In this study, mice were immunized twice with SRBC antigen at one-week intervals, and then the levels of humoral and cellular immune responses were measured. The results showed that the aqueous extract of Bene resin modulated the humoral and cellular immune responses in Balb/c mice following immunization with SRBC.<sup>8</sup> In 2014, Feng and colleagues reported the anti-inflammatory effects of other compounds present in mastic, such as carvacrol. This extract, at doses of 20-80 mg/kg in an animal model, reduced acute lung inflammation induced by LPS in mice by decreasing TNF- $\alpha$ , IL-6, and IL-1 $\beta$  levels.<sup>9</sup> In 2019, Shakarami and colleagues conducted a study titled Investigating the Therapeutic Effects of Bene Resin Extract on Inflammatory Responses in an Experimental Asthma Model. After inducing the disease using ovalbumin antigen, they treated the mice with various concentrations of Bene resin extract. The results showed that the aqueous extract of Bene resin modulated immune responses by reducing inflammatory cytokines in mice with experimental asthma.<sup>10</sup> Based on the findings of the present study, it is suggested that this extract could be an effective natural product for anti-inflammatory properties, which requires further investigation in clinical settings such as randomized controlled trials to assess its therapeutic potential and toxicity, and consequently its suitability for treating diseases with an underlying inflammatory cause.

## Conflicts of Interest Disclosures

The author declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Consent For Publication

Not applicable

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