



Literature Review: Cranberry as Prophylaxis for Dapagliflozin-Induced Urinary Tract Infections

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Abstract

Urinary tract infections [UTIs] are a common occurrence among type 2 diabetic patients using sodium-glucose cotransporter-2 [SGLT2] inhibitors to manage their diabetes. Dapagliflozin is among the most widely prescribed SGLT2i's, and it achieves the desired effect by inhibiting the reabsorption of glucose in the kidney's proximal tubule, thereby increasing the excretion of glucose via the urinary tract. However, this mechanism of action of SGLT2i's leads to glucosuria, which increases the risk of UTIs. Since cranberries contain many beneficial medicinal compounds, including proanthocyanidins, this literature review study sought to establish the potential of using cranberries as a prophylaxis for dapagliflozin-induced UTI.

Keywords: Sodium-glucose cotransporter-2; dapagliflozin; glucose absorption; Urinary tract infections; glucosuria; cranberry.

1. Introduction

The state of healthcare research has changed over the last couple of years, with researchers expanding their studies to analyze the impacts or side effects of the medication applied to common diseases. In recent years, cases of diabetes have increased, with research showing that its global prevalence is at 460 million and is expected to reach 700 million in the next twenty years [1:2303]. Diabetes is a complex chronic disease that can be caused by genetic and lifestyle factors such as poor dietary habits, overweight, and insulin resistance, among others.

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The treatment of diabetes, especially Type 2 Diabetes Meletus [T2DM], can be through pharmacologic therapy, which aims to achieve the glycemic target through lifestyle changes. Sodium-glucose cotransporter-2 [SGLT2] inhibitors are used [2:2]. Among the most used SGLT2 inhibitors is dapagliflozin, which is responsible for glucose absorption in the gut that is later excreted in the urine [3, 1136]. Even though dapagliflozin has been considered effective in addressing T2DM in most patients, it is associated with increasing cases of Urinary tract infections [UTI]. This literature review explores the potential role of cranberry as prophylaxis against UTIs induced by dapagliflozin.

2. Objectives

Despite being considered effective in addressing Type 2 diabetes, the use of SGLT2 has been linked with rising cases of UTIs. According to [6:90], UTI is a “broad term that encompasses a spectrum of infectious syndromes that affect the urinary tract anywhere from the urethra to the kidneys.” UTIs have a higher prevalence in women [50%] than in men [12%] and mainly affect people in their early 20s or after age 85 [10:1]. Research studies conducted by individual scholars, governmental, and non-governmental organizations have highlighted the risk of increased UTI infections resulting from the use of SGLT2, like dapagliflozin. In 2015, the FDA, which is responsible for regulating drugs and food products in the USA, announced that the use of SGLT2 caused a serious risk of UTI [8:2]. Another study conducted by [4:1] cited the work of Hirji and his colleagues, which showed that there was a 46.9 occurrence of UTI among 1000 patients with diabetes while the prevalence of UTI was 29.9 for 1000 individuals without diabetes.

A retrospective cohort study was conducted involving two groups of patients, all of whom had been diagnosed with type 2 diabetes. One group had patients who were using SGLT2 inhibitors, while the other groups was using other forms of medications. The study had a total of 853 patients, with the group using SGLT2 having 418 patients and the other having 435 patients. For the first group, patients were further divided into two categories: those using dapagliflozin [200, 47.85%] and those using empagliflozin [218, 52.15%]. The study results showed a higher incidence rate for UTI among patients using SGLT2, with the possibility of UTI being 33.49%, while patients using other medications had a UTI incidence rate of 11.72% [4:4]. Additionally, there was a higher possibility for patients using dapagliflozin over those using empagliflozin, with a slight difference of 1% between the two inhibitors. The research confirms that the use of SGLT2 inhibitors increases the development of UTI in diabetic patients.

The above information provides irrefutable proof that the use of dapagliflozin results in the occurrence of UTIs in diabetic patients. The main objective of this research is to analyze how cranberry can be used to address UTI cases in diabetic patients using SGLT2 inhibitors such as dapagliflozin. The review also shows how the use of dapagliflozin increases the occurrence of UTI and provides additional clinical trials that show this association.

3. Significance of the Study

This research study is significant as analyzing the role of cranberry in preventing dapagliflozin-induced UTI preventing is essential to both patients and healthcare professionals. This study is of practical value since

dapagliflozin and other SGLT2i's are among the market leaders in anti-diabetic medications that are commonly prescribed. The study results indicate that UTIs and diabetes are the two major diseases. The research study contributes to a greater understanding of avoiding and treating these diseases. The research also highlights ways healthcare officials can improve patient care and their overall well-being, as UTI is associated with high levels of discomfort and pain and may cause further complications when untreated.

4. Materials and Methods

A comprehensive literature search was conducted to identify studies evaluating the use of cranberry as prophylaxis for dapagliflozin-induced urinary tract infections [UTIs]. The electronic databases, including PubMed, Cochrane Library, Embase, and Scopus, were searched for relevant articles published between 2018 and 2024. Further, the references of the eligible articles were manually retrieved and searched to identify potentially relevant or eligible publications. Additionally, the included studies investigated the effectiveness of cranberry and cranberry products and extracts in preventing UTIs, were published in peer-reviewed journals, and were written in English. Articles that did not meet this inclusion criteria were excluded from the review. The search terms included Urinary Tract Infections[s], UTI, cranberry, glycosuria, sodium-glucose cotransporter-2, Type 2 Diabetes Mellitus, dapagliflozin, and glucose absorption. Ethical approvals were not required since all the studies included in this review were officially published in peer-reviewed journals.

5. Discussion

The utilization of SGLT2 inhibitors such as dapagliflozin in the management of type 2 diabetes is associated with increased incidences of UTIs due to the drug's mechanism of action. SGLT2i's achieve the desired effect of controlling glycemic levels by inhibiting the reabsorption of glucose in the S1 and S2 segments of the proximal tubule, where an estimated 97% of filtered glucose is reabsorbed [14:894]. The inhibition of the proximal tubule's glucose reabsorption capacity leads to increased glucose secretion through the urinary tract [6:2]. Studies by [3:1135] and [15:777861] showed that SGLT2i's prevent glucose reabsorption in the kidney, which is rechanneled to the urinary tract for excretion. According to [1:2304] and [15:211], SGLT2i's induce glycosuria which directly lowers glucose by an estimated 80 g per day through an insulin-independent process. The resultant SGLT2i's-induced glucosuria promotes uropathogenic bacterial growth, which increases the risk of UTIs [7:10]. Thus, although SGLT2i's lead to improved glycemic control by inhibiting glucose reabsorption in the proximal tubule and triggering increased glucose excretion through the urinary tract, the resultant glucosuria increases the likelihood of UTIs among type 2 diabetic people.

Cranberry has a rich history of its application as an herbal product to cure and treat illnesses as a leisure fruit or juice. The berry, which is widely grown in many parts across the globe, contains medically valuable compounds, such as flavonoids, anthocyanins, organic acids, vitamin C, and other bioactive compounds. Multiple studies have shown that proanthocyanidins enhance in vitro and urinary bacterial anti-adhesion activities, thus bolstering the maintenance of urinary tract health and relieving UTI-related symptoms such as pain and discomfort [9:2. 10:CD001321]. These proanthocyanidins are a category of defense and offense polyphenols with antimicrobial effectiveness, which prevent bacterial biofilm from forming in the urinary tract

lining and even deter the activation of Escherichia coli [E. coli]. Another study by [17:764] corroborated these findings and established that cranberries contain fungistatic benzoic acid, which impedes the adherence of p-fimbriae of E. coli in the Genito-urinary tract.

The preventive effects against UTI can be acquired by using cranberry as a fresh, dried fruit or as a juice [9:5]. Another comprehensive study by [11:120] showed that cranberries retain their efficacy against uropathogens when consumed in multiple forms, including as a dry extract, an extraction solvent of ethanol [70%], and even as capsules.[12:14] also established that cranberry prevents UTI occurrence and recurrence by impeding their attachment onto the walls of the urinary tract. [13:399] affirmed these findings in a study involving 23 women, who reported a reduction in UTIs after being subjected to cranberry juice intake for six months. Despite these positive effects of cranberry against UTIs, there are concerns that it could trigger a spike in blood sugar levels. However, the study by [17:764] and [18:782] showed that cranberry extracts did not have any effect on glycemic values. Cumulatively, the findings of these study demonstrate that cranberries are an effective nutrition-based nonantibiotic intervention to prevent and treat UTI among type 2 diabetic patients using SGLT2i's.

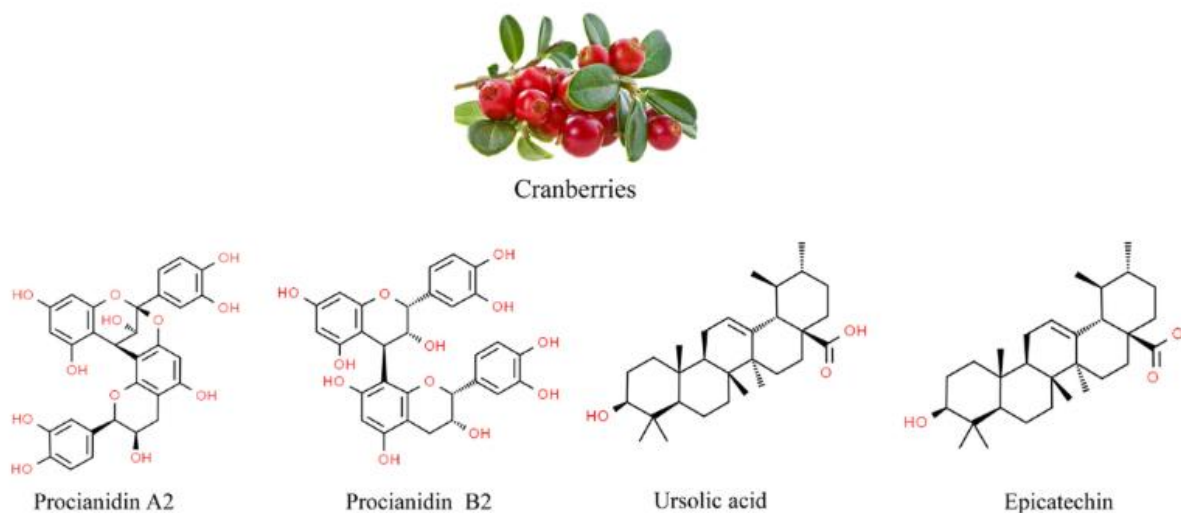


Figure 1: Cranberries

6. Conclusion

In conclusion, the use of cranberries presents a potential solution to the development of UTIs that result from the use of SGLT2 inhibitors such as dapagliflozin. Undeniably, the prevalence of diabetes has increased in recent years as a result of lifestyle changes, resulting in increased cases of obesity, among other causes. Since 2013, dapagliflozin, among other SGLT2 inhibitors, has been used by health practitioners to treat type 2 diabetes. However, despite being effective in dealing with T2DM, dapagliflozin was found to increase incidences of UTI. Multiple research studies have highlighted the connection between dapagliflozin and UTI, which necessitates a medication to treat UTI. Cranberries provide an effective solution that can be induced alongside dapagliflozin to prevent the occurrence of UTIs in diabetic patients.

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