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The Effect of Stevia Leaves as a Sugar Substitute in Reducing the Risk of Kidney Failure: A Literature Study

Riza Andrian Ibrahim[1*], Nestia Lianingsih[2], Rini Cahyandari[3]

[1]*Doctoral of Mathematics Study Program, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Sumedang 45363, Indonesia*

[2]*Master's Program of Mathematics, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jatinangor, West Java, Indonesia*

[3]*Department of Mathematics, Faculty of Science and Technology, UIN Sunan Gunung Djati Bandung*

**Corresponding author email: riza17005@mail.unpad.ac.id*

Abstract

Excessive sugar consumption has been linked to an increased risk of kidney failure, prompting research into alternative sweeteners. This literature study investigates the potential of Stevia leaves (Stevia rebaudiana) as a sugar substitute in reducing the risk of kidney failure. A comprehensive review of studies published between 2013 and 2023 was conducted using databases such as PubMed, ScienceDirect, and Google Scholar. The analysis revealed that high sugar intake, particularly from sweetened beverages, is associated with a higher risk of chronic kidney disease (CKD). Stevia, a zero-calorie sweetener, demonstrated promising results in weight management and glycemic control, both crucial factors in kidney health. Several studies reported improvements in kidney function markers, including serum creatinine and microalbumin levels, in CKD patients supplemented with Stevia. Additionally, Stevia's antioxidant properties may protect kidney tissues from oxidative stress. While the findings suggest Stevia's potential as a beneficial sugar substitute for kidney health, limitations in current research, including short study durations and unclear mechanisms of action, highlight the need for more comprehensive, long-term studies. This review concludes that Stevia shows promise as a tool in the prevention and management of kidney diseases, but further research is needed to fully understand its role and optimize its use in dietary interventions for kidney health.

Keywords: Stevia Rebaudiana, Sugar Substitute, Kidney Failure, Chronic Kidney Disease (CKD), Renoprotection.

1. Introduction

Kidney failure is a condition of decreased kidney function in filtering waste from the body's metabolism from the blood and excreting it through urine. This condition causes levels of toxins and dangerous fluids to settle in the body and can be fatal if left untreated. People with kidney failure may not feel any symptoms and can only be detected through laboratory tests. Some symptoms that can appear in people with kidney failure such as chest pain, high blood pressure or hypertension, fluid accumulation so that the body appears swollen (edema) and reduced urine production (Siloam Hospitals Medical Team, 2024).

Some risk factors that contribute to the development of kidney failure include hypertension, diabetes, and excessive sugar consumption. Sugar, especially in the form of fructose and sucrose (Karalius and Shoham, 2013), sucrose is a type of sugar that we commonly encounter. One of the most popular forms of sucrose is granulated sugar. Based on its chemical composition, sugar is basically divided into two groups, namely disaccharides and monosaccharides. Sucrose is a type of sugar that is included in the disaccharide group, while glucose and fructose are monosaccharides. Disaccharide sugar itself is formed from two monosaccharides. This means that sucrose is a sugar that is formed from fructose and glucose. Sucrose can be found naturally in fruits, vegetables, and grains. This type of sugar is also often added to various food products such as ice cream, cereals, candy, and canned foods.

Fructose is a type of monosaccharide sugar that is often also referred to as fruit sugar and can be found naturally in fruits, honey, agave, and tubers (Awuchi and Amagwula, 2021). This component can also be processed from sugar cane and corn. Artificial fructose, which is often found in various packaged foods and drinks, usually comes in the form of high fructose corn syrup. Compared to sucrose and glucose, fructose tastes the sweetest. However, this type of

sugar has little effect on blood sugar levels. However, that does not mean that fructose can be consumed excessively. In the long term, high levels of fructose can trigger an increase in triglyceride levels in the blood and increase the risk of metabolic syndrome and fatty liver (Prahastuti, 2011).

High fructose consumption, which causes diabetes, hypertension, obesity, and metabolic syndrome, increases the risk of chronic kidney disease. Uric acid can damage the kidneys directly by causing scarring of the kidneys. This can lead to increased pressure within the glomerulus (the functioning unit of the kidney) which can have a detrimental effect on the kidneys. In patients with chronic kidney disease, this can worsen the loss of protein in the urine (proteinuria).

Kidney failure occurs when the kidneys lose their ability to effectively filter waste products and excess fluids from the blood. This condition can be classified into acute kidney injury (AKI) and chronic kidney disease (CKD), which can progress to end-stage renal disease (ESRD). AKI can arise from prerenal factors, such as reduced blood flow due to dehydration or heart failure, intrinsic renal factors involving damage to kidney tissue (e.g., acute tubular necrosis), or postrenal factors due to obstruction of urine flow (e.g., kidney stones) . The underlying mechanisms often involve ischemia or nephrotoxicity, leading to cell death and inflammation. In contrast, CKD is characterized by a gradual loss of kidney function over time, commonly caused by diabetes, hypertension, glomerulonephritis, and polycystic kidney disease. The initial injury leads to compensatory hyperfiltration in remaining nephrons, which can cause further damage, ultimately resulting in fibrosis and a decline in glomerular filtration rate (GFR) (Neuen et al., 2019).

Along with the increasing public awareness of the dangers of sugar consumption, various alternative natural sweeteners have begun to be developed and popularized. One of the natural sweeteners that has begun to gain attention is stevia leaves (Stevia rebaudiana). The stevia plant is a shrub from the Asteraceae (Compositae) family, approximately 65 cm tall, has a round, segmented, multi-branched stem, and is green in color. The leaves are single, opposite, oval-shaped, have hermaphroditic flowers, a purple tubular crown, and have taproots.

2. Literature Review

2.1. Kidney failure

Kidney failure is a condition in which the kidneys are unable to perform their excretory function properly, resulting in the retention of nitrogenous waste products in the bloodstream. This occurs due to the inability of the kidneys to remove waste products, regulate electrolyte levels, participate in the synthesis of the hormone erythropoietin, and the metabolism of low molecular weight proteins such as insulin. Kidney failure can be caused by a variety of factors, including hypertension, type 2 diabetes mellitus, glomerulonephritis, polycystic kidney disease, infections, certain medications, and genetic factors. This condition is more common in men than women and its prevalence increases with age (Mohsen et al., 2023).

Based on information from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website, prevention of chronic kidney disease (CKD) Prevention strategies focus on maintaining a healthy lifestyle and managing health conditions that can increase the risk of kidney disease. Key steps include adopting a healthy diet with increased consumption of fresh fruits, vegetables, whole grains, and low-fat dairy products, and reducing salt and added sugar intake. Regular physical activity, at least 30 minutes each day, is also very important for maintaining kidney health. Maintaining an ideal body weight, getting enough sleep (7-8 hours each night), and quitting smoking are additional steps that can help prevent kidney failure. Limiting alcohol consumption and managing stress through activities such as meditation, yoga, or tai chi also play a role in maintaining overall kidney health.

2.2. The Role of Sugar in Kidney Health

In one of the studies conducted by Heo et al., (2024) entitled Sweetened Beverage Intake and Incident Chronic Kidney Disease in the UK Biobank Study, it was stated that consuming more than 1 serving of sweet drinks per day was associated with a higher risk of CKD. The fairly high sugar content in sweet drinks can increase blood sugar levels and increase the risk of diabetes. Diabetes can cause complications in the kidneys, eyes, and heart.

Kumar et al., (2023) expressed an opinion excessive sugar consumption, particularly in the form of refined sugars and high-fructose corn syrup, can have a detrimental impact on kidney health, especially for individuals with diabetes. Chronic high sugar intake leads to hyperglycemia, a condition characterized by elevated blood glucose levels, which is a significant risk factor for developing diabetic nephropathy. This condition results in structural and functional changes in the kidneys, damaging the renal microvasculature and impairing kidney function, potentially leading to end-stage renal disease (ESRD).

Excessive sugar intake, especially in the form of sugary beverages and processed foods, can lead to obesity and insulin resistance, both of which are precursors to type 2 diabetes. As diabetes progresses, it can cause damage to the blood vessels in the kidneys, impairing their ability to filter waste effectively. This damage can lead to diabetic kidney disease (DKD), which has become the leading cause of kidney failure in Indonesia, as noted in the study. Furthermore, high sugar consumption can exacerbate other risk factors for CKD, such as hypertension, by promoting weight gain

and increasing the likelihood of developing metabolic syndrome. The cumulative effect of these factors underscores the importance of reducing sugar intake as a preventive measure for maintaining kidney health (Hustrini et al., 2023).

2.3. Stevia Leaves as a Sugar Substitute

In a study by Raghavan et al., (2023) *titled "Effects of Sugar Replacement with Stevia-Based Tabletop Sweetener on Body Weight and Cardiometabolic Health in Indian Adults,"* researchers explored the impact of sugar replacement with stevia-based sweetener on body weight and cardiometabolic health. This open-label, single-arm pilot study enrolled overweight and prediabetic adults in India over a 90-day period. The 90-day study resulted in significant weight and waist circumference reduction in overweight subjects. Subjects who replaced sugar with stevia experienced an average weight loss of 1.63 kg to 2.12 kg, and a reduction in waist circumference of 1.49 to 4.78 cm. These results demonstrate the potential of stevia as a natural alternative to reduce calorie intake and improve cardiometabolic health, without adverse side effects.

In the study *"Effect of the Proportion of Stevia Leaf Extract (Stevia rebaudiana B) on the Chemical Characteristic Properties of Functional Pudding,"* Mujianto et al., (2024) explore how varying proportions of stevia leaf extract influence the physicochemical properties of functional pudding. The research highlights the potential of stevia, a natural sweetener with minimal impact on blood sugar levels, as a low-calorie alternative in dessert formulations. Through systematic experimentation, it was found that different concentrations of stevia leaf extract led to significant changes in the pudding's water, ash, fat, protein, and carbohydrate contents. Notably, the sample with the highest stevia concentration (F6) exhibited a high-water content of 88.31%, low ash content of 0.49%, moderate fat content of 0.81%, elevated protein content of 5.35%, and reduced carbohydrate content of 5.02% . These findings suggest that stevia leaf extract can be effectively used as a functional ingredient in pudding formulations, contributing to the development of healthier dessert options.

The Acceptable Daily Intake (ADI) for high-purity steviol glycosides, established by JECFA, is 4 mg/kg of body weight per day, expressed as steviol equivalents. This translates to approximately 12 mg of high-purity stevia extracts per kg of body weight per day. The ADI was determined using a safety factor of 100, accounting for potential differences between humans and animals, as well as variations within the human population, including between children and adults. To put this into perspective, a person weighing 70 kg (about 150 lbs) would have to consume approximately 40 packets of tabletop stevia sweetener daily, each containing 21 mg of steviol glycosides, to reach the maximum ADI. This calculation demonstrates the substantial margin of safety built into the ADI, ensuring that even high levels of stevia consumption pose no appreciable health risk (Ashwell, 2015).

In another study conducted by Saharudin et al., (2020) examining the effects of stevia as a sugar substitute, 73 medical students and eight doses participated by replacing sugar with commercially available stevia in their morning drinks for one week. The findings revealed that 66.7% of students liked the taste of stevia, although 74.1% experienced an aftertaste, and 65.4% felt a change in the taste of their drinks. Interestingly, 34.6% of participants reported feeling full quickly, while 16.0% noted an increase in carbohydrate cravings. Although reactions to the taste varied, 95.1% of respondents were inclined to recommend stevia for diabetic patients. However, the lecturer group showed less enthusiasm, with 66.7% disliking the taste. The study also found a significant positive correlation between the amount of stevia used and liking the taste, and a negative correlation between the perceived change in taste and its overall acceptability.

Limanto (2017) argues that stevia has several advantages, including having a sweetness level that reaches 300 times the sweetness of sucrose. In addition, stevia consumption can lower systolic and diastolic blood pressure. Low calorie content makes stevia safe for consumption by people with diabetes and obesity. The lack of genotoxicity data as a result of excessive stevia consumption, makes stevia still prohibited for consumption in several other countries including the United States and Indonesia. However, several researchers continue to warn to consume stevia within safe limits, namely 0.1 - 4 mg per kg of body weight. In addition, in-vitro studies report the potential of Stevia rebaudiana extract as an anti-cancer drug.

2.4. The relationship between Stevia and kidney health

Stevia is a zero-calorie sugar substitute, approved as safe by the FDA and EFSA. Studies have shown that stevia has antiglycemic and antioxidant properties, helps reduce blood pressure and hepatic steatosis, stabilizes atherosclerotic plaque, and improves liver and kidney health. The metabolism of steviol glycosides to steviol, which can be absorbed by the body, depends on the gut microbiota. This review discusses how stevia consumption affects the gut microbiota (Kasti et al., 2022).

In a study exploring the relationship between Stevia and kidney health, Stevia was found to have potential benefits for patients with chronic kidney disease (CKD). The randomized, placebo-controlled trial involved 97 participants who were administered Stevia capsules alongside conventional antihypertensive and antidiabetic medications for three months. Results indicated significant improvements in several biochemical parameters, including reductions in serum creatinine, serum uric acid, fasting blood sugar, postprandial blood sugar, and microalbumin levels. These findings

suggest that Stevia may contribute positively to managing CKD, although further research is needed to confirm these effects over a longer period (Rizwan et al, 2018).

Stevia rebaudiana, a plant native to Paraguay and now cultivated globally, is renowned for its high-potency sweeteners, particularly stevioside and rebaudioside A, which are significantly sweeter than sucrose. Beyond its role as a natural sweetener, Stevia exhibits various health benefits, as supported by preclinical and clinical studies. These studies suggest that Stevia and its compounds are non-toxic and possess therapeutic properties, including the ability to stimulate insulin production, improve polycystic kidney disease, and offer chemotherapeutic benefits in cancer treatment. Additionally, Stevia's rich composition, which includes flavonoids and fatty acids, contributes to its antibacterial, antioxidant, and immunomodulating effects (Peteliuk et al., 2021).

Stevia is known to contain steviol glycoside compounds that have a taste 150-300 times sweeter when compared to regular sugar, but have lower calories. Because it has a very sweet taste, the use of stevia leaf extract does not need to be as much as granulated sugar. This is what makes stevia leaves often used as a substitute for granulated sugar for diabetics. In fact, the use of stevia is known to suppress glucose levels and increase the production of the insulin hormone which functions to control glucose in the blood. In addition, stevia can help minimize the risk of liver and kidney damage which are often complications of diabetes (Tim Medis Siloam Hospitals. 2024).

3. Research Methods

3.1. Research Design

This study uses a literature study method to collect and analyze data from various relevant scientific sources. Literature study was chosen as the main approach because it allows researchers to evaluate and synthesize findings from a number of previously published studies on the effects of stevia as a sugar substitute on kidney health.

3.2. Literature Selection Criteria:

Inclusion criteria for literature selection include:

a). Research published in the last 10 years (2013-2023).
b). Research that focuses on the use of stevia as a sugar substitute.
c). Research that assesses the effects of stevia on kidney health, especially in the context of preventing or managing kidney failure.
d). Exclusion criteria include:
e). Research that is not available in full text.
f). Studies that are not conducted in humans or are not relevant to kidney health.
g). Research that does not use stevia as a primary variable.

3.3. Data Sources

Relevant literature will be searched from several credible scientific databases, including PubMed, ScienceDirect, and Google Scholar. The search will be conducted using keywords such as "stevia," "renal function," "kidney health," "chronic kidney disease," and "sugar substitute."

3.4. Data Analysis

Data obtained from the selected studies will be analyzed by comparing the results of studies related to the effects of stevia consumption on the risk of kidney failure. Identified patterns or relationships will be evaluated, and evidence supporting or refuting the hypothesis that stevia can reduce the risk of kidney failure will be identified and critically interpreted.

4. Results and Discussion

4.1. Effects of Sugar Consumption on Kidney Health

The literature review revealed a strong connection between excessive sugar consumption and increased risk of kidney problems. Key findings include:

a). High sugar intake, particularly from sweetened beverages, is associated with a higher risk of chronic kidney disease (CKD) (Heo et al., 2024).
b). Excessive sugar consumption can lead to hyperglycemia, a significant risk factor for diabetic nephropathy, potentially progressing to end-stage renal disease (ESRD) (Kumar et al., 2023).

c). Sugar overconsumption contributes to obesity and insulin resistance, precursors to type 2 diabetes, which can damage kidney blood vessels and impair filtration function (Hustrini et al., 2023).

These findings underscore the importance of reducing sugar intake as a preventive measure for maintaining kidney health.

4.2. Stevia as a Sugar Substitute

Several studies have demonstrated the potential benefits of using stevia as a sugar substitute:

a). Raghavan et al. (2023) found that replacing sugar with stevia-based sweeteners led to significant weight loss and reduced waist circumference in overweight and prediabetic adults over a 90-day period.
b). Mujianto et al. (2024) showed that stevia leaf extract could be effectively used in pudding formulations, potentially contributing to the development of healthier dessert options.
c). Saharudin et al. (2020) reported that while taste perceptions varied, the majority of participants (95.1%) were inclined to recommend stevia for diabetic patients.
d). The Acceptable Daily Intake (ADI) for high-purity steviol glycosides, established by JECFA, indicates a substantial margin of safety for stevia consumption (Ashwell, 2015).

4.3. Stevia and Kidney Health

The review of literature revealed several potential benefits of stevia for kidney health:

a). Kasti et al. (2022) reported that stevia has antiglycemic and antioxidant properties, and may help improve liver and kidney health.
b). A randomized, placebo-controlled trial by Rizwan et al. (2018) found that stevia supplementation in patients with chronic kidney disease led to significant improvements in several biochemical parameters, including reductions in serum creatinine, uric acid, and microalbumin levels.
c). Peteliuk et al. (2021) highlighted that stevia and its compounds are non-toxic and possess therapeutic properties, including the ability to improve polycystic kidney disease.
d). Tim Medis Siloam Hospitals (2024) noted that stevia use can help minimize the risk of liver and kidney damage, which are often complications of diabetes.

4.4. Limitations and Future Research Directions

While the results are promising, several limitations and areas for future research were identified:

a). Many studies were conducted over relatively short periods. Longer-term studies are needed to assess the sustained effects of stevia on kidney health.
b). Further research is required to elucidate the exact mechanisms by which stevia may protect kidney function.
c). More studies are needed to determine the optimal dosage of stevia for kidney health benefits while avoiding potential side effects.
d). Additional research should explore how stevia's effects may vary across different populations, including those with pre-existing kidney conditions.
e). Comparative studies between stevia and other sugar alternatives could provide valuable insights into their relative efficacy in protecting kidney health.

5. Discussion

The comprehensive review of literature reveals a complex interplay between sugar consumption, the use of stevia as a sugar substitute, and kidney health. This discussion aims to interpret the findings, draw connections between different studies, and explore the implications for kidney health management.

5.1. Sugar Consumption and Kidney Health Risks

The detrimental effects of excessive sugar consumption on kidney health are well-documented in the reviewed literature. Heo et al. (2024) and Kumar et al. (2023) both highlight the association between high sugar intake and increased risk of chronic kidney disease (CKD). This relationship appears to be mediated through multiple pathways:

a). Hyperglycemia resulting from high sugar intake can directly damage kidney tissues, leading to diabetic nephropathy.
b). Sugar overconsumption contributes to obesity and insulin resistance, which are precursors to type 2 diabetes – a major risk factor for kidney disease.
c). Excessive sugar intake is linked to metabolic syndrome, which includes hypertension and obesity, both of which can negatively impact kidney function.

5.2. Stevia as a Promising Sugar Alternative

The studies on stevia present it as a promising alternative to sugar, with potential benefits extending beyond simple calorie reduction:

a). Weight management: Raghavan et al. (2023) demonstrated significant weight loss and reduced waist circumference in participants who replaced sugar with stevia-based sweeteners. This is crucial, as obesity is a risk factor for both diabetes and kidney disease.
b). Multiple studies, including those by Kumar et al. (2023) and Tim Medis Siloam Hospitals (2024), suggest that stevia may help in controlling blood glucose levels. This is particularly relevant for preventing diabetic nephropathy.
c). The high Acceptable Daily Intake (ADI) for steviol glycosides, as reported by Ashwell (2015), indicates a wide margin of safety for stevia consumption. This is reassuring for its potential long-term use as a sugar substitute.
d). Mujianto et al. (2024) showed that stevia could be effectively used in food formulations, suggesting its potential as a practical sugar alternative in various dietary contexts.

5.3. Stevia and Kidney Health: Emerging Evidence

The most intriguing findings relate to stevia's potential direct benefits on kidney health:

a). Rizwan et al. (2018) reported significant improvements in several kidney function markers, including serum creatinine and microalbumin levels, in CKD patients supplemented with stevia. This suggests that stevia might have renoprotective effects beyond its role as a sugar substitute.
b). Kasti et al. (2022) highlighted stevia's antioxidant properties, which could potentially protect kidney tissues from oxidative stress – a key factor in the progression of kidney disease.
c). Peteliuk et al. (2021) noted stevia's potential in improving polycystic kidney disease, hinting at broader therapeutic applications in kidney health.

5.4. Limitations and Future Directions

Despite the promising results, several limitations in the current body of research must be acknowledged:

a). Many of the reviewed studies were conducted over relatively short periods. Long-term studies are crucial to understand the sustained effects of stevia on kidney health.
b). While benefits have been observed, the exact mechanisms by which stevia protects kidney function are not fully understood. Further research into these mechanisms could inform more targeted use of stevia in kidney health management.
c). Most studies focused on general populations or those with diabetes. More research is needed on the effects of stevia in populations with existing kidney conditions at various stages.
d). Determining the optimal dosage of stevia for maximal kidney health benefits while minimizing potential side effects is an important area for future research.
e). Studies comparing stevia with other sugar alternatives in the context of kidney health could provide valuable insights for dietary recommendations.

6. Conclusion

The reviewed literature presents a compelling case for the potential of stevia as a beneficial sugar substitute in the context of kidney health. Its ability to aid in weight management and glycemic control, coupled with possible direct renoprotective effects, positions stevia as a promising tool in the prevention and management of kidney diseases. However, the limitations in current research highlight the need for more comprehensive, long-term studies to fully understand stevia's role in kidney health.

As diabetes and chronic kidney disease continue to pose significant public health challenges, the potential of stevia to offer a safe, effective alternative to sugar is particularly relevant. Future research addressing the identified gaps could pave the way for more targeted use of stevia in dietary interventions aimed at preserving kidney function and managing kidney diseases.

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