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Antioxidant and Anti-Inflammatory Properties of Manuka Honey in Metabolic Health

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Abstract: Metabolic disorders such as obesity, type 2 diabetes, and cardiovascular diseases have become global public health crises, worsened by chronic inflammation. Manuka honey, a functional food originated from New Zealand's Leptospermum scoparium, is well-known for its unique bioactive components including methylglyoxal, polyphenolic compounds, and leptosperin, which show antioxidant, anti-inflammatory, and metabolic regulatory properties. Preclinical studies demonstrate its efficacy in reducing weight gain, improving insulin sensitivity, lowering fasting blood glucose, and protecting vascular health in animal models of metabolic dysfunction. Clinical evidence, though primarily focused on wound healing and oral inflammation, also supports its anti-inflammatory and tissue-repair capabilities. Despite its promising bioactive properties, targeted research on Manuka honey's effects on metabolic health remains limited. This paper systematically analyses current evidence on Manuka honey's bioactive components and their mechanisms of functions, focusing on the removal of antioxidant free radical and suppression of pro-inflammatory pathways.

Keywords: Manuka honey; metabolic health; methylglyoxal

1. Introduction

Metabolic health is now a global public health priority, as metabolic disorders such as obesity, type 2 diabetes, and insulin resistance reached epidemic proportions. The World Health Organization reports that 43% of adults worldwide were overweight and 16% obese in 2022, with over 8.9 billion obese adults globally. This is a more than doubling number since 1990 (from World Health Organization: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). Regionally, the IDF 2024 data indicates a global type 2 diabetes prevalence of 11.1% among 20-79-year-olds, while in China, nearly 70% of type 2 diabetes patients are overweight or obese, showing the urgent need for effective interventions (International Diabetes Federation, 2024: https://www.idf.org/). These conditions are combined with chronic inflammation and oxidative stress, which exacerbate insulin resistance and metabolic dysregulation, creating a cycle that worsens longterm health [1].

Manuka honey comes from the nectar of New Zealand's nectar of Leptospermum scoparium. It has become the leader among functional foods because of its unique biologically active ingredients. Unlike ordinary honey, Manuka honey is rich in methyl acetaldehyde (MGO), which is a landmark compound closely related to its efficacy, and its efficacy can be measured by the unique Manuka factor (UMF). In addition, Manuka honey also contains a variety of phenolic compounds, including caffeic acid, coumic acid and quarcetin, which synergize to enhance the biological activity of Manuka honey and have antioxidant and anti-inflammatory properties. MGO has obvious antibacterial effects, while phenolic compounds inhibit the pro-inflammatory pathway and reduce oxidative stress by removing free radicals. Preclinical and clinical evidence further

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supports the benefits of honey on cardiovascular metabolism. Meta-analysis shows that honey can improve fasting blood sugar, blood lipids and liver enzyme levels [2].

This article systematically reviews the current research evidence on the relationship between Manuka honey and metabolic health, focusing on its biologically active ingredients and their mechanisms of action. First of all, this article collects existing data on the antioxidant, anti-inflammatory and metabolic regulatory properties of methyl acetaldehyde (MGO) and phenolic substances in Manuka honey, and explores the link between honey and insulin resistance, obesity and type 2 diabetes. Secondly, this article analyses the existing preclinical and clinical studies, which explore the direct impact of Manuka honey on metabolic indicators (including blood sugar control, blood lipid spectrum and body composition). Finally, this paper discusses the potential of Manuka honey as a functional food aid in the management of metabolic disorders, and also points out the inconsistencies, methodological limitations (such as small sample size) and differences in UMF levels in the current research. This review aims to lay the foundation for recommendations based on evidence-based medicine to guide the role of Manuka honey in supporting metabolic health.

2. Bioactive Components of Manuka Honey

The biological efficacy of Manuka honey comes from its diverse bioactive molecules, and several key components stand out for their role in antioxidant and anti-inflammatory processes.

One of these components is methylglyoxal (MGO). It is the main influencing factor to the non-peroxide activity (NPA) of honey, which mainly relies on hydrogen peroxide to show antibacterial effects [3]. MGO is formed by the degradation of dihydroxyacetone (DHA), a compound rich in the nectar of Leptospermum scoparium. The concentration of the compound is related to the unique Manuka factor (UMF) rating, which measures the quality of Manuka honey. [4]. Which is, UMF ratings correlate to higher levels of MGO and total phenolic content, meaning stronger biological activity.

Polyphenol compounds are another source of bioactivity of Manuka honey, including flavonoids and phenolic acids. Unlike plant-based polyphenol sources, with complex macromolecules that often hinders absorption, the composition of Manuka honey minimizes polyphenol-polymer interaction and therefore do not interfere absorption. A large part of its polyphenols exist in aglycone form, which enhances gastrointestinal absorption [5]. This availability ensures that these compounds can reach tissues relevant to metabolic health, such as adipose tissue, the liver, and vascular endothelium, to make sure of their antioxidant and anti-inflammatory effects. Evidence of the high level of polyphenol content in Manuka honey can be found in comparative studies. For instance, a 2023 study found that Manuka honey contained 2–3 times higher levels of total phenolics and flavonoids than clover and acacia honeys, with corresponding increases in antioxidant capacity, measured by DPPH and FRAP assays [6].

Other bioactive components also contribute to Manuka honey's effects. Leptosperin, a unique glycoside which only exists in Leptospermum-derived honeys, modulates the interaction between antibacterial and anti-inflammatory activities, and therefore enhances the honey's ability to reduce infection caused inflammation [7]. Hydrogen peroxide, another important component, generated by the enzyme glucose oxidase present in Manuka honey, enhances MGO's non peroxide activity, further increasing antibacterial and anti-inflammatory efficacy. What's more, the synergistic interactions between these compounds strengthen Manuka honey's biological effects further more. For example, MGO reduces inflammation by inhibiting pathogenic bacteria, while polyphenols mitigate oxidative damage caused by inflammation; at last, leptosperin enhances the coordination of these processes [7].

3. Mechanisms of Antioxidant and Anti-Inflammatory Activity

3.1. Mechanisms of Antioxidant Activity

Oxidative stress is a key driver of metabolic dysfunction, and Manuka honey counteracts it through removing direct free radical. The polyphenolic compounds in Manuka honey can act as direct ROS scavengers due to their chemical structure, which includes hydroxyl groups that donate electrons to stabilize free radicals such as superoxide anion, hydroxyl radical, and peroxynitrite [6]. In vitro studies have demonstrated that Manuka honey possibly extracts effectively scavenge DPPH and ABTS radicals, with scavenging activity positively correlated with total phenolic content and UMF rating [5]. This direct scavenging reduces oxidative damage to cellular components, including lipids, proteins, and DNA, damage that contributes to insulin resistance, adipose tissue inflammation, and vascular dysfunction in metabolic diseases.

3.2. Mechanisms of Anti-Inflammatory Activity

Chronic inflammation in metabolic health is represented by the persistent activation of pro-inflammatory signaling pathways, excessive release of pro-inflammatory cytokines, and irregulate immune cell's function.

A central mechanism of Manuka honey's anti-inflammatory action is the suppression of pro-inflammatory transcription factors, particularly nuclear factor kappa B (NF-κB) and mitogen-activated protein kinases (MAPK). NF-κB is a regulator of inflammation, controlling the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6) - all cytokines that drive insulin resistance and adipose tissue inflammation in obesity and diabetes.

Manuka honey also modulates immune cell function to restore inflammatory balance. Macrophages, key immune cells in metabolic tissues, exist in two states. Pro-inflammatory M1 macrophages, which secrete pro-inflammatory cytokines, and anti-inflammatory M2 macrophages, which promote tissue repair and resolution of inflammation. Studies have shown that Manuka honey promotes the polarization of macrophages toward the M2 state, increasing the secretion of anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) [7]. Additionally, Manuka honey stimulates macrophages to release regulatory mediators that enhance tissue repair, a process critical for reversing tissue damage caused by chronic inflammation.

The antibacterial and antiviral properties of Manuka honey further increases its anti-inflammatory effects. Infections by pathogenic bacteria can trigger acute inflammation that worsens metabolic dysfunction. Manuka honey inhibits bacterial proliferation by altering cell morphology and disrupting biofilm formation. The diverse composition of Manuka honey's bioactive constituents can also strengthen its anti-inflammatory efficacy. For example, MGO reduces inflammatory triggers by inhibiting pathogen activity, polyphenols alleviate inflammatory damage through antioxidant pathways, leptosperin enhances the coordination of antibacterial and anti-inflammatory actions, and hydrogen peroxide boosts overall biological activity [7].

4. Evidence in Metabolic Health

More and more in vitro and in vivo evidence shows that Manuka honey has the potential to improve metabolic health through its antioxidant and anti-inflammatory properties.

In terms of obesity and insulin resistance, Manuka honey showed good results in preclinical models [8]. A 2023 study investigated the effect of supplementing Manuka honey on mice fed a high-fat diet (HFD) for 12 weeks [9]. The results showed that compared with the HFD control group, mice supplemented with Manuka honey (UMF 15+) gained weight and the weight of the epididymal fat pad were significantly reduced. These metabolic improvements are related to the reduction of oxidative stress and inflammation levels in the supplemented honey group. The results show that the

antioxidant and anti-inflammatory effects of Manuka honey can directly improve insulin sensitivity and reduce weight gain.

In terms of type 2 diabetes, Manuka honey also shows a protective effect. A study in 2021 showed that after supplementing Manuka honey in diabetic rats induced by streptomyculin, fasting blood sugar decreased and insulin secretion increased compared with the diabetic control group. Histological analysis shows that Manuka honey can protect pancreatic islet beta cells from oxidative damage, increase the number of beta cells, and reduce the expression of apoptotic markers such as caspase-3. These effects are attributed to polyphenolic compounds in honey, which can remove reactive oxygen (ROS) and inhibit NF-κB-mediated inflammatory reactions in pancreatic tissue [5].

Cardiovascular disease is one of the main complications of metabolic syndrome, which is also affected by oxidative stress and inflammation. Studies show that Manuka honey can improve vascular health by reducing the oxidative damage of endothelial cells and inhibiting the inflammatory process that promotes atherosclerosis. An in vivo study in 2022 showed that compared with the control group, rabbits fed a high-cholesterol diet and supplemented with Tri honey had lower serum cholesterol levels and reduced aortic plaque formation. The endothelial function of the supplemented honey group was also improved (through bloodstream-mediated vascular dilation determination), and the expression of vascular cell adhesion molecule-1 (VCAM-1) was reduced. VCAM-1 was a marker of endothelial inflammation [10].

5. Clinical Applications and Evidence

Although there is evidence that Manuka honey is beneficial to metabolic health, its clinical application is still relatively limited, and most studies focus on oral inflammation, chronic wounds and gastrointestinal diseases. However, despite limited applications, these clinical findings still provide a valuable perspective for our in-depth understanding of the efficacy of Manuka honey, laying the foundation for a more comprehensive exploration of the potential of Manuka honey in metabolic health.

In terms of chronic wounds, Manuka honey has been extensively studied and clinically approved in some areas. A 2012 trial evaluated the efficacy of UMF 15+ Manuka honey in 63 patients with diabetic foot ulcers. The results showed that 78% of the patients in the Manuka honey group healed the wound in the first week, compared with 35% in the standard treatment group. These findings show that Manuka honey can relieve inflammation and promote tissue repair in the context of metabolic diseases, supporting its potential as an inflammation-driven treatment for metabolic complications [11].

In terms of oral inflammation, Manuka honey has also shown clinical efficacy. A randomised controlled trial of 80 patients with moderate periodontitis in 2020 found that compared with the placebo group, local application of Manuka honey gel could reduce the score of gum inflammation after 8 weeks. The levels of pro-inflammatory cytokines (IL-1β, TNF-α) in the gingium sulcus fluid of patients in the honey group are also low, confirming their anti-inflammatory effect in the human body [7]. Periodontitis is associated with systemic inflammation, which can aggravate insulin resistance and metabolic disorders, so the ability of Manuka honey to reduce oral inflammation may be beneficial to metabolic health.

Despite these encouraging findings, there are still some limitations that hinder the wide clinical application of Manuka honey in the field of metabolic health. First of all, most clinical studies are small in scale and short in duration, making it difficult to evaluate the persistence of the efficacy of Manuka honey. Secondly, due to the natural source of Manuka honey, it is difficult to control the dose of active ingredients accurately. The doses of Manuka honey used in the study vary (10-50 grams/day), and the UMF levels vary, which complicates the effective comparison. Finally, the potential impact of the sugar content of Manuka honey on metabolic health needs to be carefully considered. Although the glycaemic index of Manuka honey is lower than that of refined sugar, if its fructose

and glucose content is consumed in excessive amounts, it may pose a risk to diabetics with poor blood sugar control.

6. Conclusion

Metabolic disorders caused by obesity, type 2 diabetes and insulin resistance are increasingly common global health issues, chronic inflammation and oxidative stress are the core pathogenic mechanisms. Manuka honey has a unique mixture of biologically active ingredients, including MGO, polyphenols, leptin and hydrogen peroxide. Therefore, through the combined antioxidant and anti-inflammatory effects, it is a promising choice to support metabolic health. Its bioactive constituents directly scavenge reactive oxygen species, suppress pro-inflammatory signaling pathways, modulate macrophage polarization, and protect key metabolic tissues such as pancreatic beta cells, adipose tissue, and vascular endothelium. Preclinical evidence has already shown its effectiveness in improving blood sugar control, reducing weight gain, reducing lipid levels and reducing the formation of atherosclerotic plaques. On the other hand, clinical research also provides valuable support. For instance, the efficacy of Manuka honey in the treatment of oral inflammation and ulcers has been proven to solve inflammation and promote human tissue repair. These findings further demonstrate its potential for solving inflammatory-driven metabolic problems. However, major challenges still hinder its extensive clinical application in health, as small-scale, short-term clinical trials limit the evaluation of long-term efficacy and safety, and its inherent sugar content raises concerns about poor diabetes control if consumed in excess amounts.

In summary, the unique bioactive characteristics and preclinical evidence of Manuka honey do support its role as a promising functional food for metabolic health. Its therapeutic potential lies not only in individual components but in the synergistic interplay between MGO, polyphenols, and complex carbohydrates, which provides a multi-targeted approach to systemic homeostasis. Although the current clinical data and trials is limited, they still lay the foundation for targeted investigation. Future research should prioritize large-scale, longitudinal randomized controlled trials (RCTs) to establish standardized dosing protocols that maximize anti-inflammatory benefits while neutralizing the risks of its intrinsic sugar load. Furthermore, exploring the impact of Manuka honey on the gut-metabolic axis—specifically its prebiotic-like effects on microbiota composition—could unlock new dimensions of its efficacy. It is believed that through more long-term and standardized further research, Manuka honey can become a valuable adjuvant drug for traditional therapies, providing a natural and reliable method to alleviate metabolic disorders and their complications. Ultimately, as the paradigm shifts towards integrative and precision nutrition, Manuka honey stands as a sophisticated candidate for mitigating the global burden of chronic metabolic diseases through evidence-based dietary intervention.

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