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THE POTENTIAL ROLE OF BEETROOT JUICE IN HYPERGLYCEMIA MANAGEMENT: A REVIEW OF MECHANISMS AND CLINICAL OUTCOMES

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ABSTRACT: *Hyperglycemia, characterized by elevated blood glucose levels, is a significant health concern that affects millions of individuals worldwide. It has been associated with long-term complications affecting the cardiovascular, renal, and nervous systems. Beetroot juice (BRJ), rich in nitrates, betalains, and antioxidants, has gained attention for its potential role in mitigating hyperglycemia and improving insulin sensitivity. This review evaluates the available scientific evidence on the hypoglycemic effects of beetroot juice, explores its proposed mechanisms of action, and discusses its potential as a complementary therapy for diabetes management. By analyzing studies, we found that beetroot juice may help manage hyperglycemia by enhancing insulin sensitivity through its nitrate content, which converts to nitric oxide. Clinical evidence indicates it may lower fasting blood glucose and improve glycated hemoglobin A1c (HbA1c) levels, though results vary. While beetroot juice shows promise as a supplementary treatment for hyperglycemia, more research is needed to determine the optimal dosage, long-term effects, and interactions with other diabetes management strategies.*

KEYWORDS: Beetroot juice, Hyperglycemia, Diabetes mellitus, Nitric oxide, Antioxidants.

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INTRODUCTION

The prevalence of diabetes mellitus continues to rise globally according to the International Diabetes Federation (IDF, 2022), creating an urgent need for novel strategies to manage hyperglycemia and its associated complications. Hyperglycemia, characterized by elevated blood glucose levels, is a primary feature of diabetes mellitus (Olumese & Oboh, 2016). It leads to serious complications such as cardiovascular diseases, neuropathy, nephropathy, and retinopathy (Ali et al., 2020: Pecoits-Filho et al., 2016).

Management strategies often include lifestyle modifications, oral hypoglycemic agents, and insulin therapy. Conventional antidiabetic medications are effective but usually come with side effects that limit long-term adherence (Olumese & Oboh, 2016). Therefore, natural therapies, such as plant-based interventions, are being explored for their safety and efficacy. One such natural intervention is beetroot juice (BRJ), derived from *Beta vulgaris*, which is rich in bioactive compounds, particularly nitrate, polyphenols, and betalains (Kale et al., 2018; Mirmiran et al., 2020). Beetroot has medicinal properties that can cure various illnesses (Shivani *et al.,* 2020), including protection against heart disease and colon cancer (Kavalcova *et al.,* 2015).

BRJ exhibits potential anti-diabetic and cardioprotective effects and has promising potential in reducing blood pressure through its vasodilatory effects, largely attributed to its nitrate content, which enhances nitric oxide (NO) production in the body (Domínguez et al., 2017; Mirmiran et al., 2020). Recently, emerging studies suggest that beetroot juice may also influence glucose metabolism, insulin sensitivity, and oxidative stress, all of which are crucial in the pathogenesis of diabetes and its complications (Mirmiran et al., 2020). This manuscript reviews the current evidence on the role of beetroot juice in managing hyperglycemia and the mechanisms underlying its therapeutic potential.

Nutrient and Bioactive Composition of Beetroot Juice

Beetroot juice is derived from the taproot of *Beta vulgaris*, commonly known as beet. It is rich in Nitrates (Cava et al., 2012; Kale et al., 2018), polyphenols, betalains, flavonoids, ascorbic acid, carotenoids, and saponins (Chhikara et al., 2019). Beetroot is one of the richest natural sources of dietary nitrates, which can be converted into nitric oxide (NO) in the body. NO is crucial in vascular health and glucose metabolism (Kale et al., 2018). BRJ is also abundant in diverse mineral elements (table 1) like sodium, calcium, magnesium, potassium, phosphorus, zinc, iron, and copper (Mirmiran et al., 2020; Mathangi and Balasaraswathi, 2019).

Beetroot is a rich source of flavonoids and phenolic compounds. Recent research showed the total phenolic acids content in beetroot was 30.81 gallic acid equivalent/g dry weight (DW) (Desseva et al., 2020). Four main groups of flavonoids namely betavulgarin, cochliophilin A, betagarin, and dihydroisorhamnetin have been identified in beetroot (Vulić et al., 2014). Other flavonoids in beetroots include 5-hydroxy-6, 7-methylenedioxyflavone, 3, 5-dihydroxy-6, 7-methylenedioxyflavanone, 2, 5-dihydroxy-6, and 7-methylenedioxy isoflavone (Rana et al., 2022). Carotenoids are abundant in beetroot and act as potent antioxidants and oxygen radical scavengers (Lim et al., 2023).

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Betalains which make up to ~70–100% of the phenolic composition of beetroot (Mirmiran et al., 2020), especially betanin, give beetroot its deep red color and have been shown to exhibit anti-inflammatory and antioxidant activities (Aliahmadi et al., 2021; Karimzadeh et al., 2022). Interestingly, the consumption of betalains may promote the growth of *Akkermansia* sp. which has beneficial effects against metabolic disorders such as insulin resistance and diabetes (Song et al., 2016). Oxalic acid, a metal ion chelator that promotes the formation of nephrolithiasis is relatively abundant in beetroot juice (Mirmiran et al., 2020). An average content in beetroot juice equals 300–525 mg/L, (Mirmiran et al., 2020).

Table 1: Mineral Composition of Beetroot

Minerals	Average value (mg/100g)
Iron	0.75 ±1.20
Potassium	30.12 ± 0.29
Calcium	12.20±1.20
Manganese	0.79 ± 1.98
Copper	0.09 ± 0.47
Sodium	72.58 ± 1.12
Zinc	0.21 ± 1.01

Source: *Kale et al., 2018*

Mechanisms of Beetroot Juice in Hyperglycemia Management

Nitrate-Nitric Oxide Pathway

Research indicates that beetroot juice consumption can enhance insulin sensitivity, which is a critical factor in hyperglycemia management. Insulin sensitivity refers to how responsive cells are to insulin, allowing glucose to be absorbed from the bloodstream. According to Wootton-Beard et al. (2014), insulin liberation and absorption are important for glucose transportation and uptake from digested food. Highly carbohydrate-containing food causes hyperglycemia which in turn arouses a rapid rise in blood insulin known as insulinaemia. Insulin resistance which is major in type 2 diabetes may result from continuous hyperglycemia and hyperinsulinemia. The high nitrate content of beetroot when converted to nitric oxide (NO) in the body has shown to improve endothelial function and blood flow, potentially enhancing glucose delivery to peripheral tissues and improving insulin sensitivity (Andrew et al., 2024; Clifford et al., 2015). According to Nyström et al. (2012), rats administered nitrite showed an increase in insulin secretion; this could be attributed to an increase in islet blood flow. Additionally, Jiang et al. demonstrated that giving dietary nitrite for four weeks lowers insulin and fasting glucose levels (Jiang et al., 2014).

Carlström suggests that NO may increase glucose uptake by skeletal muscle via activation of the AMP-activated protein kinase (AMPK) pathway (Carlström, 2021), which is involved in energy metabolism and insulin signaling. AMPK activation increases glucose uptake into muscle cells by promoting the translocation of glucose transporters (GLUT4) to the cell membrane. This leads to increased glucose utilization, helping lower blood glucose levels. In another research, Harrison and Cia, (2016) revealed that inhibition of Angiotensin-Converting Enzyme (ACE) by NO reduces angiotensin II production and enhances bradykinin levels. This interaction improves insulin sensitivity, glucose metabolism and endothelial function. Researchers have also demonstrated that NO is crucial in modulating insulin signaling

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pathways, making tissues more responsive to insulin. (Khalif et al., 2015). Through the combined effects of NO production and antioxidant activity, beetroot juice improves glucose uptake in muscle tissues by increasing the action of insulin and GLUT4 transporters.

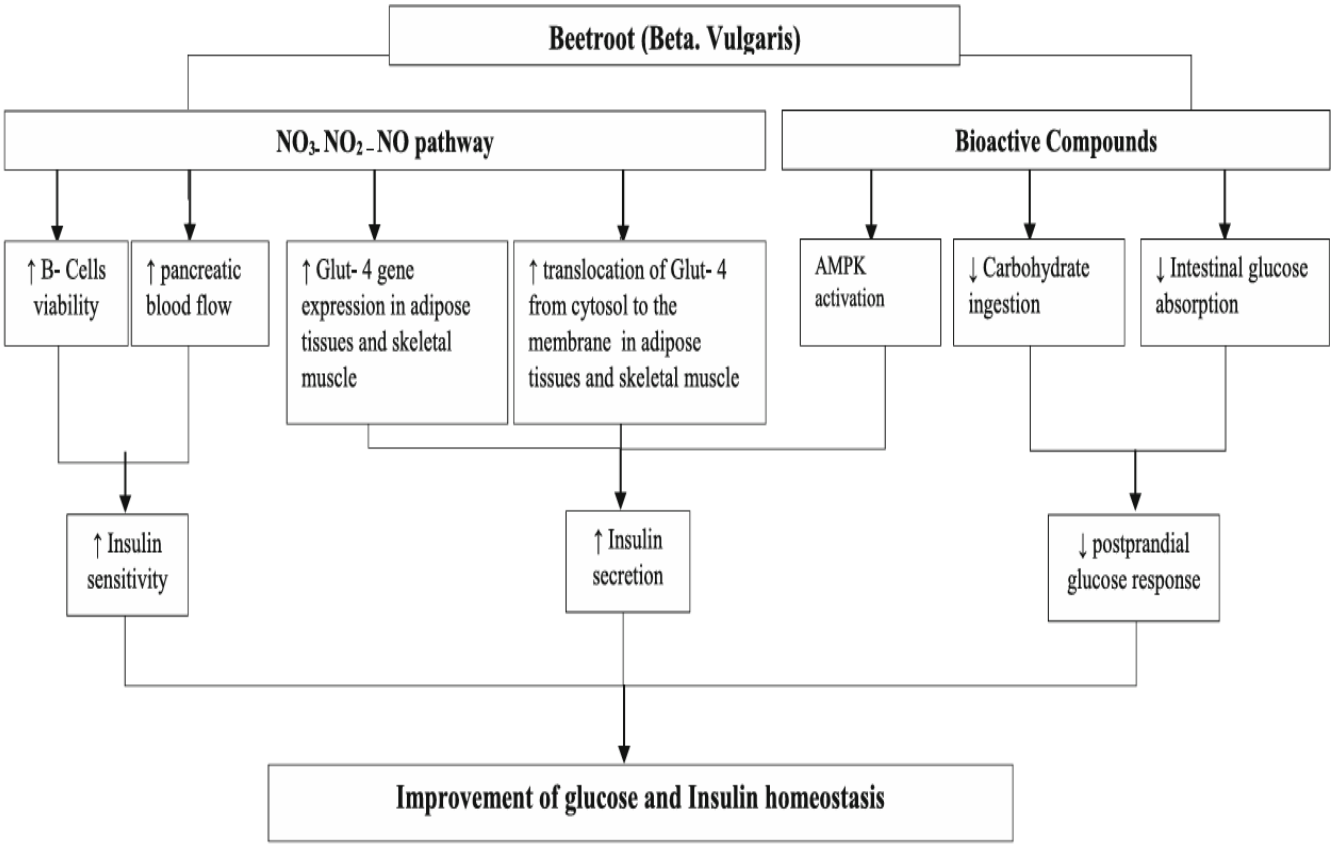

Fig 1: The SGC-cGMP pathway is triggered by NO, which lowers renovascular resistance and improves renal function. Reduction of angiotensin II type I receptor gene expression results in the production of NO2-S-nitrosothiol, enhances renal blood flow, and relaxes blood vessels. AMPK: Adenosine Monophosphate-activated Protein Kinase, NO: Nitric Oxide, SGC Soluble Guanylate Cyclase, cGMP Cyclic Guanosine Monophosphate

Source: *Mirmiran et al. (2020)*

Antioxidant Properties

Under aerobic conditions, biological systems come into contact with oxidants, mainly reactive oxygen species (ROS) and reactive nitrogen species (RNS). RNS refers to the oxidation states and reactive adducts of NOS products, whereas ROS are created when incomplete oxygen reduction occurs (D'Autreaux andToledano, 2007). Oxidative stress, caused by imbalance between endogenous oxidants and antioxidants, leads to impaired NO bioavailability and vascular dysfunction, affecting the expression of endothelial nitric oxide synthase (eNOS) in cardiovascular diseases like diabetes (Pitocco et al., 2010). Oxidative stress, which is intimately linked to hyperglycemia, is a major factor in the development of insulin resistance and β-cell dysfunction in the pancreas. In another study, Nishiwaka et al observed that rapid mitochondrial fragmentation brought on by hyperglycemia counteracts the Krebs cycle's

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generation of ROS-generating substrate (Nishiwaka et al., 2000), this leads to an increase in ROS production, which in turn triggers the intracellular synthesis of advanced glycation end-products (AGEs) precursors and the overexpression of AGE receptors and their activating ligands.

Baião (2017) opine that, with the high levels of betalains, a class of antioxidants known for their anti-inflammatory and free radical-scavenging abilities, antioxidants and nitrates, beetroot juice can mitigates the harmful effects of hyperglycemia-induced mitochondrial fragmentation and ROS overproduction. By reducing oxidative stress, enhancing mitochondrial function, and preventing excessive formation of AGEs and their interaction with RAGE, beetroot juice helps protect cells from the damaging cycle of oxidative stress and inflammation, ultimately benefiting glucose metabolism and reducing complications associated with hyperglycemia (Li et al., 2017).

Inhibition of Carbohydrate-Digesting Enzymes

Another possible mechanism by which beetroot juice may control hyperglycemia is through the inhibition of carbohydrate-digesting enzymes like α-amylase and α-glucosidase. Carbohydrates when converted to glucose provide energy for the cells of the body. Glycosidic linkages of α-D-(1, 4) in carbohydrates are cleaved by α-amylase to produce oligosaccharides, which are further cleaved to monosaccharide glucose by α-glucosidase (Hurtado, 2018). By preventing glucose metabolism and the hydrolysis of carbohydrates, beetroot may help prevent diabetes directly. The primary causes of hyperglycemia in diabetes patients are increased gluconeogenesis in the liver and glucose produced during the breakdown of carbohydrates (Jiang et al., 2020).

According to Montiel-Sánchez et al. (2021) and other research findings, betanins found in beetroot can inhibit α-amylase and α-glucosidase, which reduces the amount of glucose released from diet. By increasing pyruvate kinase and glucokinase and lowering gluconeogenic enzymes like fructose-1, 6-bisphosphatase and glucose-6-phosphatase in the liver, bethanin ingestion can also increase glycolysis (Dhananjayan et al., 2017). It has been revealed that polyphenols, such as flavonoids, phenolic acids, proanthocyanidins, and tannins, found in beetroot juice can alter postprandial glycemia (de Bock et al., 2012).

Glycemic Control and Hemodynamic Improvement

Beetroot juice has been shown to exert favorable effects on both glycemic control and cardiovascular health. In patients with type 2 diabetes, consumption of beetroot juice was linked to improved fasting glucose levels and reduced blood pressure due to its nitrate content. The reduction in blood pressure indirectly aids in reducing the risk of diabetes-related complications, especially cardiovascular diseases (Andrew et al., 2024).

Anti-Inflammatory Action

Chronic inflammation is a significant contributor to the progression of insulin resistance and type 2 diabetes. The betalains in beetroot juice possess strong anti-inflammatory properties that can help mitigate the low-grade systemic inflammation often seen in diabetic patients, thereby improving insulin sensitivity and helping regulate blood glucose levels. Betanin consumption can also promote glycolysis by activating glucokinase and pyruvate kinase while decreasing gluconeogenic enzymes such as glucose-6-phosphatase and fructose-1,6-bisphosphatase in the

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liver (Dhananjayan et al., 2017). These actions help lower blood sugar levels by increasing the utilization of glucose for energy and reducing the production of new glucose, which is beneficial for managing hyperglycemia, particularly in individuals with insulin resistance or type 2 diabetes (Li et al., 2017). Studies show that beetroot juice can reduce the levels of pro-inflammatory cytokines, which contribute to insulin resistance and hyperglycemia (Clifford, 2015).

Clinical Evidence Supporting Beetroot Juice in Hyperglycemia Management

Several small-scale clinical studies have begun to investigate the effects of beetroot juice on glycemic control. In a randomized controlled trial, participants with type 2 diabetes who consumed beetroot juice for two weeks showed modest improvements in fasting blood glucose levels and insulin resistance markers compared to a placebo group (Al-Harbi et al., 2021). In a randomized cross-over study, administering 270 mL of beetroot juice to healthy adults suppressed the postprandial glycemic response and reduced both the peak and duration of elevated blood glucose levels. Compared to a sugar-matched control drink, beetroot juice demonstrated beneficial effects (Chang et al., 2018).

Data from a recent study by Olumese and Oboh involving 30 healthy participants demonstrated a further reduction in blood glucose levels by 34.5% after four weeks of consuming a 10% beetroot juice solution (Olumese and Oboh, 2016), compared to baseline and washout periods. However, this reduction was not observed after just two weeks of the intervention. Similar to its hypotensive effects, these findings suggest that sustained consumption of beetroot juice may be required to achieve lasting improvements in blood glucose and insulin responses (Wootton-Beard et al., 2014).

An observational study conducted by Wootton-Beard et al on the phytochemical composition of 225 mL beetroot juice in 16 healthy adults examined its postprandial effects. Three samples, each containing 50g of available carbohydrates, were tested: beetroot juice with lemon (sample 1), a sugar-matched control drink with sucrose, fructose, and glucose (sample 2), and glucose alone (sample 3). The study found that the glycemic and insulin responses were higher for beetroot juice with lemon (sample 1) compared to the other two drinks. Both beetroot juice samples (1 and 2) produced significantly lower glycemic responses than the glucose-only drink (sample 3). Although insulin response was lower with beetroot juice compared to the control drink, the difference was not statistically significant. These findings suggest that the polyphenol-rich content of beetroot juice may contribute to delayed rises in postprandial glucose and insulin levels (Wootton-Beard et al., 2014).

Kumar (2016) et al. treated diabetic rats with either 400 mg/kg of ethanolic extract of beetroot juice (EEBT) or 5 mg/kg of Glibenclamide. The study showed that EEBT reduced serum triglyceride (TG) and cholesterol levels, with effects comparable to Glibenclamide. After 21 days of treatment, EEBT significantly lowered cholesterol and TG levels compared to untreated diabetic rats. The findings suggest that beetroot juice may help reduce blood glucose levels and insulin resistance similar to standard diabetes medication. These studies suggest that beetroot's bioactive compounds enhance insulin secretion and sensitivity.

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However, results from clinical trials remain mixed, with some studies failing to show significant hypoglycemic effects. The variability in outcomes may be due to differences in study design, population characteristics, and dosage of beetroot juice.

Potential Synergy with Conventional Treatments

Given its mechanisms of action, beetroot juice may serve as an adjunct therapy for managing hyperglycemia, especially in individuals with early-stage insulin resistance or metabolic syndrome. Its nitrate content could complement the actions of conventional diabetes medications like Glibenclamide, which also targets AMPK activation (Sravan Kumar et al., 2016). However, larger clinical trials are needed to confirm these synergies and establish optimal dosing protocols.

Limitations and Considerations

High levels of beetroot consumption can result in beeturia, a harmless condition where urine or stool turns pink or red due to the presence of betanin, a pigment in beets. While it may seem alarming, beeturia is generally benign and temporary. The pigment is not fully broken down in some individuals, leading to its excretion via the kidneys. This condition is observed in 10-14% of people but can also be linked to iron deficiency or low stomach acid, which affects the body's ability to process certain nutrients. For most people, the discoloration fades shortly after stopping beetroot intake. Additionally, due to its nitrate content, individuals with oxalate kidney stones or low blood pressure should exercise caution when consuming high amounts of beetroot juice, as it may exacerbate these conditions.

Furthermore, there is a need for more large-scale, long-term clinical studies to confirm the effectiveness of beetroot juice in hyperglycemia management and to establish standardized dosing regimens.

IMPLICATION TO RESEARCH AND PRACTICE

Beetroot juice's potential therapeutic benefits can be enhanced by exploring its biochemical pathways, including nitric oxide content and antioxidant properties. Further clinical trials and comparative studies could evaluate its efficacy and safety. Interdisciplinary collaboration between nutritionists, healthcare providers, and researchers is crucial.

CONCLUSION

Beetroot juice, with its rich composition of nitrates, antioxidants, and anti-inflammatory compounds, offers significant potential as a complementary therapy for hyperglycemia management. Its ability to improve insulin sensitivity, reduce oxidative stress, inhibit carbohydrate-digesting enzymes, and lower blood pressure makes it a promising candidate for dietary intervention in diabetes management. While preliminary studies indicate potential benefits, more robust, long-term clinical trials are needed to fully understand its role in diabetes management. If proven effective, beetroot juice could become part of a broader dietary strategy to help mitigate the growing burden of diabetes.

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FUTURE RESEARCH

Future research could focus on the effects of beetroot juice on blood glucose levels in different populations; including people with type 1 and type 2 diabetes, long-term consequences of consistent consumption on insulin sensitivity, glycemic management, and general metabolic health and effects of beetroot juice on gut flora and its financial implications in comparison to conventional treatments

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