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Vitamin C as adjuvant therapy in diabetes management

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Abstract:

Diabetes mellitus is a long-term metabolic condition marked by high blood sugar levels due to issues with insulin secretion, its action, or a combination of both.Effective management of blood glucose levels is essential to prevent complications associated with diabetes. Recent studies have highlighted the potential role of Vitamin C, a vital water-soluble vitamin, in diabetes management. This review aims to explore the relationship between Vitamin C and diabetes, focusing on its antioxidant properties, effects on glucose metabolism, and implications for diabetes-related complications.

Vitamin C, or ascorbic acid, is renowned for its antioxidant capabilities and essential functions in various biological processes. Emerging research underscores its significance in glucose metabolism, particularly regarding insulin sensitivity and diabetes management. This article examines how Vitamin C influences glucose metabolism through mechanisms such as insulin signaling, modulation of oxidative stress, reduction of inflammation, and facilitation of glucose transport.

Additionally, the review discusses recent findings on Vitamin C's effects on glycemic control and its potential to alleviate diabetes-related complications. By elucidating these relationships, this review provides insights into the therapeutic potential of Vitamin C in enhancing metabolic health and improving outcomes for individuals with diabetes.

Keywords: Vitamin C, Diabetes, Antioxidant, Insulin Resistance.

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1. Introduction

Vitamin C, scientifically referred to as ascorbic acid, is a vitamin that dissolves in water , is essential for various bodily functions and is vital for many physiological processes. It functions as a strong antioxidant and is important for immune support [1]. Additionally, Vitamin C serves as a cofactor in several enzymatic reactions [2]. Its antioxidant characteristics come from its ability to neutralize free radicals and regenerate other antioxidants like Vitamin E [3]. Furthermore, it protects cells from oxidative stress, which is a major factor in the onset of diabetes and its complications [4].

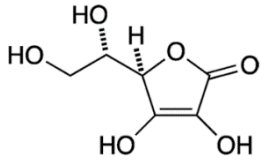

Figure1: Vitamin C Structure

1.1. Vitamin C functions as a potent water-soluble antioxidant in several ways:

Direct Scavenging of Free Radicals: Vitamin C can directly interact with free radicals like superoxide radicals, hydroxyl radicals, and singlet oxygen, effectively neutralizing them. This process helps to prevent oxidative damage to lipids, proteins, and nucleic acids [5], which in turn reduces oxidative stress on pancreatic β-cells and enhances insulin secretion [6].

Regeneration of Other Antioxidants: Vitamin C also plays a role in regenerating other antioxidants, such as Vitamin E, thereby bolstering the body's antioxidant defenses and protecting cells from oxidative harm [7].

Metal Ion Chelation: Vitamin C has the ability to bind with metal ions, such as iron and copper, which can catalyze free radical formation through Fenton reactions. By chelating these metal ions, Vitamin C helps to diminish the risk of oxidative stress [8].

Influence on Gene Expression: Research has demonstrated that Vitamin C can influence the expression of genes related to oxidative stress responses and antioxidant defense mechanisms. For instance, it can promote the expression of heme oxygenase-1, an enzyme known for its antioxidant properties [9].

2. Health Benefits of Vitamin C

1. Immune Support and Infection Resistance

Vitamin C boosts immune defense by strengthening epithelial barrier function and increasing phagocytic activity [1]. A meta-analysis indicated that vitamin C supplementation can lessen both the duration and severity of respiratory infections [10]. It enhances the activity of leukocytes, supports the integrity of epithelial barriers, and modulates cytokine production [11]. Additionally, it has been shown to stimulate the production of white blood cells, which are crucial for combating infections [12].

2. Cardiovascular Health

Vitamin C enhances endothelial function and diminishes oxidative stress, potentially reducing the risk of cardiovascular disease. Its antioxidant properties help prevent the oxidation of LDL cholesterol, a significant factor in the development of atherosclerosis [13].

3. Skin Health and Wound Healing

Vitamin C is crucial for the hydroxylation of proline and lysine residues during collagen synthesis, which is vital for the structure of skin, blood vessels, bones, and connective tissues [14].

4. Cognitive Function and Neuroprotection

Vitamin C may offer protection against neurodegenerative diseases by counteracting oxidative stress in the brain. Studies suggest that individuals with higher dietary intake of Vitamin C may experience a lower risk of cognitive decline [15].

Unlike most animals, humans cannot synthesize Vitamin C due to a mutation in the L-gulono-γ-lactone oxidase (GULO) gene, making dietary sources essential [16]. Vitamin C is plentiful in fruits and vegetables, particularly in citrus fruits, strawberries, kiwi, bell peppers, and leafy greens [17].

3. Diabetes mellitus

Diabetes mellitus (DM) is a chronic condition characterized by inadequate insulin secretion or insulin resistance [18]. It affects nearly half a billion people worldwide, with projections indicating that this number could rise to 700 million by 2045 [19]. The prevalence of abnormal glucose tolerance among adults is expected to reach 8.0% by 2030 and increase to 8.6% by 2045 [20]. Poor glycemic control can lead to serious complications, including retinopathy, neuropathy, and nephropathy [21].

Various strategies, including physical activity, diet, and dietary supplements, have been proposed to improve DM complications [22-26]. There is also evidence that oxidative stress and chronic low-grade inflammation contribute to the progression and onset of DM. Therefore, a healthy diet rich in antioxidants may help reduce the risk of developing diabetes [27, 28].

Optimal antioxidant intake may lower the likelihood of developing DM and its associated complications, as antioxidant supplements can normalize lipid peroxidation levels and cellular markers of oxidative stress [28]. Oxidative reactions may exacerbate DM by promoting insulin resistance and hindering insulin secretion [29]. The antioxidant properties of Vitamin C can mitigate oxidative stress, potentially lowering the risk of DM [30].

Some studies have shown that Vitamin C supplementation can significantly reduce hemoglobin A1c (HbA1c) and fasting blood glucose (FBG) levels [31, 32]. However, other research has found no significant effects of Vitamin C supplements on HbA1c, FBG, or insulin levels [33, 34].

Effective diabetes management typically includes lifestyle changes, glucose monitoring, and pharmacological treatments. Recently, there has been increasing interest in the role of dietary antioxidants, particularly Vitamin C, in enhancing glycemic control and reducing diabetes-related complications.

Oxidative stress is crucial in developing insulin resistance and advancing diabetes [35]. By scavenging reactive oxygen species (ROS) and regenerating other antioxidants like Vitamin E, Vitamin C helps alleviate oxidative damage, potentially improving insulin sensitivity and glucose metabolism [36].

4.Vitamin C and glucose metabolism

Several studies have suggested that Vitamin C may influence glucose metabolism through various mechanisms:

- Enhancing Insulin Sensitivity: Vitamin C may improve insulin sensitivity by modulating the signaling pathways involved in insulin action [37].
- Reducing Inflammation: Chronic inflammation is a characteristic of type 2 diabetes. Vitamin C may exert anti-inflammatory effects, indirectly enhancing insulin sensitivity and glycemic control [38].
- Regulating Glucose Transporters: Vitamin C has been shown to upregulate glucose transporter proteins, facilitating glucose uptake in tissues [39].

A randomized controlled trial by Rahman et al. evaluated the impact of Vitamin C supplementation on glycemic control in patients with type 2 diabetes. Participants received 500 mg of Vitamin C daily for 12 weeks, resulting in significant reductions in fasting blood glucose levels and HbA1c, suggesting improved insulin sensitivity. The study indicated that Vitamin C enhances insulin signaling pathways, possibly through AMPK activation [40].

A meta-analysis by Nascimento et al. reviewed multiple studies assessing Vitamin C supplementation's effects on glycemic control and found significant improvements in fasting blood glucose and HbA1c levels across different populations, highlighting its potential as an adjunct therapy for diabetes management [41]. A cross-sectional study indicated that individuals with higher dietary Vitamin C intake had a lower risk of developing type 2 diabetes mellitus (T2DM), particularly among those with elevated BMI. This protective effect may be due to Vitamin C's antioxidant and anti-inflammatory properties, as well as its role in enhancing insulin sensitivity [42].

Vitamin C has been shown to enhance the expression and translocation of GLUT4, thereby increasing glucose uptake in muscle and adipose tissues:

- Insulin Signaling Pathway: In addition to its effects on AMPK, Vitamin C may amplify insulin signaling pathways that facilitate GLUT4 translocation. Insulin binding to its receptor triggers a cascade of signaling events that lead to GLUT4 movement to the cell membrane [43]. Vitamin C may enhance this response, promoting increased glucose uptake.
- Direct Modulation of GLUT4: Some studies suggest that Vitamin C can directly influence GLUT4 expression and activity, independently of insulin. This mechanism may provide an alternative pathway for enhancing glucose uptake, particularly in insulin-resistant states [39].

5.Vitamin C and Insulin Resistance

Insulin resistance is a key feature of type 2 diabetes, and improving insulin sensitivity is crucial for effective diabetes management. This section explores the impact of Vitamin C on insulin resistance.

Vitamin C may enhance insulin sensitivity through several mechanisms, including:

- **Reduction of Oxidative Stress**: By decreasing oxidative stress, Vitamin C may enhance insulin signaling pathways and improve glucose uptake in tissues [35].
- **Modulation of Inflammatory Cytokines**: Vitamin C has been shown to lower levels of pro-inflammatory cytokines, which contribute to insulin resistance [38].

A study demonstrated that Vitamin C supplementation improved insulin sensitivity in overweight and obese individuals with insulin resistance [44]. Additionally, a meta-analysis indicated significant reductions in insulin resistance parameters, including HOMA-IR, in diabetic patients [45].

Insulin sensitivity refers to how responsive cells are to insulin, the hormone responsible for facilitating glucose uptake. Impaired insulin sensitivity is a primary contributor to the development of T2DM. Vitamin C has been shown to enhance insulin sensitivity through several pathways:

- **AMP-Activated Protein Kinase (AMPK) Activation**: AMPK is crucial for regulating cellular energy homeostasis. Vitamin C activates AMPK, leading to increased glucose uptake in muscle cells and improved insulin sensitivity. This activation promotes the translocation of glucose transporter type 4 (GLUT4) to the cell membrane, facilitating glucose uptake [39, 43].
- **Reduction of Lipid Accumulation**: Excessive lipid accumulation in tissues can lead to insulin resistance. Vitamin C inhibits lipid accumulation and promotes fatty acid oxidation, which contributes to improved insulin sensitivity [37].

Chronic inflammation is closely linked to the development of insulin resistance and T2DM. Vitamin C exerts anti-inflammatory effects that can positively influence glucose metabolism:

- Reduction of Pro-inflammatory Cytokines: Vitamin C decreases levels of cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are involved in insulin resistance [38]. By modulating inflammation, Vitamin C may mitigate its adverse effects on insulin signaling.
- Regulating Nuclear Factor Kappa B (NF-κB): NF-κB is a transcription factor that regulates inflammatory gene expression. Vitamin C can inhibit NF-κB activation, leading to reduced inflammation and improved insulin sensitivity [46].

6.Vitamin C and Diabetes-Related Complications

Diabetes is associated with several complications, including cardiovascular disease, neuropathy, retinopathy, and nephropathy. Vitamin C may offer protective effects against these complications:

Cardiovascular Disease: Individuals with diabetes are at higher risk for cardiovascular diseases due to oxidative stress and inflammation. Vitamin C's antioxidant properties may help reduce this risk. A systematic review found that Vitamin C supplementation was associated with lower blood pressure and improved endothelial function in diabetic patients [42].

Diabetic Neuropathy: This common complication involves nerve damage due to hyperglycemia and oxidative stress. Research demonstrated that Vitamin C supplementation improved nerve conduction velocity and reduced neuropathic symptoms in patients with diabetic neuropathy [47].

Diabetic Retinopathy: A leading cause of blindness among diabetic patients, diabetic retinopathy may be mitigated by Vitamin C, which protects retinal cells from oxidative damage and inhibits progression in animal models [48].

7. Conclusion

Vitamin C is an essential nutrient that offers a wide range of health benefits, from supporting immune function to aiding in collagen synthesis. Its emerging role in diabetes management, particularly through its antioxidant properties and effects on glycemic control, highlights its potential as a complementary strategy for individuals with diabetes. While the current evidence is promising, further research is crucial to determine optimal dosages and treatment protocols for Vitamin C supplementation.

Incorporating Vitamin C-rich foods into the diet can enhance overall well-being and may help mitigate diabetes-related complications. As diabetes prevalence continues to rise globally, understanding the mechanisms by which Vitamin C influences glucose metabolism will be vital for developing effective therapeutic approaches. Future studies should prioritize these areas to fully unlock the potential of Vitamin C in diabetes management, ultimately leading to improved health outcomes for those affected by this condition.

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