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A Systemic Review of an Anti-Diabetic Drug Ertugliflozin

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ABSTRACT:
The US, EU, and other territories have approved ertugliflozin, an inhibitor of sodium-glucose cotransporter 2 (SGLT2) that is selectively used to treat type 2 diabetes (T2DM). Inhibitors of the sodium-glucose cotransporter 2 (SGLT2) are the newest treatment option for type 2 diabetic mellitus (T2DM). as this review summarizes. By means of a glucose-independent process called glycosuria, they lessen the toxicity of glucose and enhance the activity of β-cells and insulin sensitivity. Clinical trials yielded encouraging results: SGLT2 considerably reduces body weight and blood pressure (BP), improves glycaemic control, and offers higher cardiovascular protection. The novel, highly selective, and reversible SGLT2 inhibitor ertugliflozin is the subject of this review. Glycosylated haemoglobin (HbA1c), According to clinical trials that have been reported thus far, ertugliflozin can lower blood pressure, body weight, and both when used alone or in conjunction with oral antidiabetic medicines in people with type 2 diabetes.

Keywords: Diabetic Mellitus, Antidiabetic, inhibitor of sodium glucose co-transporter 2, Ertugliflozin, Pharmacokinetics, Mechanism, Ketoacidosis.

I. INTRODUCTION:

Diabetes mellitus:

One metabolic illness that is included in this class is diabetes mellitus, characterized by a protracted duration of increased blood sugar levels. Due to its widespread impact and two main forms (Type I and Type II), it can be categorized as one of the major diseases of the world. Diabetes's side effects include the risk of renal failure, lower limb amputation, stroke, and cardiac arrest.

One of the most common non-communicable diseases in the world is diabetes mellitus.India is met with a number of obstacles in managing diabetes, such as the disease's increasing incidence in areas that are both rural and urban, low public awareness of the condition, a lack of adequate healthcare facilities, high treatment costs, inadequate glycaemic control, and an increase in common complications. Injections under the skin, up to four times a day, are the most popular way of administering insulin for diabetes.

The administration of insulin can be intrusive, which has led to issues with patient compliance and consequently affected patient outcomes. This is especially true for long-term insulin therapy. Type 1 diabetes is also on the rise, even though type 2 diabetes mellitus which causes over 90% of all cases of diabetes is the main culprit behind the epidemic.

Diabetes type I is a chronic metabolic disease involving the lipids, carbs, and proteins The most prevalent endocrine condition, "Sugar" diabetes is another term for diabetes mellitus (DM). It is primarily brought on by either too little or no insulin., or less frequently, by a decrease in insulin action (insulin resistance). By 2025, there will be 69.9 million diabetes subjects in India, according to estimations from the International Diabetes Federation (IDF). Currently, there are about 40.9 million diabetic individuals nationwide. The pancreas secretes the hormones insulin and glucagon respectively. Alpha (ß) cells release insulin.

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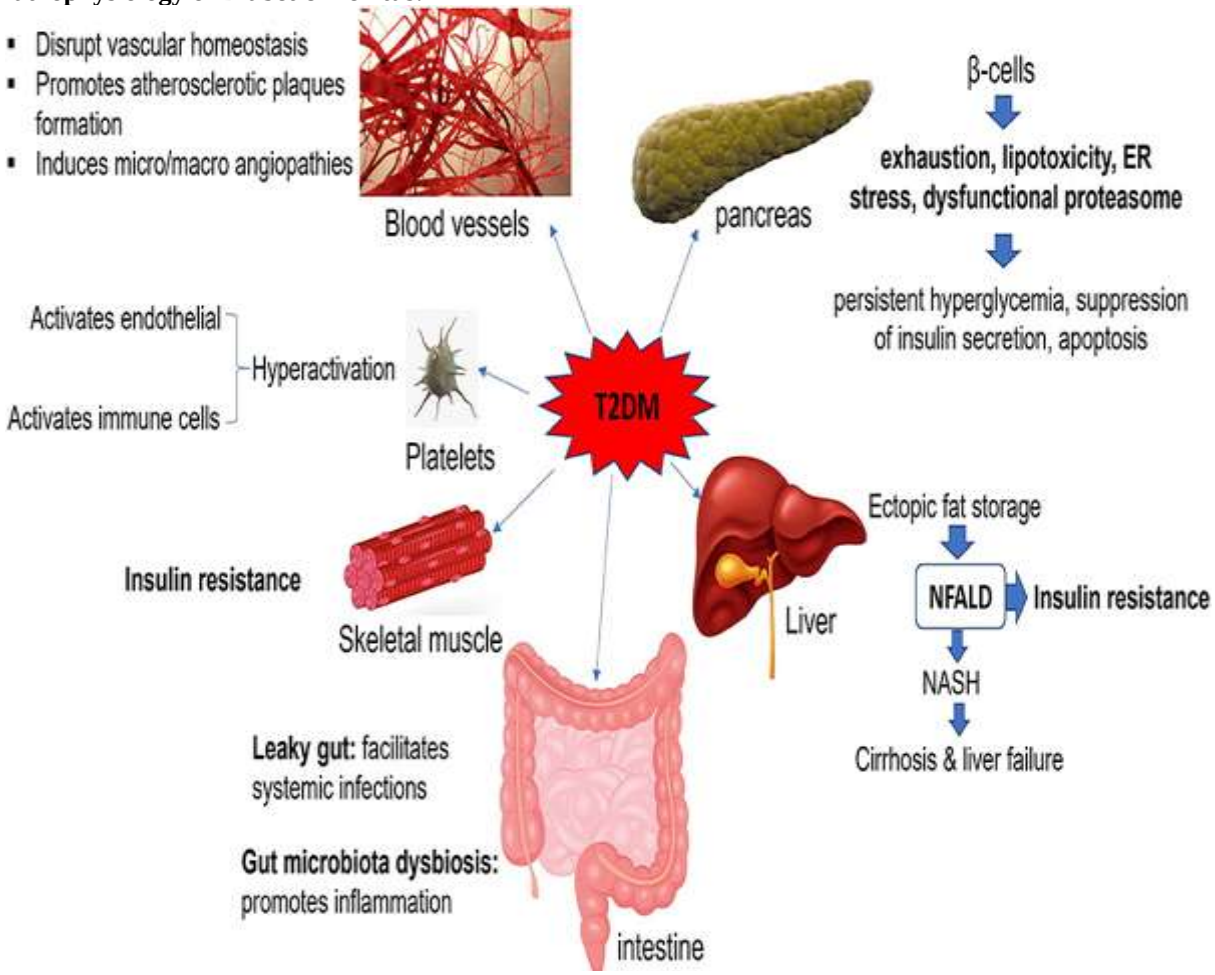
Pathophysiology of Diabetic Mellitus:



Insulin for Diabetes Mellitus

Insulin is a hormone that our bodies produce to keep our blood glucose levels within normal limits. It is produced by pancreatic beta cells. The primary function of insulin is to transport glucose from the bloodstream into the body's cells, where it is converted into energy. If you do not have enough insulin, glucose accumulates in your bloodstream instead of entering your cells to provide energy.

Type 1 diabetes occurs when the body does not produce insulin, so insulin must be injected on a daily basis to stay alive. Type 2 diabetes occurs when the body either does not produce enough insulin or the insulin produced does not function properly. Insulin injections are sometimes required to regulate blood glucose levels.

Epidemiology Of Diabetes Mellitus

The prevalence of diabetes is rapidly increasing in the United States and around the world. Globally, an estimated 285 million people had diabetes in 2010, with type II accounting for approximately 90% of cases. According to the International Diabetes Federation, approximately 381 million people had diabetes in 2013, and its prevalence is rapidly increasing.

In 2005, it was estimated that over 20 million people in the United States had diabetes. Approximately 30% of these individuals had undiagnosed conditions. Age, ethnicity, a family history of diabetes, smoking, obesity, and physical inactivity all increase the risk of developing diabetes.

Diabetes-related complications, such as cardiovascular disease, kidney disease, neuropathy, blindness, and lower-extremity amputation, are a major cause of morbidity and mortality among diabetics, imposing a significant economic burden

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on the US healthcare system. People with diabetes are living longer lives as treatment for the disease and its complications improves. This longer life span will contribute to an increase in diabetes morbidity, particularly among the elderly and minorities. The number of people diagnosed with diabetes in the United States is expected to reach 48.3 million by 2050.

Randomized controlled trials show that intensive lifestyle interventions can prevent or delay the onset of diabetes in high-risk people. Furthermore, adequate and consistent control of blood sugar, blood pressure, and blood lipid levels can prevent or postpone the onset of diabetes-related complications in people with diabetes. Effective interventions at both the individual and population levels are critical for slowing the diabetes epidemic and reducing diabetes-related complications in the United States.

This report describes the current diabetes epidemic, as well as the health and economic consequences of diabetes complications for individuals and the healthcare system. The report also suggests ways to control the epidemic.According to the IDF diabetes atlas (2021), 10.5% of adults aged 20 to 79 have diabetes, with nearly half unaware of the condition. Diabetes affects an estimated 250 million people worldwide, and the figure is expected to rise to 350 million by 2030.

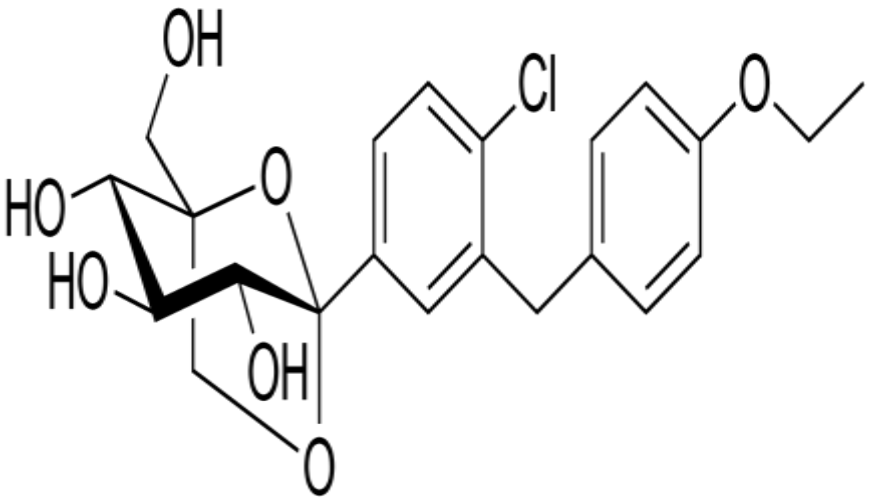
Ertugliflozin

Introduction:

One medication ERTUIFLIZIN is used to treat type 2 diabetes. The sodium glucose co-transporter (SGLT2) is inhibited by it. As type 2 accounts for around 90% of the glomerulus's total blood glucose levels, SGLT2 inhibitors lower postprandial and fasting blood glucose levels (SGLT). glucose uptake reversal. They also increase urine glucose excretion. The selective sodium glucose co-transporter-2 (SGLT2) inhibitor ertugliflozin is taken orally. that causes a reduction in plasma glucose and haemoglobin A1c (A1C) in people having diabetes mellitus type 2 (T2DM), Along with glucose excretion in urine (UGE).

A recently identified chemical compound is called Ertugliflozin (1S, 2S, 3S, 4R, 5S). Phenyl-4-Chloro-3-(4ethoxybenzyl)5-[4-Methoxy-3-(4ethoxybenzyl)phenyl]Octane-2,3,4-triol-1-hydroxymethyl-6,8-dioxabicyclo [3.2.1]. When men and women use ertugliflozin instead of placebo, there is a greater mycotic infection incidence in the genitalia of both groups.

Structure of Ertugliflozin:



Mechanism of Action of Ertugliflozin:

Comparable to further SGLT2 inhibitors, ertugliflozin functions by obstructing the transfer of glucose from the glomerular filtrate across the proximal epithelial cells' apical membrane. This leads to a decrease in renal reabsorption of filtered glucose and an increase in urine glucose excretion. The enzymes UGT1A9 and UGT2B metabolize ertugliflozin primarily, in addition CYP3A4 and CYP3A5 and CYP2C8 contributing very little. Ertugliflozin does not activate CYPs 1A2, 2B6, or 3A4 and does not inhibit CYP450 isoenzymes (CYPs) 1A2, 2C9, 2C19, 2C8, 2B6, 2D6, or 3A4. Since Consuming ertugliflozin would lower the

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likelihood of having significant interactions with medications that are processed by these common enzymes, this could be advantageous for individuals with type 2 diabetes who have problems and are taking many medications. Ertugliflozin functions similarly to other SGLT2 inhibitors.

Since taking ertugliflozin would lower the likelihood of having significant interactions with medications that are processed by these common enzymes, this could be advantageous for individuals with type 2 diabetes who have problems and are taking many medications.

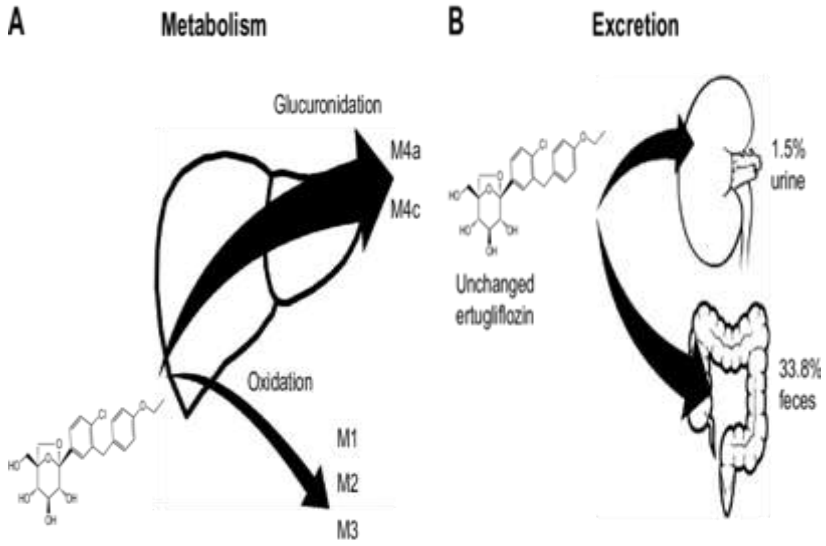

Figure: Hepatic Metabolism of Ertugliflozin

Pharmacokinetics:

The sodium-glucose cotransporter-2 inhibitor ertugliflozin (SGLT2), is administered orally. Its oral bioavailability ranges from 70 to 90%, and it is efficiently absorbed. Tmax (median) is one hour during a fast and two hours following a high-fat meal. O-glucuronidation by UGT1A9 and UGT2B7 is the main method of metabolism, producing inactive metabolites. Feces (41%) and urine (50%) are the routes of elimination. Half-life exceeds sixteen hours.

Adverse Effects:

Urinary tract infections and genital mycotic infections have been linked to ertugliflozin.

Using either a DPP-4 or an SGLT2 inhibitor together, hypoglycaemia is uncommon unless the patient is already taking an antihyperglycemic medication. It may result in hypovolemia, dehydration, and severe renal damage due to sodium loss. Together, they can result in ketoacidosis, usually in people with type 1 diabetes. Lower-limb amputations were linked to the use of ertugliflozin in clinical studies in 0.2% of individuals getting the 5 mg dose and 0.5% to those receiving the 15 mg dose

II. CONCLUSION:

Ertugliflozin provides a special kind of treatment for type 2 diabetes. Ertugliflozin has advantages in terms of improved blood pressure, body weight, and blood glucose regulation. Adverse outcomes include sporadic hypoglycaemia and vaginal fungal infections. Preliminary research indicates that there is no elevated danger related to heart conditions. Extended-duration clinical trials are necessary. though.

Another effective SGLT2i in order to treat type 2 diabetes is ertugliflozin. Its insulin-independent approach works to reduce your body mass, arterial pressure, and HbA1c both alone or in conjunction with other glucose-lowering medications, just like other gliflozins. Genetic variations have been partially attributed to documented individual variability in responsiveness to SGLT2.As a result, finding Using pharmacogenetic indicators to forecast treatment outcome may be crucial to maximizing advantages as well as minimizing adverse consequences in customized treatment

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