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Olive Oil and Type 2 Diabetes: Understanding the Gene Expression Mechanisms behind Insulin Resistance and Metabolic Health

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a major public health concern worldwide, characterized by insulin resistance, impaired glucose metabolism, and a higher risk of cardiovascular complications. Insulin resistance is the key feature of T2DM, where the body's cells become less responsive to insulin, resulting in elevated blood glucose levels. While genetic factors contribute to T2DM, lifestyle factors, particularly diet, play a significant role in the development and management of the disease. Among dietary fats, olive oil, especially Extra Virgin Olive Oil (EVOO), has gained attention for its beneficial effects on metabolic health. It is a cornerstone of the Mediterranean diet, which is associated with lower risks of developing T2DM and cardiovascular diseases. Understanding the molecular mechanisms by which olive oil affects gene expression related to insulin resistance and metabolic health is crucial for harnessing its therapeutic potential. Olive oil is rich in Monounsaturated Fatty Acids (MUFAs), primarily oleic acid, and contains a variety of bioactive compounds such as polyphenols (e.g., hydroxytyrosol, oleuropein), antioxidants, and vitamins. These components contribute to its anti-inflammatory, antioxidant, and insulin-sensitizing properties. The primary active compounds in olive oil—oleic acid and polyphenols—are thought to be responsible for its effects on gene expression related to glucose metabolism, lipid metabolism, and inflammation, all of which are central to the pathogenesis of T2DM. Oleic acid, the most abundant monounsaturated fatty acid in olive oil, has been shown to improve insulin sensitivity and reduce the risk of developing insulin resistance.
insulin resistance.

Description

Olive oil polyphenols, such as hydroxytyrosol, oleuropein, and tyrosol, are potent antioxidants and anti-inflammatory agents. Chronic low-grade inflammation is a key contributor to the development of insulin resistance and T2DM. Olive oil polyphenols have been shown to modulate the expression of inflammatory cytokines and transcription factors that are involved in insulin resistance, such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6), and nuclear factor-kappa B (NF-κB). In T2DM, elevated levels of pro-inflammatory cytokines interfere with insulin signaling, promoting insulin resistance. Olive oil polyphenols counteract this by downregulating the expression of these inflammatory markers. For instance, studies have shown that hydroxytyrosol can suppress the activation of NF-κB, a key transcription factor involved in the inflammatory response, thereby reducing chronic inflammation and improving insulin sensitivity. Additionally, olive oil polyphenols increase the expression of adiponectin, an anti-inflammatory cytokine produced by adipose tissue, which improves insulin sensitivity. The regulation of genes involved in glucose and lipid metabolism is essential for maintaining metabolic health. In T2DM, dysregulation of these genes contributes to impaired glucose uptake, increased hepatic glucose production, and excessive fat accumulation. Olive oil components, particularly oleic acid and polyphenols, influence the expression of several genes involved in these processes [1].

Insulin resistance, a hallmark of T2DM, occurs when insulin signaling pathways become impaired. One of the primary pathways involved in insulin action is the phosphoinositide 3-kinase (PI3K)/Akt pathway, which regulates glucose uptake in muscle and adipose tissue. Studies have shown that oleic acid can enhance the activation of this pathway, improving glucose transport by increasing the expression of Glucose Transporter 4 (GLUT4), an insulin-sensitive transporter responsible for glucose uptake into cells. Oleic acid also increases the phosphorylation of insulin receptor substrates (IRS-1 and IRS-2), which are essential for the downstream activation of the PI3K/Akt pathway. As a result, insulin signaling is enhanced, leading to improved glucose metabolism and reduced blood glucose levels. Additionally, oleic acid modulates the expression of genes related to lipogenesis and lipolysis, such as Fatty Acid Synthase (FAS) and Hormone-Sensitive Lipase (HSL), promoting healthy lipid metabolism and reducing fat accumulation in insulin-sensitive tissues [2].

Excessive fat accumulation in tissues, particularly in the liver and skeletal muscles, is a key factor in the development of insulin resistance and T2DM. Olive oil, through its MUFA content, influences the expression of genes involved in fatty acid oxidation and lipid synthesis. Oleic acid increases the expression of genes related to fatty acid oxidation, such as peroxisome Proliferator-activated Receptor alpha (PPAR-α) and Carnitine Palmitoyltransferase 1 (CPT1). These genes promote the utilization of fatty acids for energy, reducing fat accumulation in tissues and improving insulin sensitivity. Moreover, olive oil components can help reduce the expression of genes involved in lipogenesis, such as FAS, thereby decreasing the synthesis of new fat. This reduction in lipogenesis, coupled with enhanced fatty acid oxidation, contributes to a healthier lipid profile and improved insulin sensitivity, both of which are crucial for preventing and managing T2DM.

Oxidative stress and inflammation are significant contributors to insulin resistance and metabolic dysfunction in T2DM. The antioxidants in olive oil, such as hydroxytyrosol, oleuropein, and vitamin E, can protect cells from oxidative damage by neutralizing reactive oxygen species (ROS). Oxidative stress leads to the activation of inflammatory pathways, which interfere with insulin signaling and promote insulin resistance. By modulating the expression of antioxidant genes, olive oil polyphenols help restore the balance between ROS and antioxidants, reducing oxidative damage and improving insulin sensitivity. For example, hydroxytyrosol has been shown to increase the expression of antioxidant enzymes such as Superoxide Dismutase (SOD) and catalase, which protect cells from oxidative stress. In addition to their antioxidant effects, polyphenols also modulate the expression of inflammatory genes, as previously mentioned, thereby reducing inflammation and improving metabolic function [3,4].

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Clinical studies have provided strong evidence supporting the role of olive oil in improving insulin sensitivity and reducing the risk of T2DM. For instance, the PREDIMED study (Prevención con Dieta Mediterránea) demonstrated that individuals who consumed a Mediterranean diet supplemented with extra virgin olive oil had a significantly lower incidence of T2DM compared to those on a low-fat diet. The beneficial effects were attributed to the anti- inflammatory, antioxidant, and insulin-sensitizing properties of olive oil. Moreover, randomized controlled trials have shown that replacing saturated fats with olive oil leads to improvements in insulin sensitivity, glucose metabolism, and lipid profiles in individuals at risk of T2DM. These studies highlight the potential of olive oil as a therapeutic dietary intervention for the prevention and management of T2DM [5].

Conclusion

The components of olive oil, particularly oleic acid and polyphenols, play a significant role in modulating gene expression related to insulin resistance, glucose metabolism, and inflammation. Through their effects on key molecular pathways, such as insulin signaling, lipid metabolism, and antioxidant defense, olive oil can improve insulin sensitivity, reduce inflammation, and help maintain metabolic health. These mechanisms highlight the importance of incorporating olive oil, especially extra virgin olive oil, into the diet as a preventive and therapeutic measure for T2DM. The growing body of evidence supports the idea that a diet rich in olive oil, particularly as part of the Mediterranean diet, can contribute to better metabolic health and a reduced risk of T2DM. Further research is needed to explore the full potential of olive oil in the management of T2DM and its underlying molecular mechanisms.

Acknowledgment

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Conflict of Interest

There are no conflicts of interest by author.

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