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DERLEME / REVIEW

Mad Honey and Its Possible Biological Mechanisms in Alleviating Chronic Obstructive Pulmonary Disease

Deli Bal ve Kronik Obstrüktif Akciğer Hastalığını Yatıştırmada Yardımcı Olabilecek Potansiyel Mekanizmaları

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease is a progressive respiratory condition characterized by airflow limitation, chronic inflammation, and structural damage in the lungs The disease is primarily caused by long-term exposure to irritants, particularly cigarette smoke and, leading to airway remodeling, fibrosis, and oxidative stress. Although, current treatments help manage symptoms, they do not offer a definitive cure, and the morbidity and mortality rates are still high with very significant healthcare costs. Therefore, there is growing interest in alternative and natural remedies that may complement conventional therapies. One such substance is mad honey a rare and potent type of honey derived from the nectar of Rhododendron species, particularly Rhododendron ponticum and Rhododendron luteum.

Conclusion: In this commentary, we explore the possible mechanisms, by which mad honey could alleviate Chronic Obstructive Pulmonary Disease symptoms and improve lung function,considering different molecular and biological aspects.

Keywords: Chronic obstructive pulmonary disease, mad honey, rhododendron, inflammation

ÖZ

Giriş: Kronik Obstrüktif Akciğer Hastalığı nefes darlığı, kronik enflamasyon ve akciğerlerde yapısal hasar ile kendini gösteren ilerleyici bir hastalıktır. Hastalığa, hava yolu yeniden şekillenmesi, fibröz ve oksidatif strese yol açan, özellikle sigara dumanı ve çevresel kirleticiler gibi irritan maddelere uzun-süreli maruziyet sebep olmaktadır. Güncel tedaviler semptomları yönetmeye yardımcı olsa da kesin bir tedavi sağlamamakta ve çok ciddi sağlık masraflarıyla birlikte, morbidite ve mortalite oranları hâlâ oldukça yüksek seyretmektedir. Bu sebepten, güncel tedavilere eşlik eden alternatif ve doğal tedavilere olan ilgi her geçen gün artmaktadır. Bunlara örnek olarak ender bulunan ve Rhododendron türlerinden, özellikle Rhododendron ponticum ve Rhododendron luteum, elde edilen 'Deli Bal' verilebilir.

Sonuç: Bu tartışmada, Deli Bal'ın Kronik Obstrüktif Akciğer Hastalığı semptomlarını yatıştırma ve akciğer fonksiyonlarını geliştirmede yardımcı olma potansiyeli taşıyan mekanizmalar, farklı moleküler ve biyolojik mekanizmalar göz önünde bulundurularak incelenmiştir.

Anahtar Sözcükler: Kronik obstrüktif akciğer hastalığı, deli bal, rhododendron, inflamasyon

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by airflow limitation, chronic inflammation, and structural damage in the lungs (1–5). It includes chronic bronchitis and emphysema, with symptoms such as persistent cough, excessive mucus production, wheezing, and shortness of breath. The disease is primarily caused by long-term exposure to irritants, particularly cigarette smoke and environmental pollutants, leading to airway remodeling, fibrosis, and oxidative stress (2–4).

While current treatments, including bronchodilators, corticosteroids, and mucolytic agents, help manage symptoms, they do not offer a definitive cure. As a result, there is growing interest in alternative and natural remedies that may complement conventional therapies. One such substance is mad honey, a rare and potent type of honey derived from the nectar of

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Rhododendron species, particularly Rhododendron ponticum and Rhododendron luteum (6–8). This unique honey contains grayanotoxins, which interact with ion channels in the body, producing physiological effects that range from mild euphoria to serious neurotoxicity (6–9).

Despite its toxicity at high doses, mad honey has been traditionally used for its medicinal properties, including its anti-inflammatory, bronchodilatory, and analgesic effects. Recent studies suggest that mad honey's bioactive compounds might offer potential benefits for COPD patients by reducing inflammation, relaxing airway muscles, and modulating immune responses. This commentary explores the possible biological mechanisms by which mad honey could alleviate COPD symptoms and improve lung function.

Anti-Inflammatory Effects in Copd Management

Chronic Obstructive Pulmonary Disease and Chronic Inflammation

Chronic obstructive pulmonary disease is characterized by chronic airway inflammation, primarily driven by the overactivation of immune cells such as neutrophils, macrophages, and T-lymphocytes (2–4). This results in excessive production of inflammatory cytokines like tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8), which perpetuate tissue damage and airway remodeling (2–5).

Mad Honey's Anti-Inflammatory Properties

Mad honey contains polyphenols, flavonoids (e.g., quercetin, kaempferol), and diterpenes, which have been shown to exhibit potent anti-inflammatory effects (9,10).

Inhibit Pro-Inflammatory Cytokines: Studies suggest that flavonoids can suppress the activation of NF-κB, a transcription factor that regulates inflammatory cytokine production in COPD (10,11). By inhibiting NF-κB, mad honey may help reduce airway inflammation and tissue damage (9–11).

Modulate Oxidative Stress: COPD is associated with increased oxidative stress (2), which exacerbates lung injury. Polyphenols in mad honey act as antioxidants, scavenging reactive oxygen species (ROS) and protecting lung cells from oxidative damage (9,10).

Reduce Airway Hyperresponsiveness: Chronic inflammation in COPD leads to excessive airway narrowing and bronchial hyperreactivity (2–4). The anti-inflammatory properties of mad honey may help reduce airway sensitivity, leading to improved breathing (10,11).

Bronchodilatory and Smooth Muscle Relaxation Effects

Chronic Obstructive Pulmonary Disease and Airway Constriction

Airway narrowing due to bronchoconstriction, mucus hypersecretion, and structural remodeling is a major problem in COPD, leading to persistent breathing difficulties (1–5). Conventional bronchodilators, such as β2-agonists and anticholinergics, help relax airway smooth muscles, but they often have side effects, including increased heart rate and tremors (12).

Mad Honey's Effects on Smooth Muscle Relaxation

One of the most intriguing aspects of mad honey is its neuromodulatory effects via grayanotoxins. These toxins interact with voltage-gated sodium channels (VGSCs) in excitable tissues, leading to altered neuronal signaling and muscle relaxation (9,13).

Bronchodilation mechanism

Grayanotoxins cause sustained depolarization of airway smooth muscle cells (9,13), which may lead to calcium channel modulation and relaxation of bronchial muscles.

This mechanism is similar to how some bronchodilators work by reducing muscle contractility and improving airflow (14).

As a result, mad honey could act as a natural bronchodilator, helping COPD patients breathe more easily.

Reduced cough sensitivity

Persistent coughing in COPD results from airway irritation and hyperresponsiveness (1,2).

The neural desensitization effects of grayanotoxins might modulate vagal nerve activity, reducing cough frequency and severity.

These effects suggest that mad honey could be useful as a natural adjunct therapy for COPD patients struggling with airway constriction and persistent coughing.

Mucolytic And Expectorant Properties

Excess Mucus Production in COPD

One of the defining characteristics of chronic bronchitis, a major subtype of COPD, is excessive mucus secretion due to goblet cell hyperplasia. This leads to airway obstruction, bacterial infections, and increased disease exacerbations (5,15).

Mad Honey's Potential Role in Mucus Clearance

Hydration and enzymatic activity

Like regular honey, mad honey has hygroscopic properties (attracting water), which may help loosen thick mucus.

Honey contains enzymes such as glucose oxidase, which generate small amounts of hydrogen peroxide (11), exhibiting mild mucolytic effects.

Ciliary function enhancement

Proper ciliary movement is essential for clearing mucus from the airways (5).

Polyphenols in mad honey may stimulate ciliary motility, aiding in mucus clearance and preventing bacterial accumulation.

These mucolytic and expectorant properties suggest that mad honey could help COPD patients manage excessive mucus production, reducing airway obstruction and infection risk.

Immunomodulatory Effects: Balancing the Immune Response

Immune Dysregulation in COPD

Chronic obstructive pulmonary disease patients experience chronic immune activation, often leading to excessive neutrophilic inflammation and a weakened antiviral response. This imbalance increases susceptibility to respiratory infections, which worsen COPD symptoms (1,3).

Immunomodulatory Mechanisms of Mad Honey

Neutrophil regulation

Flavonoids in mad honey have been shown to reduce neutrophil infiltration into the airways, decreasing excessive inflammation (16).

This could help prevent further lung tissue damage.

Antimicrobial properties

Mad honey exhibits broad-spectrum antimicrobial effects, potentially reducing secondary bacterial infections in COPD patients.

The presence of hydrogen peroxide and other bioactive compounds may inhibit bacterial growth, particularly pathogens like Haemophilus influenzae and Pseudomonas aeruginosa, which commonly infect COPD patients.

Modulation of adaptive immunity

By influencing the balance of Th1 and Th2 responses, mad honey may help control excessive immune reactions while preserving the body's ability to fight infections (17).

These findings suggest that mad honey could support COPD patients by reducing excessive inflammation while enhancing antimicrobial defenses.

Neurophysiological and Analgesic Effects

COPD-Associated Pain and Discomfort

Many COPD patients suffer from chronic chest discomfort, muscle fatigue, and anxiety due to breathing difficulties (18,19). Traditional painkillers may not always be suitable due to their side effects.

Mad Honey's Role in Pain Relief

Neural modulation

Grayanotoxins interact with the nervous system, leading to temporary neural desensitization (9,13).

This could help alleviate chest tightness and respiratory discomfort associated with COPD.

Mild sedation and anxiety reduction

Many COPD patients experience anxiety and breathlessness-related panic episodes (19).

The psychoactive properties of mad honey may promote mild euphoria and relaxation, reducing anxiety and improving sleep quality.

Safety Considerations and Risks

Despite its potential benefits, mad honey comes with toxicity risks. Excessive consumption can cause nausea, vomiting, dizziness, hypotension, and even cardiac arrhythmias (6–8).

Safe dosage: Low and controlled doses are essential.

Contraindications: Individuals with heart disease, hypotension, or neurological disorders should avoid mad honey.

Medical supervision: COPD patients should consult healthcare professionals before using mad honey as a complementary therapy.

Conclusion

Mad honey holds promise as a natural adjunct therapy for COPD, thanks to its anti-inflammatory, bronchodilatory, mucolytic, immune-modulating, and analgesic properties. While preliminary evidence suggests potential benefits, clinical studies are needed to determine safe dosages and efficacy. If used correctly, mad honey could provide symptomatic relief and improved lung function, offering a complementary approach to COPD management.

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