



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Sodium-Glucose Co-Transporter 2 Inhibitors in Type 2 Diabetes Mellitus

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ARTICLE INFO

Published: 07 Jul. 2025

Keywords:

Type 2 Diabetes, Sodium Glucose Co-transporter 2 Inhibitor (SGLT 2), Diabetes mellitus, Bexagliflozin, Canagliflozin.

DOI:

10.5281/zenodo.15825999

ABSTRACT

This review gives a detailed look at the latest logical styles used in the pharmaceutical field. Type 2 diabetes mellitus is a long-term metabolic condition that not only affects blood sugar levels but also significantly increases the risk of heart-related complications. More importantly, SGLT2 inhibitors have shown remarkable benefits in protecting both heart and kidney function, making them valuable beyond just blood sugar control. Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are a newer group of antidiabetic drugs that lower blood sugar levels by preventing the kidneys from reabsorbing glucose, leading to its removal through urine. It focuses on Sodium Glucose Co-transporter 2 (SGLT2) inhibitors—Empagliflozin, Dapagliflozin, Canagliflozin, Bexagliflozin, & Ertugliflozin. These medicines come in various forms, like active pharmaceutical ingredients (APIs), liquid solutions, & bright capsules. It is commonly known that SGLT2 inhibitors help control type 2 diabetes. They work by blocking the SGLT2 protein in the kidneys, which leads to getting rid of glucose and helps manage blood sugar levels. This review also provides detailed insights into the chemical structure, molecular properties, IUPAC names, formulas, mechanisms of action, and potential side effects of these drugs. This comprehensive summary supports both academic research and pharmaceutical development by offering updated insights into the evaluation of these antidiabetic agents.

INTRODUCTION

Hyperglycemia, a key feature of diabetes mellitus, is a long-term metabolic condition that arises due to problems with insulin production, insulin function, or both. Diabetes mellitus is classified

into two primary forms: Type 1 diabetes, an autoimmune condition that leads to the destruction of insulin-producing beta cells, and Insulin resistance and relative Insulin production deficiencies are often associated with type 2 diabetes. The global prevalence of diabetes has

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



increased substantially in recent decades, driven by factors such as obesity, sedentary lifestyles, and an aging population. According to the International Diabetes Federation (2023), an estimated 537 million adults worldwide were living with diabetes in 2021, with projections suggesting that this number will rise to 643 million by 2030 (Cho et al., 2023). Early detection and intervention are critical, as diabetes is associated with a range of severe complications, including retinopathy, neuropathy, nephropathy, and cardiovascular disease [1]. Recent research underscores the importance of pharmacological interventions, alongside lifestyle modifications, in the effective management of diabetes. Notably, new classes of medications, such as Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitors and Glucagon-Like Peptide-1 (GLP-1) receptor agonists, have shown promise in improving glucose control and reducing cardiovascular risk. Furthermore, ongoing studies investigating genetic and environmental factors contributing to the pathogenesis of diabetes continue to enhance our understanding of this complex disease [2].

Types of Diabetes Mellitus Include:

- **Type 1 Diabetes Mellitus (T1DM):**
For patients with this kind of condition (T1DM), insulin therapy must be administered continuously.
- **Type 2 Diabetes Mellitus (T2DM):**
This is not an emergency involving insulin.
- **Type 3 Diabetes Mellitus (T3DM):**
It is linked to a number of hormonal disorders, most notably acromegaly, and drugs like glucocorticoids; Oral anti-diabetic therapy typically makes it better.
- **Type 4 Diabetes Mellitus (T4DM):**
Using or not using insulin, this needs to be handled.

Type 2 Diabetes Mellitus:

Dysregulation in the metabolism of proteins, lipids, and carbohydrates is a hallmark of type 2 diabetes mellitus (T2DM), which results in dysregulated blood glucose levels [3]. Maintaining blood glucose within a specified range is the major objective of T2DM management in order to avoid long-term problems [4]. Although type 2 diabetes can occur at any age, middle-aged and older people are the ones who are diagnosed with it most frequently. Being overweight or obese, having a family history of the condition, and being 45 years of age or older are risk factors for acquiring type 2 diabetes. Furthermore, some groups are more vulnerable than others, such as African Americans, Hispanic/Latino, American Indian, Asian American, and Pacific Islander communities. Recent studies have broadened our knowledge of the pathophysiology of type 2 diabetes by demonstrating that it is not exclusively caused by insulin resistance but rather results from at least eight different pathogenic processes. Impaired incretin function, peripheral tissue insulin resistance, elevated hepatic glucose generation, increased lipolysis, altered renal control of glucose homeostasis, incorrect α -cell glucagon secretion, and inappropriate β -cell insulin secretion are some of these processes. The intricacy of type 2 diabetes is highlighted by this multifaceted pathophysiology, which also emphasizes the necessity of focused treatment strategies [5].

SGLT2 Inhibitors:

Gliflozins, also known as sodium-glucose cotransporter 2 inhibitors, are a class of anti-diabetic medications that have been found to enhance renal and cardiovascular outcomes in individuals with and without diabetes. We'll go over the several suggested modes of action for SGLT2i in this review. Gliflozins inhibit renal glucose reabsorption by blocking the SGLT2

cotransporters in the proximal tubules, which causes glucosuria [6]. SGLT2 inhibitors are antihyperglycemic drugs that work by targeting the SGLT2 proteins located in the proximal convoluted tubules of the kidneys, helping to lower blood sugar levels. These drugs prevent the tubular lumen's filtered glucose from being reabsorbed. The Food and Drug Administration (FDA) has approved four SGLT-2 inhibitors so far for adult use: Canagliflozin, Dapagliflozin, Empagliflozin, and Ertugliflozin. Each of the four agents has a different set of approved uses, but

they can all be used by adults with type 2 diabetes mellitus (DM) to better regulate their blood sugar as an addition to diet and exercise [7,8].

Table 1: List of SGLT 2 Inhibitors Drugs

Drugs
Bexagliflozin
Canagliflozin
Dapagliflozin
Ipragliflozin
Empagliflozin
Ertugliflozin
Sotagliflozin

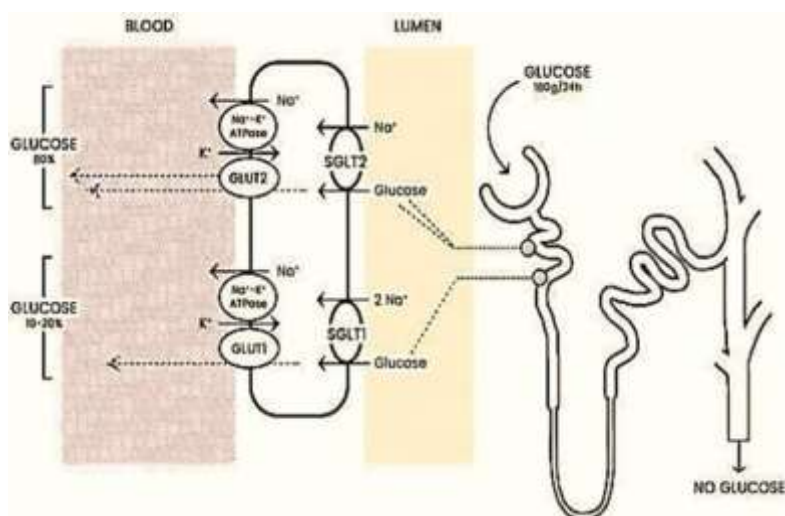


Figure 1: Sodium-glucose co-transporter (SGLT) protein localization and mode of action. The proximal (S1) segments include SGLT2, whereas the S2 and S3 sections of the proximal tubule contain SGLT1.

1. Bexagliflozin:

A glucose molecule, two benzene rings—one connected to the glucose and the other to a methylene group—and a methylene bridge that joins them make up the fundamental structure of SGLT2 inhibitors, including dapagliflozin [9]. An effective and highly selective SGLT2 inhibitor named bexagliflozin is being studied for approval to treat type 2 diabetes. Theracos, Inc. had originally developed it as EGT1442/EGT0001442. situated in Marlborough, Massachusetts [10]

- **Structure:**

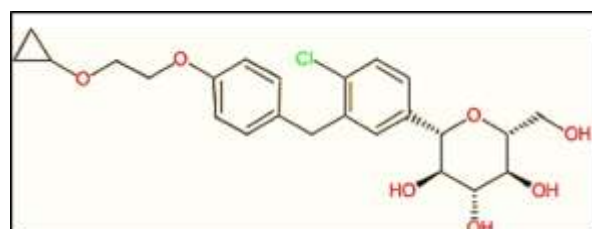


Fig.2: Structure of Bexagliflozin

- **IUPAC name:** 22S,3R,4R,5S,6R)-2-[4-chloro-3-[[4-(2-cyclopropoxyethoxy) phenyl] methyl] phenyl]-6-(hydroxymethyl) oxane-3,4,5-triol.
- **Brand name:** BRENZAVY
- **Molecular formula:** C₂₄H₂₉ClO₇
- **Molecular weight:** 464.94g/mol

Mechanism of action:

Bexagliflozin is considered a highly effective agent for inhibiting the sodium-glucose co-transporter 2 (SGLT2), making it a valuable option in the treatment of type 2 diabetes. Since most glucose reabsorption takes place in the early portion of the kidney's proximal tubule, SGLT2 transporters are primarily found there. It transports salt and glucose from the tubular lumen to the epithelium. Bexagliflozin works by blocking SGLT2 in the kidneys, which reduces glucose reabsorption and promotes its excretion through the urine. Consequently, Bexagliflozin lowers blood glucose levels in people with type 2 diabetes mellitus (T2DM) regardless of insulin sensitivity. These additional effects' mode of action is not entirely understood, but it's plausible that it depends on the Bexagliflozin-induced initial natriuresis and subsequent modifications to tissue sodium management. In addition to increasing glucose management. [11,12] Additionally, bexagliflozin can reduce albuminuria, high blood pressure, and weight loss. [13]

Side effect:

An SGLT2 inhibitor under investigation called bexagliflozin is used to treat type 2 diabetes. The following are the main adverse effects linked to bexagliflozin:

- I. Genital mycotic Infection:**
Elevated risk of yeast infections, especially in females.
- II. Urinary Tract Infection (UTIS):**
Increased frequency of UTIs in comparison to placebo.
- III. Dehydration:**
Possibility of dehydration due to increased urine.
- IV. Hypoglycemia:**

It poses a concern when combined with insulin or insulin secretagogues.

2. Canagliflozin:

Among the substitute oral antidiabetic medicaments of the sodium – glucoseco-transporter 2(SGLT2) inhibitor class is canagliflozin [14]. An asset of sodium glucoseco-transporter 2(SGLT2) called canagliflozin was created to treat grown-ups with type 2 diabetes. It decreases nephro glucose absorption by lowering the renal glucose (RTG) and accelerated urine glucose excretion (UGE). This lowers plasma glucose degrees and causes a net calorie loss. In several Phase 3 trials, canagliflozin helped cases with T2DM whose current treatment plans were n't furnishing enough control over their blood pressure (BP), body weight, or glucose situations. It was also generally well permitted by a large group of cases. A previous pooled disquisition showed that in a global population of Hispanic/ Latino and non- Hispanic/ Latino cases with T2DM, canagliflozin's effectiveness and safety profile were original [15]

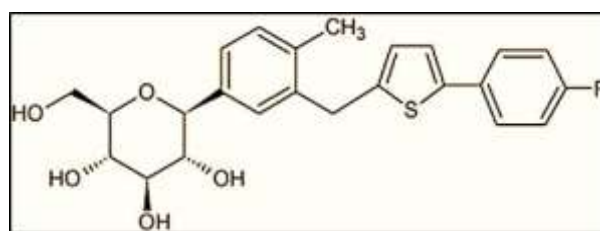
• Structure:

Fig.3: Structure of Canagliflozin

- IUPAC name:** (2S,3R,4R,5S,6R)-2-[3-[[5-(4-fluorophenyl) thiophen-2-yl] methyl] -4-methylphenyl] 6(hydroxymethyl) oxane-3,4,5 triol.
- Brand name:** Invokana
- Molecular weight:** 444.5g/mol
- Molecular formula:** C₂₄H₂₅FO₅S

Mechanism of action:

Reduces glucose reabsorption by inhibiting the kidney's Na-glucose co-transporter 2 (SGLT-2), which raises urine glucose excretion and lowers plasma glucose. The proximal tubule expresses SGLT-2, which helps reabsorb about 90% of filtered glucose.

Side effects [16,17]

Common side effect of canagliflozin is:

- I. Urinary tract infections
- II. Genital mycotic infections
- III. Dehydration

Additionally, it raises the chance of lower limb amputations, especially in those with a history of vascular disease.

3. Dapagliflozin:

A very effective, reversible, and specific sodium-glucose cotransporter-2 inhibitor, dapagliflozin is prescribed globally to treat type 2 diabetes [18]. Dapagliflozin increases the amount of glucose excreted in the urine by blocking renal glucose absorption, which decreases blood glucose levels independently of insulin secretion. It has been demonstrated that dapagliflozin, either as a monotherapy or in combination with metformin, glimepiride, pioglitazone, sitagliptin, or insulin, improves glycemic indices in individuals with type 2 diabetes [19].

- **Structure:**

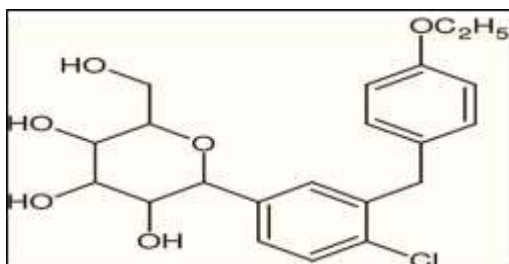


Fig.4: Structure of Dapagliflozin

- **IUPAC name:** (2S,3R,4R,5S,6R)-2-[4-chloro-3-[(4-ethoxyphenyl) methyl] phenyl]-6-(hydroxymethyl) oxane-3,4,5-triol.
- **BRAND NAME:** Forxiga
- **Molecular weight:** 408.9g/mol
- **Molecular formula:** C₂₁H₂₅ClO₆

Mechanism of action:

By significantly lowering glucose absorption, dapagliflozin, a specific and reversible SGLT2 inhibitor, lowers blood sugar levels without the need for insulin. Dapagliflozin Insulin levels and boosts the production of glycogen in T2DM patients [20,21].

Side effect:

I. Genital Infection:

Men and women are more susceptible to genital fungal infections [22].

II. Urinary Tract Infection (UTI):

There have been reports of a higher UTI incidence [23,24].

III. Dehydration and Volume Depletion:

Osmotic diuresis may cause low blood pressure and dehydration [25].

IV. Ketoacidosis:

Diabetic ketoacidosis's risk, especially for those with type 1 diabetes [26,27].

V. Kidney Issues:

Potential for acute renal damage in some individuals [28].

VI. Bone Fracture:

An elevated risk of bone fractures is suggested by certain studies [29].

4. Empagliflozin:

A number of major microvascular and macrovascular problems are linked to type 2 diabetes mellitus (T2DM), a chronic, progressive, and complex illness [30]. Compared to other

members of the class, empagliflozin is a new inhibitor that exhibits greater selectivity for the SGLT2 over other SGLT receptors. Empagliflozin has been recommended for marketing authorization by the European Medicines Agency Committee for Medicinal Products for Human Use, and a new drug application has been filed with the US Food and Drug Administration [31].

• **Structure:**

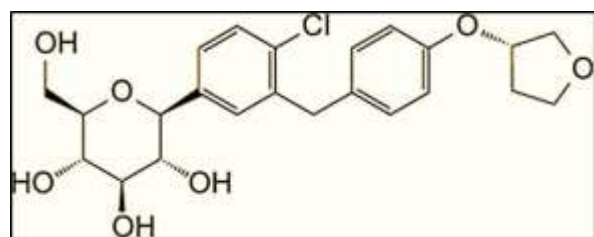


Fig.5: Structure of Empagliflozin

- **IUPAC name:** (2S, 3R, 4R, 5S, 6R) -2- [4-chloro -3- [[4-[(3S)-oxolan-3-yl] oxyphenyl] methyl] phenyl]-6(hydroxy methyl) oxane- 3, 4, 5-triol.
- **Brand name:** Jardiane
- **Molecular formula:** C₂₃H₂₇CO₇
- **Molecular weight:** 450.9g/ml

Mechanism of action:

Empagliflozin inhibits SGLT2, boosting the elimination of glucose in the urine while lowering renal reabsorption. The drug lowers blood sugar levels without the assistance of insulin. Urine glucose excretion increased. When exposed to 10 mg and 25 mg daily, patients with type 2 diabetes increased their intake by 64 to 78 grams, respectively. Empagliflozin's diuretic effects reduce volume and salt load, which results in intravascular contraction. Additionally, empagliflozin has been linked to reduce blood pressure and decrease weight without affecting the pace of the heart [32,33].

Side effects:

The main purpose of empagliflozin, an inhibitor of sodium-glucose cotransporter 2 (SGLT2), is to treat type 2 diabetes. It has possible adverse effects in addition to its potential effectiveness. These are several of the significant negative consequences.

I. Genital mycotic infection:

Empagliflozin can make genital fungal infections more likely, especially in women.

II. Urinary Tract Infection (UTI):

The use of empagliflozin is associated with a higher incidence of UTIs [34].

III. Dehydration and Volume Depletion:

Dehydration brought on by the diuretic action can cause hypotension or dizziness, especially in the elderly or those taking diuretics [35].

IV. Ketoacidosis:

Diabetic ketoacidosis (DKA) is an uncommon but potentially fatal condition that can strike people with type 2 diabetes even when they do not exhibit normal risk factors [36,37].

V. Bone Fracture:

There have been worries about SGLT2 inhibitors, such as empagliflozin, raising the risk of bone fractures [38].

CONCLUSION:

Sodium-glucose co-transporter 2 (SGLT2) inhibitors, including Bexagliflozin, Canagliflozin, Dapagliflozin, and Empagliflozin, represent a promising therapeutic class for the management of type 2 diabetes mellitus (T2DM). These agents are effective as monotherapy, particularly in patients with newly diagnosed diabetes. Available data support a favorable safety profile for SGLT2 inhibitors, although long-term studies are still required to fully assess their impact on cardiovascular outcomes and potential long-term risks. Given their unique mechanism of action, which involves the inhibition of glucose reabsorption in the kidneys, SGLT2 inhibitors

have the potential to evolve as a novel and integral component of T2DM treatment regimens. However, the literature review has also highlighted various side effects associated with these medications, underscoring the importance of monitoring for adverse events during their use. To maximize their therapeutic use and get a deeper understanding of their long-term safety and effectiveness, more study is required.

FUTURE SCOPE:

Despite the growing body of evidence supporting the efficacy and safety of SGLT2 inhibitors in the management of type 2 diabetes mellitus (T2DM), several areas warrant further research:

1. Long-Term Safety Profiles: Ongoing post-marketing surveillance and long-duration clinical trials are essential to assess the chronic safety risks, including renal function decline, bone health, and rare adverse effects like diabetic ketoacidosis.
2. Cardiorenal Protection: Further studies are needed to delineate the specific mechanisms by which SGLT2 inhibitors confer cardiovascular and renal protection, particularly in non-diabetic populations.
3. Personalized Medicine: Research into pharmacogenomics may enable patient-specific therapy, allowing clinicians to predict therapeutic efficacy and minimize side effects based on genetic and metabolic profiles.
4. Combination Therapies: Future studies should explore optimal combinations of SGLT2 inhibitors with other anti-diabetic and cardioprotective agents to enhance overall treatment outcomes.
5. Analytical Advancements: Continued innovation in analytical techniques (e.g., miniaturized, rapid, and cost-effective methods) will improve monitoring of drug levels, efficacy, and patient compliance in clinical settings.
6. Broader Indications: Expanding the clinical application of SGLT2 inhibitors beyond T2DM, such as in type 1 diabetes, heart failure, and chronic kidney disease, requires more focused and condition-specific research.

REFERENCES

1. Kahn SE. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. *Lancet*. 2014 Mar 22;383(9922):1068–83.
2. Davies MJ, et al. Standards of medical care in diabetes—2023. *Diabetes Care*. 2023 Jan;46(Suppl 1): S1–291.
3. DeFronzo RA, et al. Type 2 diabetes mellitus. *Nat Rev Dis Primers*. 2015 Jul 23;1:15019.
4. Kant R, et al. Optimization of a single HPLC-PDA method for quantifying multiple antidiabetic drugs using central composite design. *Bioorg Chem*. 2019 Oct;91:103111.
5. Seman L, et al. Empagliflozin (BI 10773), a potent and selective SGLT2 inhibitor, induces dose-dependent glucosuria in healthy subjects. *Diabetes Obes Metab*. 2013 Nov;15(11):920–8.
6. Fonseca-Correa JI, Correa-Rotter R. Sodium-glucose cotransporter 2 inhibitors mechanisms of action: A review. *Front Med (Lausanne)*. 2021;8:777861.
7. Nespoux J, Vallon V. Renal effects of SGLT2 inhibitors: an update. *Curr Opin Nephrol Hypertens*. 2020 Mar;29(2):190–8.
8. Abdul-Ghani MA, et al. Efficacy and safety of SGLT2 inhibitors in the treatment of type 2 diabetes mellitus. *Curr Diab Rep*. 2012 Jun;12(3):230–8.
9. Bhattacharya S, et al. Structural insights of SGLT2 inhibitors: A novel class of antidiabetic agents. *Eur J Med Chem*. 2020 Oct;204:112523.



10. Azzam O, et al. Bexagliflozin for type 2 diabetes: an overview of the data. *Expert Opin Pharmacother*. 2021 Nov;22(16):2095–103.
11. Cowie MR, Fisher M. SGLT2 inhibitors: mechanisms of cardiovascular benefit beyond glycaemic control. *Nat Rev Cardiol*. 2020 Oct;17(10):620–31.
12. U.S. Food and Drug Administration. BRENZAVVY (bexagliflozin) tablets for oral use. 2023 [cited 2025 Jun 20]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214373s000lbl.pdf
13. Allegretti AS, et al. Safety and effectiveness of bexagliflozin in patients with T2DM and stage 3a/3b CKD. *Am J Kidney Dis*. 2019 Sep;74(3):328–37.
14. Karagiannis T, et al. Canagliflozin in the treatment of type 2 diabetes: an evidence-based review. *Diabetes Ther*. 2014 Dec;5(2):353–68.
15. Lavallo-González FJ, et al. Efficacy and safety of canagliflozin in Latin American patients with T2DM. *Diabetes Ther*. 2015 Dec;6(4):619–29.
16. Kale N, et al. Review on SGLT2 inhibitors. *Asian J Pharm Res Dev*. 2023 Apr;11(2):98–106.
17. U.S. FDA. SGLT2 inhibitors may cause ketoacidosis and serious UTIs. [Internet]. [cited 2025 Jun 20]. Available from: <https://www.fda.gov/drugs/drug-safety-and-availability>
18. Dhillon S. Dapagliflozin: A review in type 2 diabetes. *Drugs*. 2019 Jul;79(10):1135–46.
19. Vivian EM. Dapagliflozin: A new SGLT2 inhibitor for type 2 diabetes. *Am J Health Syst Pharm*. 2015 Mar;72(5):361–72.
20. Saeed MA, Narendran P. Dapagliflozin for type 2 diabetes: a literature review. *Drug Des Devel Ther*. 2014;8:2493–505.
21. Zhao SD, et al. Renal outcomes in Asian T2DM patients on SGLT2 inhibitors: meta-analysis. *J Diabetes Metab Disord*. 2021;20(2):1–10.
22. Ferrannini E, et al. Metabolic response to SGLT2 inhibition in type 2 diabetic patients. *Diabetologia*. 2014;57(12):2640–52.
23. Hanas J. *Diabetes and metabolism*. Basel: Karger; 2016.
24. Majewski C, Bakris GL. Blood pressure reduction: benefit of SGLT2 inhibitors. *Diabetes Care*. 2015;38(3):429–30.
25. Zaccardi F, et al. SGLT2 inhibitors in T2DM: systematic review and meta-analysis. *Diabetologia*. 2016;59(5):823–33.
26. Wiviott SD, et al. Dapagliflozin and cardiovascular outcomes in T2DM. *N Engl J Med*. 2019 Jan;380(4):347–57.
27. Wanner C, et al. Empagliflozin and kidney disease progression in T2DM. *N Engl J Med*. 2016 Jul;375(4):323–34.
28. Heerspink HJL, et al. Effect of dapagliflozin in CKD with/without T2DM: DAPA-CKD trial. *Lancet Diabetes Endocrinol*. 2020;8(7):582–93.
29. Perkovic V, et al. Canagliflozin and renal outcomes in T2DM and nephropathy. *N Engl J Med*. 2019 Jun;380(24):2295–304.
30. Aroda VR, Eckel RH. Reassessing glycaemic control in CVD risk in T2DM. *Diabetes Care*. 2018;41(2):266–74.
31. White JR Jr. Empagliflozin, an SGLT2 inhibitor for T2DM: evidence review. *Diabetes Ther*. 2015;6(4):425–38.
32. Liakos A, et al. Empagliflozin in T2DM: systematic review and meta-analysis. *Diabetes Obes Metab*. 2014;16(10):984–93.
33. Heise T, et al. Acute effects of empagliflozin with/without diuretics in T2DM. *Clin Ther*. 2016;38(8):1830–42.
34. Zinman B, et al. Empagliflozin, CV outcomes, and mortality in T2DM. *N Engl J Med*. 2015 Nov;373(22):2117–28.

35. Wanner C, et al. Empagliflozin and kidney disease in T2DM. *N Engl J Med.* 2016 Jul;375(4):323–34.
36. Burke KR, et al. SGLT2 inhibitors: review of DKA and risk factors. *Diabetes Obes Metab.* 2017;19(4):524–32.
37. Bonora BM, et al. SGLT2 inhibitors and diabetic ketoacidosis: literature review. *Diabetes Obes Metab.* 2018;20(1):25–33.
38. Ye Y, et al. SGLT2 inhibitors: effect on bone metabolism and fracture risk. *Diabetes Obes Metab.* 2018;20(1):25–33

HOW TO CITE: Smita Aher, Sakshi Khandbahale, Pratiksha Batwal, Sodium-Glucose Co-Transporter 2 Inhibitors in Type 2 Diabetes Mellitus, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 7, 764-772. <https://doi.org/10.5281/zenodo.15825999>