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Review Article

SGLT Inhibitors As Antidiabetic Agents

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ABSTRACT

One of the most prevalent metabolic diseases that significantly raises the burden of disease on the world health system is diabetes mellitus. Diabetes mellitus (DM) is linked to several illnesses and medical disorders, including atherosclerosis, obesity, hypertension, and cardiovascular diseases. Type 1 diabetes, Type 2 diabetes, and gestational diabetes are the three main forms of diabetes mellitus. Many medication classes, including insulin, biguanides, sulfonylureas, metformin, DPP4 inhibitors, GLP-1 inhibitors, and SGLT2 inhibitors, are used to treat or manage diabetes mellitus. Included in this review are the types of diabetes mellitus, medications that treat the condition, and the sodium/glucose co-transporter [SGLT2] inhibitors. Large proteins called sodium/glucose co-transporters (SGLT) enhance the transport of sugars like fructose, galactose, and fructose while also transporting sodium. across a cell's plasma membrane from a range of tissues. The kidney's reabsorption of glucose is enhanced by SGLT receptors. Reduced reabsorption of glucose and increased excretion of glucose through the urine are the results of SGLT2 inhibitor inhibition. FDA-approved medications that are used to manage or control diabetes mellitus include canagliflozin, dapagliflozin, and empagliflozin.

INTRODUCTION

Under normal physiological conditions, most healthy individuals can maintain tight glucose homeostasis by regulating glucose production, re-absorption, and utilization. The importance of this homeostatic mechanism is evident from the fact that despite extreme variations in glucose intake, only a fraction of individuals develop either diabetes or hypoglycemia. In healthy adults, about 180 g of glucose is filtered daily by the renal glomeruli and is completely reabsorbed in the proximal convoluted tubule (PCT).[2] This is achieved by passive transport via facilitated glucose transporters (GLUTs), and active co-transport through sodium-glucose co-transporters (SGLTs). There are six identified SGLTs, of which two (SGLT1 and SGLT2) are considered most important. Here, a review of the role of SGLT2 inhibitors (SGLT2i) in Type 2 diabetes mellitus (T2DM) management, clinical

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pharmacology including mechanism of action, and the pragmatic placement of these molecules in the existing oral anti-diabetic drug arena is presented.[3]

2 Diabetes Mellitus:

A chronic illness involving the metabolism of proteins, lipids, and carbohydrates is diabetes mellitus. Diabetes mellitus is characterized by a poor or insufficient insulin secretory response, which results in impaired utilization of carbohydrates (glucose), as well as the hyperglycemia that follows. Diabetes mellitus (DM), sometimes known as "sugar diabetes," is the most prevalent endocrine condition. It typically arises from an insufficient or absent insulin supply, or in rare cases, from impaired insulin action (insulin resistance). According to projections from the International Diabetes Federation (IDF), there are around 40.9 million diabetic people in India, and by 2025, that number is expected to increase to 69.9 million. Four [4]. Both glucagon and insulin hormones are released by the pancreas. The beta (ß) cells and alpha (α) cells are found in the islets of Langerhans and release insulin and glucagon, respectively. Insulin transfers glucose into the muscles, liver, and adipose tissue, lowering blood glucose levels through glycogenesis. While erythrocytes and neural tissue do not require insulin for glucose use, alpha (α) cells are crucial for blood glucose regulation because they produce glucagon, which raises blood glucose levels by speeding up the process of glycogenolysis.[5]

Approximately 422 million individuals globally suffer from diabetes, with the majority residing in low- and middle-income nations. The disease is directly responsible for 1.5 million fatalities annually. Over the past few decades, there has been a steady rise in both the number of cases and the incidence of diabetes. In [12] Diagnosing diabetes mellitus involves. -fasting blood glucose level is higher than 6.1–7.0 mmol/L **[6]**-Glucose after meals >200 mg/dl. -HbA1c > 6.5 percent. The following are the three main forms of diabetes mellitus that need to be treated appropriately.

1] Type 1.

2] Type 2

3] Gestational diabetes mellitus (GDM) **[7]**

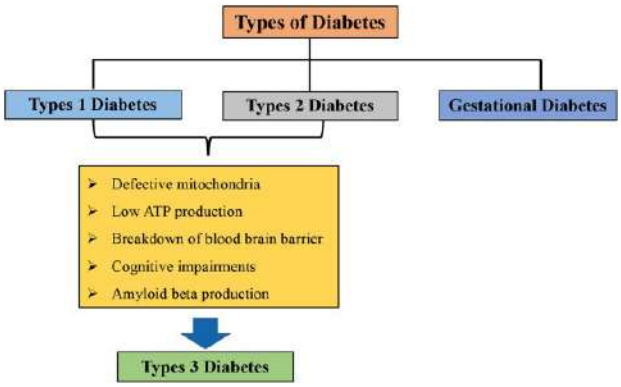

Fig no.1: Types of Diabetes.

2.1 Diabetes mellitus Type 1

Insulin insufficiency is the outcome, which is brought on by the autoimmune beta cells' death. These types of diabetes are sometimes known as juvenile diabetes or insulin-dependent diabetes mellitus (IDDM). In these, the patient—who was mostly a child—needed to take an insulin dose regularly, regardless of age. Insulin is the only treatment for this diabetes.

2.2 Diabetes mellitus type 2

Diabetes causes the pancreatic beta cells to gradually disappear as a result of decreased insulin output. These types of diabetes are sometimes known as adult-onset diabetes or noninsulin-dependent diabetes mellitus (NIDDM). These are referred to as "insulin-resistant" cells because the insulin receptors on insulin-responsive cells do not react to insulin as they should. Diabetes is managed with injections or oral medications.

2.3 GDM, or gestational diabetes mellitus

In some cases, pregnancy-related diabetes that was not present before delivery was discovered in the second or third trimester. the risk factors for gestational diabetes development. In certain

instances, metformin and insulin are used to treat this diabetes.[**8]**

3. Classification of anti-diabetic agent

1) **Bigaunides-** Metformin, Buformin, Phenoformin, Proguanil, Polyaminopropyl Biguanide
2) **Sulfonylureas**
a) **First Generation-** Chlorpropamide, Tolbutamide, Acetohexamide, Metahexamide, Metahexamide
b) **Second Generation**- Glipizide, Glibunuride, Glyclazide, Gliquidone.
3) **Glucagon- Like Peptide-1 (Glp-1) Receptor Agonists**- Exenatide, Liraglutide, Lixisenatide
4) **Glucose Co-Transporter 2 Inhibitor (SGLT-2)-** Canagliflozin, Dapagliflozin, Empagliflozin
5) **Alpha Glycosidase Inhibitors** - Acarbose, miglitol
6) **Meglitinides**- Nateglidnide, Repaglinide, Mitiglinide.
7) **DPP-4 Inhibitors**- Sitagliptin, Saxagliptin, Linagliptin, alogliptin
8) **Thiazolidiones (Tzds)-** Rosaglitazone, Pioglitazone. **[9]**

1) Biguanides:

Phenoformin, buformin, and metformin are three biguanide-containing medications for which antidiabetic activity has been observed. Because of lactic acidosis, the use of buformin and phenoformin has been ceased. Metformin is one of the biguanides that is utilized globally. The first line of treatment for DM is metformin. Metformin is an insulin-sensitizing medication that works by gluconeogenic gene expression to sustain its antihyperglycemic effects. Metformin decreases CAMP, which in turn lowers the expression of the gluconeogenic enzyme, and inhibits the liver's mitochondrial respiratory chain, which activates AMPK and improves insulin sensitivity[10,11]. Oral absorption of metformin does not result in lactic acidosis. Proguanil and chlorproguanil are biguanides used as antimalarials Chlorhexidine and polyhexanide are disinfectants.

2) Sulfonylureas:

This is most widely used as an oral anti-diabetic agents. Sulfonylureas stimulate insulin release by binding to the SUR-1 subunit of ATP ATP-sensitive potassium channel (KATP) of pancreatic b-cells and inducing channel closure. Therefore potassium flow across the plasma membrane is inhibited leading to depolarisation this opens the calcium channel there is the uptake of extracellular calcium which activate the cytoskeletal system and causes translocation of secretory granules to the cell surface and extrusion of insulin through exocytosis This results in fusion of secretory granules with plasma membrane causes the release of insulin into the extracellular space to reach the capillary blood flow, therefore, sulfonyl ureas administered carefully since it causes hypoglycemia and hyperinsulinemia. Sulfonylureas have multiple formulations at minimum side effects with low cost with maximum efficacy in controlling hyperglycemia.[12,13] It is administered in conjunction with insulin and other oral anti-diabetic agents. Glipizide, gliburnuride, gliclazide, and gliquidone are second-generation medications that have fewer adverse effects and are more potent than first-generation medications (chlorpropamide, tolbutamide). Sulfonylureas must be broken down in the liver and eliminated through the urine. Disulfiram-like reactions are caused by first-generation sulfonylureas. In **[14]**

3) GLP-1 receptor agonists:

GLP-1 receptors are found in numerous bodily tissues, but they affect the GIT that makes them appropriate for type 2 diabetes. After meals, GLP1 reduces the release of glucagon and increases the release of insulin-mediated by glucose. GLP1 has a half-life of one to two minutes because it is broken down by the enzyme DPP4.In [**15**] The

pancreatic islet releases insulin in response to glucose when GLP1 is present. Additionally, it has been demonstrated to decrease food intake, suppress the improper release of glucagon after a meal, and empty the stomach. GLP1 stimulates insulin secretion in several ways, such as the direct blockage of ATP-dependent potassium channels, which increases intracellular calcium levels and ATP production. One such technique is the usage of sulphonylureas. which promotes depolarization and the exocytosis of insulin granules from pancreatic cells (**16).**

4) Alpha glycosidase inhibitors (AGIs)

This class of anti-diabetic medications is used to treat type 2 diabetes. AGIs primarily lower the level of glycosylated hemoglobin and aid in lowering the concentration of postprandial insulin. (**17**) AGIs work by slowing down and preventing the small intestine from absorbing carbs. By postponing the absorption of carbohydrates in the gut, they competitively inhibit the enzymes sucrose, maltase, and iso-maltase at the brush border of enterocytes, which are involved in converting non-absorbable oligo into absorbable form.[**18]** Alpha-glucosidase is the first-line medication for type 2 diabetes when taken orally. It is taken three times a day before eating. Diarrhea is the most frequent GI upset caused by AGIs [**19**].

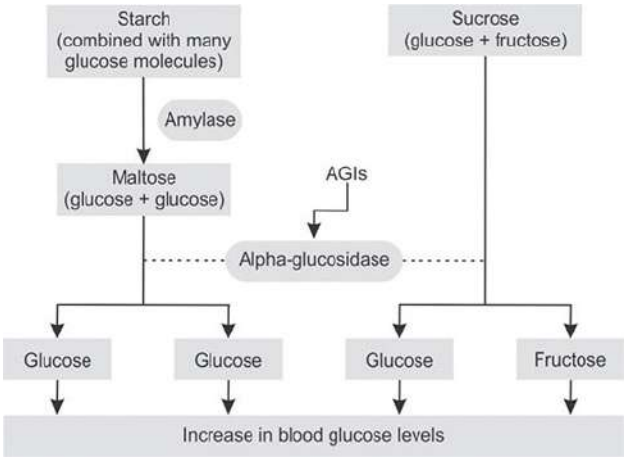

Fig no.2 Inhibitory effect of alpha glycoside

5) DDP 4 inhibitors drugs

Saxagliptin, Vitagliptin, and Sitagliptin are DDP 4 inhibitors. These are the more recent class of diabetes medications used to treat type 2 diabetes.**[20]** DPP4 breaks down the incretins that the intestinal cells release after a meal, which raises the secretion of insulin. It is used in conjunction with sulfonylureas and metformin to treat type 2 diabetes and diabetic ketoacidosis.[**21]**

6) Thaizolidinediones (TDZs)

The oral active medicines for diabetes are called thiazolidinediones. These are regarded as insulin-sensitive substances, similar to biguinoids.**[22**] The first medication for TZDs to hit the market is troglitazone. However, because of hepatotoxicity, these drugs are no longer produced or offered for sale.[**23]** The nuclear receptor PPAR is strongly activated by TDZs, which are abundant in adipose tissue, muscle, liver, and pancreatic cells. [**24**] Due to their tendency to cause fluid retention, TDZs should not be used in patients with cardiac problems. Long-term usage of TDZs also raises the risk of bone fracture in women. Reference [**25]**

7) Meglitinides:

Medication: mitiglinide, repaglinide, and ateglinide. These are a more recent family of diabetes medications that raise insulin production by obstructing potassium channels that are sensitive to ATP.[**26]** Meglitinides are used to treat type 2 diabetes and have a brief half-life. Meglitinide side effects include hypoglycemia, which is brought on by an increase in insulin secretion. Patients suffering from liver dysfunction or renal failure should not take this class of medication. The oral diabetic medications are displayed in the **table below (number 1).[46]**

Class of Oral Antidiabetic Medication	Mechanism To Control Glucose Levels	Generic Name	Brand Name
Sulfonyl ureas	Improve insulin production	Chlorpropamide Glimepiride Glipizide	Diabinese Amaryl Glucotrol
Maglitinides	Improve Insulin Production	Repaglinide Nateglinide	Prandin Starlix
Biguanides	Reduce Hepatic Glucose Output And Increase Uptake Of Glucose By The Periphery Including Skeletal muscle	Metformin	Glucophage
Thiazolidinediones	Substantially Attenuated Insulin Resistance	Rosiglitazone	Avandia
DPP4 Inhibitors	Inhibition Of DPP4 Enzyme Prolongs And Enhances Activity Of Incretins That Play An Important Role In Insulin Secretion And Control Blood glucose Level	Sitagliptin	Januvia
Alpha Glucoside	Slow The Digestion Of Starch	Acarbose	Precose

Table 1: Oral anti-diabetes agent.

8) Sodium-glucose co-transporter 2 inhibitors (SGLT2 inhibitors):

The kidney's sodium-glucose cotransporter-2 (SGLT2) is now crucial to the management of type 2 diabetes mellitus (T2DM). In 1933, Smith and colleagues reported that intravenous phlorizin (phloretin-2'-β-Dglucopyranoside) blocked the reabsorption of filtered glucose [**27**]. DeFronzo and his associates discovered fifty years ago that phlorizinizing diabetic rats reduced their hyperglycemia and improved their insulin sensitivity, indicating that phlorizin may be used to treat type 2 diabetes.[**28**] Phlorizin was initially used to treat infections such as fever, malaria, and other infections. The phalozin derivative cana has greater SGLT2 inhibitory action than SGLT1 inhibitory activity.[**29]**

4. SGLTs (Co-factors that resemble glucose)

Scientist Crane used the deposition of glucose molecules at the brush edge of intestinal epithelial cells to illustrate the active cotransport theory. that related sodium ion transit along their gradient.**[30**] The first co-transports of sodium/glucose and sodium/proline were discovered on the rabbit's intestinal brush edge. There are about 220 members of the SGLTs family (gene symbol: SLC5A) in both mammalian and bacterial cells. Eleven human genes encoding members of the SGLT family have been found, ranging from epithelial cells to nerve cells.[**31**] Sodium-glucose cotransporters (SGLTs) are members of the membrane protein family. They help the proximal convoluted tubule and intestinal epithelium carry substances such as glucose, amino acids, different ions, and vitamins.[**32]**

4.1 Sodium Glucose Like Cofactor 1 (SGLT1):

The human protein SGLT1, sometimes referred to as solute carrier family 5 member 1, is encoded by the SLC5A1 gene. The protein SGLT1, which is membrane-bound, has a mass of 75 k Dalton. The S3 segment, kidney (renal proximal convoluted tubule), small intestine, and heart are the organs where it is primarily present in cell membranes. The ratio of sodium to glucose transported by the SGLT1 protein is 2:1. Although SGLT1 has a limited ability to transport glucose and galactose, it has a greater affinity for them. Although SGLT1 is an essential transporter for glucose uptake in the gastrointestinal tract, its impact on the kidneys is less important (around 10% reabsorption of glucose is seen). Genetic disorders known as are caused by mutations in the SGLT1 gene.

GGM stands for glucose-galactose malabsorption. A rare autosomal recessive illness can cause potentially fatal diarrhea in newborns. When

dietary sugars like glucose, galactose, and lactose are eliminated, diarrhea stops. In people without this illness, SGLT1 is essential for the proper functioning of oral rehydration therapy because it allows sodium, glucose, and water to be transported by accelerating the absorption of water. Because it is believed that inhibiting the SGLT1 receptor reduces gastrointestinal glucose absorption, causes weight loss, and lessens postprandial hyperglycemia, researchers have been interested in this receptor.**[33]** **Shown in fig.2) [34]**

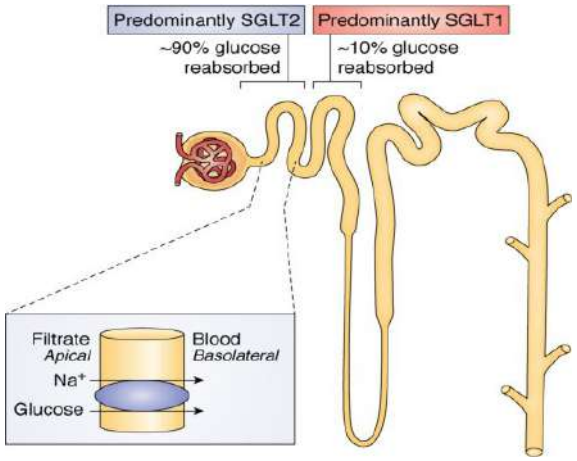

Fig. no. 3: Structure of SGLT1.

4.2 Sodium Glucose Like Co-factors 2 (SGLT2)

The second membrane-bound member of the SGLT family that is encoded by the human SLC5A2 gene is called SGLT2.SGLT2 differs from SGLT1 in that it has a higher capacity but a lower affinity for glucose and galactose. The transport of these sugar molecules happens at a stoichiometric ratio of 1:1 between the sodium ion and the sugar molecule. This is the main co-transporter, which is mostly expressed in the kidneys and is responsible for 90% of glucose absorption. This receptor is located in the kidneys' proximal tubule's S1 and S2 segments' apical membrane (**fig. 3). (35)**

Characteristic	SGLT1	SGLT2
Location	Small intestine; later part of PCT (segment 3)	Early PCT (segment 1, 2)
Capacity	Low	High
Affinity	High	Low
Contribution to glucose reabsorption	10%	90%
Disease state if mutation/deficiency occurs	Glucose-galactose malabsorption	Familial renal glucosuria
Physical manifestations of disease state	Diarrhea at few days age	None
Course	Fatal without glucose free/galactose free diet	Benign
Inhibitors	Phlorizin	Currently available SGLT2i

Table. no.2 A comparison between SGLT2 and SGLT1

4.3 Sodium glucose-like cofactors three, or SGLT3

The SLC5A4 gene family encodes SGLT3, the third membrane-bound protein, which was initially discovered by the chromosome 22 genome project. Skeletal muscles, the small intestine, the kidneys, and the nicotinic acetylcholine receptor are the main locations for this. Human SGLT3 is a simple glucose-gated ion channel found in muscle and neuronal membranes, however, it has been shown to on the functional research employing expression from laevis oocytes, which shows that it does not function as a sodium/glucose transporter. In the plasma membrane of skeletal muscle, cholinergic neurons, and other organs, SGLT3 is not a sodium/glucose sensor.**[36]**

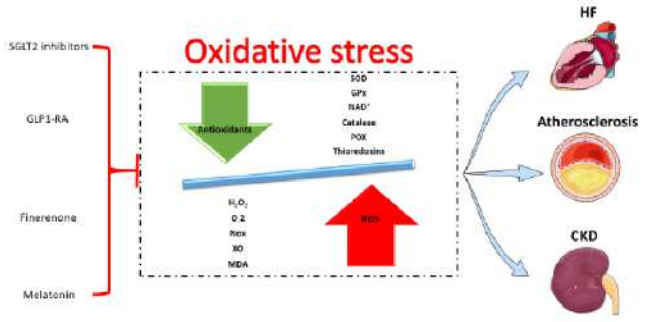

Fig.no.4 Reactive oxygen species (ROS) can be reduced and antioxidant system activity can be strengthened by substances that have antioxidant properties, such as melatonin, finer enone, glucagon-like peptide-1 receptor agonists (GLP1-RA), and sodium-glucose cotransporter-2 (SGLT2) inhibitors. In the end, there is a reduction in the burden of oxidative

stress-related illnesses such as heart failure (HF), atherosclerosis, and chronic kidney disease (CKD).

Transporter	Tissues*	Type of transport	Notes	Sensitive to insulin?
SGLT	Renal tubules, intestinal epithelia (apical membrane)	Secondary active transport	Responsible for the absorption (intestine) and reabsorption (renal tubule cells) of glucose.	No
GLUT1	Pancreatic beta cells, hepatocytes	Facilitated diffusion	Pancreatic beta cells: important for gauging blood glucose levels in humans. Hepatocytes: bi-direction transport of glucose when influenced by hormones, such as thyroid hormone.	No
GLUT2	Pancreatic beta-cells, hepatocytes, intestinal epithelium, kidney	Facilitated diffusion	Hepatocytes: important for the bi-directional transport of glucose with regards to hepatic glucose metabolism.	No
GLUT3	CNS	Facilitated diffusion	Very high affinity for glucose.	No
GLUT4	Skeletal muscle, cardiac muscle, adipose tissue	Facilitated diffusion	Expression regulated by insulin.	Yes

*Most transporters are found in a variety of tissues, but are expressed in higher concentrations in specific cell-types.

Table. no.03 There is currently not enough information available on the SGLT4, SGLT5, and proteins. The distribution of tissues, substrate, SGLT members, and function-encoding genes.[37]

5. A mutation in SGLT1 causes the pathophysiology of GGM.

A hereditary condition called glucose-galactose malabsorption (GGM) is connected to the SGLT gene family. Mutations in the SGLT1 gene cause life-threatening diarrhea in newborns with this rare autosomal recessive illness. GGM is a disorder that causes severe diarrhea because the body is unable to absorb glucose and galactose. Dietary sweets can be eliminated to control diarrhea, but reintroducing these sugars can cause them to flare up again very fast. The presence of the kidney-associated SGLT2 transporter, linked to glucose reabsorption, explains why autosomal recessive renal glycosuria manifests in diabetics. Two younger brothers and their parents were the subjects of DNA sequencing to study the genesis of two mutations: a heterozygous mutation that appeared in an exon in SGLT2.] The GGM patient then cut off all sugar-containing items from their diet because these foods can induce diarrhea and other health issues. The SGLT1 receptor handles glucose and galactose, while the facilitated fructose transporter (GLUT5), a separate carrier, transports fructose across the brush boundary. SLUT2 in the basolateral membrane facilitates the transfer of glucose, galactose, and fructose across the cell membrane and into the blood **(fig. 5) [38]**

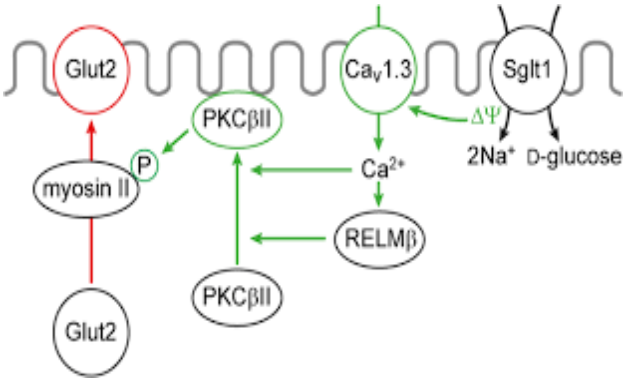

Figure 5: Sugar transfer model involving basolateral sodium-potassium pumps, GLUT2 sugar transporter, and SGLT1 and GLUT5 transporters.

6. Structure and functions of SGLT:

Vibrio parahaemolyticus provided the crystal structure of SGLT, which is 60% identical to human SGLT1. The SGLT structural model has two COOH-terminal and one NH2-terminal half, and it predicts 14 transmembrane α-helices (TMH). Research on these transporters shows that the sugar moiety is carried by the COOH-terminal half of the transporter, whereas the sodium ion is carried by the NH2-terminal half. NH2-terminal attachment to sodium ions causes the proteins to undergo a conformational shift that allows for the binding and translocation of sugars. According to this study, the TMHs numbered 10–13 are essential for SGLT1's sugar translocation pathway to remain intact.[**39**].

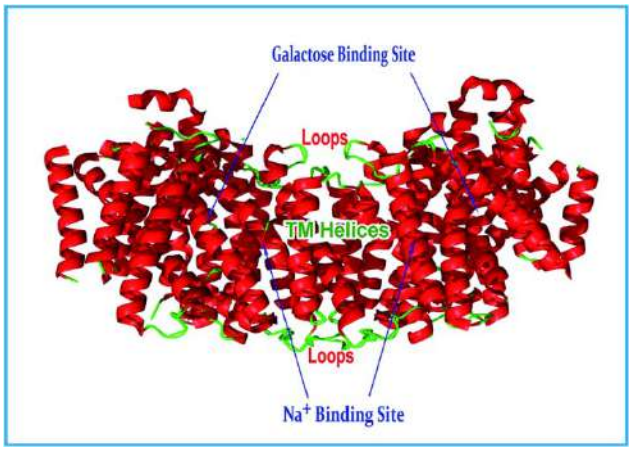

Fig. no. 6 Crystal structure of the SGLT protein.

In the crystal structure, researchers found two significant binding sites, which are: Na+ and

galactose binding sites: This site's purpose is to pinpoint the exact location and point of reference of the sugar molecule. The hydrophobic residues of the extracellular and intracellular gates are separated by this binding site. Because of the densitometric resemblance between Na+ and water, it is challenging to properly find the sodium binding site on vSGLT. Sequence alignment studies on the LeuT structure indicate that the sodium binding site is situated 10 Å from the substrate-binding site, at the intersection of the TM2 and TM9 helices.**[40]**

6(a) Functions:

During SGLT1's mutagenesis study, cysteines were substituted for the residues at positions 457, 468, and 499. This results in the transporter being vulnerable to methanethiosulfonate (MTS) when it is in the C2 conformation. The accessibility of the cysteine residues to MTS is prevented if the MTS reaction is carried out with glucose/phlorizin in the presence or absence of sodium ions, or the presence of sodium ions alone (during depolarization of the membrane potential). The accessibility of certain acids (457, 468, and 499) to MTS directly correlates with the likelihood of proteins adopting the C2 conformation. The primary finding of these studies was that the translocation pathway, which is accessible in the C2 conformation, depends on the transporter residues 457, 468, and 499.

It is proposed that one or more TMHs in the 10–13 helical bundle rotate, causing a significant conformational shift to occur. Water and urea are transported when sugar translocation in a cell necessitates a significant alteration in helical rotation. In such transport, the stoichiometry of sodium ions:glucose: water was determined to be 2:1:250 under these circumstances. In the small intestine, SGLT1 is in charge of absorbing glucose and galactose, while SGLT2 is in charge of reabsorbing glucose in the kidney. **[41]**

7. SGLT inhibitors:

A class of pharmaceuticals that are prescribed to treat high blood glucose by blocking both SGLT1 and SGLT2.

7.1 SGLT1 inhibitors:

They lessen post-meal glucose impale and enhance glycaemic management by postponing and decreasing small intestinal glucose absorption. The FDA has examined Sotagliflozin, the first oral SGLT1 inhibitor, for use in treating adult patients with type 2 diabetes mellitus in addition to insulin. This medication inhibits SGLT2 as well. Research has demonstrated that individuals with type 2 diabetes mellitus who take sotagliflozin in addition to optimal insulin therapy have reduced weight and hemoglobin A1c levels after a year of treatment, as well as a low incidence of severe hypoglycemia. as seen in **fig. 7. In [42]**

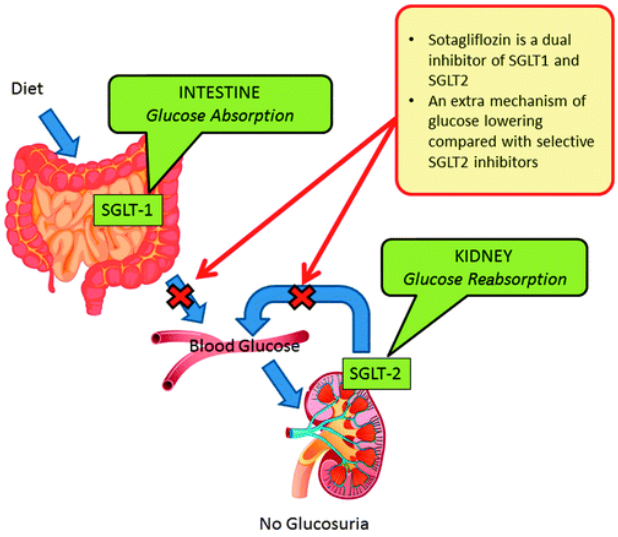

Fig. no. 7: Mechanism of action of Sotaglifloz

7.3 SGLT2 Inhibitors:

Prescription drugs in the SGLT2I class have FDA approval for usage in conjunction with diet and exercise to help adults with type 2 diabetes mellitus reduce their blood glucose levels. Canagliflozin, dapagliflozin, and empagliflozin are SGLT2I medications. Table 3 is a list of SGLT2 inhibitors that are approved by the FDA or the European Medicines Agency and are available globally**. [43]**

8. SGLT2 inhibitors' positive benefits in preclinical and clinical research

Surprisingly, SGLT2 inhibitor medication for type 2 diabetes mellitus decreased hospitalization for heart failure and all causes of mortality by about 30%. It also decreases the risk of cardiovascular death. If the patient suffers from heart disease, chronic renal illness, or atherosclerosis failure of the SGLT2i is preferred. The benefits of SGLT2 inhibitors are numerous. that boost cardiac energy, decrease blood pressure, increase diuresis or natriuresis metabolism, reduce inflammation, aid in weight loss, and enhance glucose regulation.

The effects of SGLT2 inhibitors on glucose excretion by the kidneys are distinct from those of insulin. The side effects of older medications, such as hypoglycemia and liver damage, are lessened by SGLT2i.The. The results of a more recent class of antihyperglycemic drugs are positive.

CONCLUSION

Diabetes mellitus is a serious, long-term metabolic illness linked to metabolism. A sizable fraction of the global population is impacted. It has been connected to several other illnesses and ailments, including atherosclerosis, hypertension, obesity, and cardiovascular diseases. A diabetic's lifetime is typically included in the diabetes mellitus management period, necessitating a multidisciplinary approach that includes dietary adjustments and medicinal treatments such as antidiabetic medicines. This article covers all available research on SGLTs as potential targets for the treatment of diabetes as well as substances that have inhibitory effects against SGLTs, including medications now undergoing clinical development. This review offers a comprehensive summary of the studies on SGLT inhibition as an antidiabetic target that has been published in the last five years. destined to act as an all-inclusive resource for researchers.

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