"Role of Glibenclamide in Diabetes Treatment"

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Abstract:- The review article provides a comprehensive overview of Glibenclamide, also known as glyburide, as an oral anti-diabetic drug used in the treatment of type 2 diabetes mellitus. It covers the drug's discovery, physicochemical properties, pharmacokinetic properties, mechanism of action, methods of synthesis, medical applications, side effects, treatment of overdose, contraindications, interactions, conventional and novel commercial formulations, and patents. Glibenclamide functions by binding to sulfonylurea receptors, stimulating insulin release from pancreatic beta cells, and enhancing tissue sensitivity to insulin, thereby improving glycemic control. It is often prescribed as an adjunct to diet and exercise when lifestyle changes alone are insufficient for glycemic control. The drug has been shown to significantly reduce HbA1c levels and improve long-term outcomes in type 2 diabetes patients. However, hypoglycemia is a common side effect, particularly with high or mistimed doses, and other adverse effects include liver dysfunction, allergic reactions, and occasional gastrointestinal issues. Contraindications for Glibenclamide include type 1 diabetes, diabetic ketoacidosis, severe renal or hepatic impairment, pregnancy, or breastfeeding. Close monitoring and patient education are essential to mitigate these risks. Overall, the abstract provides a comprehensive overview of Glibenclamide's role in the treatment of type 2 diabetes mellitus.

Keywords:- Glibenclamide, Glyburide, Diabetes mellitus Type 2.

Discovery and further history :- Glibenclamide also known as glyburide was discovered in 1966 by collaborative efforts of the German pharmaceutical companies of Hoechst and Boehringer Mannheim. It was approved in 1984 by FDA of United states to use as medicine of diabetes mellitus type 2.[1] An antibacterial sulfonamide medication called 2254 RP (pamino-benzenesulphonyl-isopropylthio-diazole) was prescribed to patients during the early years of World War 11, and Marcel Janbon, a physician in Montpellier, France, noticed that these patients occasionally experienced symptoms of hypoglycemia. August Loubatieres, a physiologist, was tasked by Janbon to test the compound's ability to lower blood sugar levels in dogs. Loubatieres reported that normal fasting, non-pancreatectomized dogs receiving 2254 RP developed hypoglycemia. He came to the conclusion that the chemical likely triggered the release of insulin from the islets of the normal fasted dog, and that this insulin was responsible for the onset of hypoglycemia.[2] Glibenclamide was introduced into

clinical practice in 1969. Glyburide is called as second generation sulfonylureas since it has much greater hypoglycemic potency per milligram than the first generation drugs. Prior to 1984, Hoechst-Rousseau conducted clinical trials outside of the United States including around 5053 patients receiving glyburide treatment. In November 1974, 3124 patients in the United States received glyburide treatment thanks to financing from the Upjohn Company. 1017 patients finished at least 24 months of therapy, according to the data. Glyburide is a safe and effective medicine for the treatment of individuals with type 2 diabetes, according to the findings of these studies.[2]

Physicochemical Properties :- Glibenclamide has IUPAC Name as 1-{4{2-(5-chloro-2-methoxy-benz-amido)ethyl}benzenesulphonyl}-3-cyclohexylurea.[3] With Molecular weight of 494g.

Solubility:- Glibenclamide is insoluble in water. But it is soluble in Alcohol with 330 parts and 36 parts in chloroform and also with 250 parts in methanol. The formation of water soluble salts with alkali hydroxides takes place. Melting Point of Glibenclamide has been reported in many studies in the range of 168° to 174℃. The UV absorption spectra of glibenclamide in the chosen medium displayed a maximum at 300 nm, and following addition of the prescribed quantity of strong hydrochloric acid, it displayed a very pronounced absorption maximum at 229.5 nm, leaving the other at 300 nm in the original spectrum.[4] An infrared spectra of glibenclamide was obtained using a Perkin-Elmer Model 357 grating spectrometer from a potassium bromide disc. The spectrum and reported spectra are in agreement 1163, 1333, 1471, 1515, 1613, and 1724 cm are the primary peaks. Assignments for the peaks found for glibenclamide can be determined based on results from an analysis of the infrared spectra of many sulfonylurea derivatives: 1333 cm1 1 to -S02-N-; 1163 cm (split peak) to -S02; 3363 and 3313 cm to urea N-H stretch; 1515 cm to urea, amide II. Many of the absorption maxima have been found to become less intense as a result of salt production.[3] Using a Perkin-Elmer R32 (90MHz) spectrometer, the NMR spectrum for glibenclamide in dimethylsulphoxide-D6 (DMS) was obtained. The figures' designations are consistent with those written by Hajdetal, who also included the signal generated by the -S02-NH proton (offset) at 10.27 ppm. When the spectrum is calculated using trifluoroacetic acid as the solvent, the -CO-NH- proton that was detected in DMS as a doublet at 6.27ppm vanishes.[3]

Pharmacokinetic Properties:- this is defined as "what the body does to the drug," and it is often explained in terms of four vital processes: absorption, distribution, metabolism, and elimination, or ADME.

Absorption:- Glibenclamide is well absorbed from the digestive tract after being administered orally. Its variable bioavailability ranges from 50% to 80% as a result of significant first-pass liver metabolism. Its rate and degree of absorption can be impacted by food intake.[10]

Distribution:- Glibenclamide binds largely to plasma proteins, particularly albumin, and shows little binding to red blood cells. It has a very wide volume of distribution, indicating broad tissue dispersion.[10]

Metabolism:- The cytochrome P450 enzyme system, in particular CYP2C9, is principally responsible for the hepatic metabolism of Glibenclamide. M1 and M2, which are pharmacologically inactive, are two of the main metabolites. Genetic variations in CYP2C9 may affect how Glibenclamide is metabolised, which might affect how each person responds to a medicine. [10]

Elimination:- Renal excretion is the primary route of elimination for Glibenclamide and its metabolites. In people with normal renal function, the medication has a half-life of between 10 and 24 hours. The elimination half-life may be extended in individuals with poor renal function, necessitating dosage modifications.[10]

C_{max}:- Glibenclamide's Cmax, or peak plasma concentration, can change based on a number of parameters, including the dose given, the features of each patient, and the medication's formulation. Within 2 to 4 hours, the peak plasma concentration is attained. In therapeutic dosages, the highest concentration attainable might range from 0.3 to 1.5 micrograms per millilitre (g/mL).[5]

T_{max}:- The amount of time provided, the characteristics of each patient, and the formulation of the drug can all affect how long it takes for Glibenclamide to reach its maximum plasma concentration (T_{max}). Glibenclamide is typically quickly absorbed from the gastrointestinal system after oral treatment. Glibenclamide normally reaches its Tmax after 2 to 4 hours.[9]

T_{half} :- The amount of time it takes for half of a medicine to be cleared from the body is known as the half-life of Glibenclamide. The half-life can change based on the

features of each patient as well as variables like kidney and liver function as well as the medication's precise formulation. In people with normal renal function, the elimination half-life of Glibenclamide normally varies from 10 to 24 hours. It's crucial to remember that in individuals with compromised renal function, the half-life might be extended. [9]

Mechanism of working:- Glibenclamide, which is commonly referred to as glyburide, is a sulfonylurea class of oral antidiabetic medication. Its mechanism of action primarily involves stimulating insulin release from the beta cells of the pancreas and improving tissue sensitivity to insulin. Glibenclamide enters into the blood stream and reaches pancreatic beta cells after administration.[11] Glibenclamide interacts with a particular receptor known as the sulfonylurea receptor 1 (SUR1) inside beta cells. This binding inhibits the activity of ATP-sensitive potassium (KATP) channels, which are typically open at rest. Glibenclamide produces cell membrane depolarization by inhibiting KATP channels. Voltage-gated calcium channels open as a result of this depolarization, letting calcium ions into the beta cells. Calcium ion influx induces exocytosis of insulin-containing vesicles, resulting in insulin release into the bloodstream. The enhanced insulin secretion caused by glibenclamide helps to compensate for the decreased insulin synthesis and release found in type 2 diabetes patients. Glibenclamide lowers blood glucose levels and improves glycemic control by providing an extra stimulus for insulin release. The effect of glibenclamide on insulin sensitivity is another significant part of its mode of action. Insulin resistance is a primary contributor to high blood glucose levels in type 2 diabetes.[12] Glibenclamide has been proven to increase tissue insulin sensitivity, allowing cells in the body to use glucose more effectively. The exact mechanism through which glibenclamide enhances insulin sensitivity is unknown. Glibenclamide, on the other hand, is thought to enhance the number and activity of insulin receptors on target cells, increasing glucose absorption and utilisation. This insulin sensitivity effect contributes to the reduction of insulin resistance seen in type 2 diabetes.[12] It should be noted that the effectiveness of glibenclamide in enhancing insulin sensitivity varies across individuals. Diet and physical exercise are two lifestyle variables that might alter insulin sensitivity and should be considered in addition to pharmaceutical therapy. While glibenclamide has been shown to be effective in decreasing blood glucose levels, it is critical to use this medication with caution. To avoid hypoglycemia, a possible adverse

effect of glibenclamide medication, blood glucose levels must be closely monitored. When blood sugar levels go too low, symptoms such as dizziness, disorientation, sweating, and weakness arise. To ensure the safe and successful administration of Glibenclamide, patients must be educated on the signs, symptoms, and management of hypoglycaemia.[12] The medicine works by inhibiting the ATP-sensitive K+ channel, which depolarizes cells and releases insulin.

Medicinal Uses:- Glibenclamide, sometimes referred to as glyburide, is an oral diabetic medicine that belongs to the sulfonylureas pharmacological class. Type 2 diabetes mellitus is the primary condition it is used to treat. It is characterized by elevated blood sugar levels caused by either insulin resistance or insufficient insulin production..[14]

Treatment of Type 2 diabetes mellitus:- Glibenclamide is oral anti-diabetic drug, it acts by lowering blood glucose levels and boost pancreatic insulin secretion also enhance tissue insulin sensitivity. When diet and exercise alone are insufficient for controlling blood sugar levels, it is routinely recommended. It can only use in diabetes type 2 since it does not show any effect in the case of type 1 diabetes mellitus, since no insulin is produced in pancreas and Glibenclamide demands some pancreatic insulin secretion. The main mechanism of action of Glibenclamide involves stimulating the release of insulin from the beta cells in the pancreas. It acts by binding to sulfonylurea receptors on the pancreatic beta cells, which leads to closure of ATP-sensitive potassium channels. This closure leads to membrane depolarization and subsequent influx of calcium ions, triggering the release of insulin. By increasing insulin secretion, Glibenclamide helps to overcome the reduced insulin production often seen in type 2 diabetes. Another important aspect of Glibenclamide action is its ability to enhance tissue sensitivity to insulin, also known as insulin sensitization. It achieves this by increasing the number and activity of insulin receptors on target cells, allowing for more efficient utilization of glucose. This helps to counteract the insulin resistance commonly observed in type 2 diabetes, where tissues become less responsive to the effects of insulin. When dietary adjustments and exercise alone are insufficient to achieve optimal glycaemic control, Glibenclamide is often given as an adjuvant to these efforts. It is accessible in oral tablet form, making it easy for patients to take. One of the key aims of type 2 diabetes management is to establish and

maintain good glycaemic control, because prolonged hyperglycaemia can lead to a variety of problems impacting numerous organ systems.[14] Glibenclamide reduces the risk of serious consequences by lowering blood glucose levels. It helps to balance blood sugar levels and prevent the long-term harm associated with hyperglycaemia by boosting insulin production and enhancing insulin sensitivity. Furthermore, Glibenclamide has been demonstrated to lower glycosylated haemoglobin (HbA1c) levels. HbA1c is a metric of average blood glucose levels over the past two to three months, and lowering HbA1c is an essential therapeutic goal in diabetes care. When taken correctly, Glibenclamide can help reduce HbA1c levels, indicating enhanced long-term glycaemic management. An additional benefit of Glibenclamide is its relatively quick beginning of action, which allows for an immediate drop in blood glucose levels. This is especially effective in circumstances where urgent glycaemic control is required, such as during acute bouts of hyperglycaemia. However, it is crucial to highlight that the usage of Glibenclamide in type 2 diabetes should be tailored to the patient's specific needs, taking into account characteristics such as age, renal function, liver function, and other comorbidities. In individuals with poor renal or hepatic function, dosage changes may be required to prevent drug build-ups and associated harmful effects. [15]

Adverse Effects:- Side effects are characterised as temporary issues that go away with drug withdrawal, and occasionally even with continued use. Toxicology is the term used to describe an aberration in organ function that lasts until the medicine is stopped.[8] There might be some negative consequences from glyburide. Even though not all of these adverse effects are likely to occur, if they do, medical treatment may be required.[7]

1) **Skin related diseases:-** Glibenclamide may result in skin problems such dermatitis, skin eruptions, and photosensitivity (increased sensitivity to sunlight).[16]
2) **Allergic symptoms:** Skin rashes, itching, hives, and swelling are just a few of the allergic symptoms that Glibenclamide may bring on. Anaphylaxis, a severe allergic reaction that can be fatal, is exceedingly rare.[16]
3) **Gastrointestinal Effects:** Glibenclamide may result in gastrointestinal disturbances such as nausea, vomiting, stomach pain, diarrhoea, and

constipation. Generally speaking, these adverse effects are minor and transient.[16]

4) **Low blood sugar levels**, or hypoglycaemia, are Glibenclamide most frequent side effect. It may happen if the dosage is too high or if not enough food is consumed. Dizziness, disorientation, sweating, shakiness, and weakness are all signs of hypoglycaemia. To avoid consequences, hypoglycaemia must be promptly diagnosed and treated.[16]
5) **Effects on the Liver:** In a small percentage of instances, Glibenclamide has been linked to liver impairment. Jaundice (yellowing of the skin and eyes), dark urine, exhaustion, and stomach discomfort are possible symptoms. Periodic liver function tests should be monitored, and any symptoms of liver impairment should be immediately reported to a medical expert.[16]
6) **Haematological Effects:** Glibenclamide unusual effects on blood cell counts might result in anomalies in the haematology. This may involve alterations in platelets (thrombocytopenia), leukopenia, and anaemia of the red and white blood cells, respectively. It is advised to regularly check blood cell counts when using Glibenclamide.[16]
7) **Weight Gain:** A side effect of Glibenclamide treatment is weight gain. This is explained by better glycaemic control and a bigger appetite. Regularly checking weight and committing to a healthy lifestyle will help effectively manage weight fluctuations.[16]
8) **Cardiovascular Effects:** According to certain research, sulfonylureas, such as Glibenclamide, may be linked with a higher risk of cardiovascular events. The overall cardiovascular risk must be assessed on an individual basis because the research is not yet solid.[16]

Treatment of Overdose:- When a patient consumes more Glibenclamide than is recommended, an overdose may result. Due to the increased risk of severe hypoglycaemia (low blood sugar levels), an overdose might result in potentially dangerous consequences. In situations of Glibenclamide overdose, immediate identification and effective care is crucial.[17]

Glibenclamide Overdose Symptoms[17]:-

1) **Hypoglycaemia:-** The main issue with Glibenclamide overdose is severe hypoglycaemia, which can cause seizures, loss of consciousness, coma, disorientation, dizziness, extreme perspiration, shivering, palpitations, and impaired vision. An early response and action are necessary for hypoglycaemia.
2) **Gastrointestinal Disturbances:-** An overdose may result in gastrointestinal symptoms such as diarrhoea, abdominal discomfort, nausea, and vomiting.
3) **Cardiovascular Effects:-**In a small percentage of cases, Glibenclamide overdose can cause cardiovascular symptoms like tachycardia, hypotension, and cardiac arrhythmias.
4) **Neurological effect:-** Glibenclamide overdoses can have neurological side effects, including weakness, lethargy, aberrant reflexes, difficulty speaking, and in severe cases, breathing difficulties.

Glibenclamide Overdose Treatment[17]:-

1) **Administration of glucose:-** The main objective of therapy is to raise blood glucose levels in order to stop or control hypoglycaemia. The mainstay of Glibenclamide overdose therapy is the injection of glucose. Treatment options include oral glucose administration, intravenous (IV) glucose infusion, and intramuscular (IM) glucagon injection, depending on the severity of the symptoms and blood glucose levels. The best way to provide glucose and the dosage will be decided by healthcare specialists.
2) **Seeking Immediate Medical Attention:** It's critical to get help right away if a Glibenclamide overdose is suspected.
3) **Observation and Medical Attention:** Patients who overdosed Glibenclamide might need to be monitored and given medical attention for a while. This makes it possible for medical personnel to keep a watch for any delayed or repeated hypoglycaemia episodes and address any potential issues that could develop.
4) **Supportive treatments:** To control symptoms and stabilise the patient, supportive treatments may also be required in addition to the administration of glucose. This can entail preserving an open airway, giving oxygen support, and attending to any further overdose-related problems.

5) **Prevention of Future Overdoses:** After a Glibenclamide overdose, it's important to assess the factors that contributed to the overdose and take precautions to avoid it happening again. The patient and family members should get education and counselling on drug adherence, dose guidelines, and potential hazards.
6) **Close Monitoring:** To guarantee appropriate correction of hypoglycaemia and stop recurrence, blood glucose levels must be monitored continuously. It may be necessary to monitor the patient often at first, including taking fingerstick blood glucose readings, and then on a regular basis until they have stabilised.

Contraindications:- The term "contraindications" refers to particular situations or health issues where it is deemed risky or potentially hazardous to use a particular medicine. Glibenclamide can show some contraindications in some patients. This medical conditions can be serious, and consulting a medical professional immediately is important. Here are the following contraindications of Glibenclamide.[18]

1) Pregnancy and lactation:- During the pregnancy, use of Glibenclamide by the mother is not safe, since it cross the placenta and growing foetus can get affected by the drug. It is recommended to avoid the use of Glibenclamide during the first trimester. Glibenclamide can be passed to baby by the breastfeeding as well. [18]
2) Glibenclamide shouldn't be taken by anyone who have a known hypersensitivity or adverse response to the medication or any of its ingredients. Hypersensitivity symptoms might include skin rashes, itching, hives, swelling, or breathing problems. If an allergic response is believed to have occurred, immediate medical treatment should be sought. [18]
3) Glibenclamide is largely excreted through the kidneys in cases of severe renal impairment. Therefore, medication clearance may be compromised in those with severe renal impairment, who also have a higher risk of drug build-up. In these circumstances, Glibenclamide usage should be avoided or closely monitored. [18]
4) Glibenclamide is not recommended for treating the type 1 diabetes, which is distinguished by a lack of insulin synthesis. Glibenclamide is unsuccessful in

people with type 1 diabetes who need exogenous insulin because it works by causing the pancreatic beta cells to produce more insulin. [18]

5) Glibenclamide is not advised for use in those who have diabetic ketoacidosis (DKA). A fatal side effect of diabetes, DKA is known by elevated blood sugar, ketone generation, and metabolic acidosis. Instead of oral diabetes drugs like Glibenclamide, DKA is treated with insulin therapy and fluid replenishment. [18]
6) Glibenclamide has the ability to conceal the signs of adrenal insufficiency, which is characterised by insufficient hormone synthesis by the adrenal glands. As Glibenclamide can inhibit the release of glucagon, a hormone essential for the synthesis of glucose under stress, its usage in people with adrenal insufficiency raises the risk of a possibly fatal adrenal crisis. [18]
7) Glibenclamide shouldn't be used in those who are diabetic coma or pre-coma sufferers. These serious diabetic consequences are linked to mental changes, metabolic issues, and electrolyte abnormalities. In these cases, prompt medical attention is necessary, usually incorporating insulin and hydration treatment. [18]

Interaction:- Drug interactions between Glibenclamide and other substances may alter the efficacy, security, and metabolism of the latter. These interactions may happen as a result of other drugs' effects on Glibenclamide metabolism, their binding to plasma proteins, or changes in blood glucose levels. To make the most use of Glibenclamide therapeutically, it is crucial to be aware of these possible interactions. Intriguing medication interactions include the following:[19]

1) **Protein bound drug:-** When taken concurrently with other highly protein-bound medications, there is the potential for a pharmacokinetic interaction and a potential Glibenclamide of hypoglycaemia effects.[7]
2) **Drugs Affecting Hepatic Microsomal Enzymes** :- By CYP2C9, glyburide is mostly metabolised. It's important to think about possible interactions with CYP2C9 inducers or inhibitors.[7]
3) **Beta-Blockers:** Non-selective beta-blockers, such propranolol, might hide hypoglycaemia’s tell-tale signs, making it challenging to identify low blood sugar levels. Patients using Glibenclamide plus beta-blockers need to closely monitor their blood sugar levels and be alert to any signs of hypoglycaemia.[19]

4) **Rifampicin:** The antibiotic rifampicin, which is used to treat Tuberculosis and other diseases, might speed up the metabolism of Glibenclamide, lowering its levels in the blood and possibly reducing its effectiveness. In patients on rifampicin, careful blood glucose monitoring and Glibenclamide dose adjustment may be required.[19]
5) **Sulphonamide Antibiotics:** By displacing Glibenclamide from plasma protein binding sites, certain sulphonamide antibiotics, such as sulfamethoxazole, may raise its levels in the blood. Potentially, this might raise the risk of hypoglycaemia. When providing these medications together, it may be required to monitor blood glucose levels and change the Glibenclamide dosage.[19]
6) **Nonsteroidal anti-inflammatory medicines (NSAIDs):** NSAIDs may counteract the blood glucose-lowering benefits of Glibenclamide. They could raise blood glucose levels and lessen Glibenclamide efficacy. In patients using NSAIDs, regular blood glucose checks and dose adjustments for Glibenclamide may be required.[19]

Vascular Effect :- The main observation that can be derived from the recent review is that the targeting of KATP channels has no consequence on vasoconstriction at the basal resting vascular tone.[20] It is worth noting, however, that Glibenclamide does have the ability to reduce the vasodilation that is induced by levcromakalim and other KCOS. What is particularly interesting is that the observed effect of Glibenclamide is similar to the effect of the newly developed CGRP monoclonal antibodies, which only constrict arteries that have been pre-dilated without altering the baseline tone.[20] The relationship between Glibenclamide and other vasoactive compounds, such as CGRP and GTN, known to trigger migraine attacks, has been found to be paradoxical. Moreover, there is a scarcity of information regarding the influence of Glibenclamide on human cranial arteries when researched in vivo.[20] **Neurological Finding:-** The discussion of the potential of Glibenclamide as a neuroprotective antidementia drug, specifically in the context of cognitive impairment associated with diabetes mellitus, holds no significance.[21] The examination delves into the multifaceted impacts of Glibenclamide on the central nervous system (CNS) and its potential role in averting cognitive decline. Moreover, it presents an insight into the molecular mechanisms behind cognitive dysfunction in diabetes and other diseases, and posits that Glibenclamide may possess neuroprotective and anti-dementia properties. Empirical

investigations indicate that Glibenclamide impedes neuroinflammation and cellular demise within the CNS, thus offering possible therapeutic advantages. In any case, more investigation is needed to determine the clinical effectiveness of Glibenclamide in preventing dementia in diabetic patients.[21]The studies have demonstrated the inefficacy of Glibenclamide in clinical studies aimed at provoking headaches, ascribing this to the drug's restricted interaction with the pertinent subtype of KATP channel. Simulations indicate diminished levels of occupancy for the vascular subtype, thereby implying the requirement for new inhibitory compounds to investigate the inhibition of KATP channel in the treatment of migraines.[22]

Conclusion :-The review article provides an examination of Glibenclamide, also known as glyburide which's an oral medication used for managing type 2 diabetes mellitus. It covers aspects such, as the drugs properties, how it works, its medical applications, side effects, treatment for overdose situations where it should not be used and interactions with other drugs. Glibenclamide functions by stimulating the release of insulin from beta cells and improving the body’s response to insulin, which helps blood glucose levels. It is recommended for type 2 diabetes patients when dietary changes and physical activity alone are not enough to achieve control over blood sugar levels. The article provides information on the drugs peak concentration in the bloodstream how quickly it reaches that point and how long it stays in the body. It also mentions that Glibenclamide has limited solubility in water and is distributed throughout the body extensively. Side effects may include blood sugar levels (hypoglycaemia) skin conditions, gastrointestinal issues and potential risks to health. In case of an overdose on Glibenclamide immediate medical attention is necessary. Treatment involves administering glucose and providing care. The article also discusses interactions with drugs, situations where its use should be avoided or monitored closely due, to conditions or medications being taken simultaneously. Additionally highlighted are vascular consequences of using Glibenclamide as well as emphasizing the importance of avoiding future overdoses while educating patients and their families about medication adherence and possible risks.

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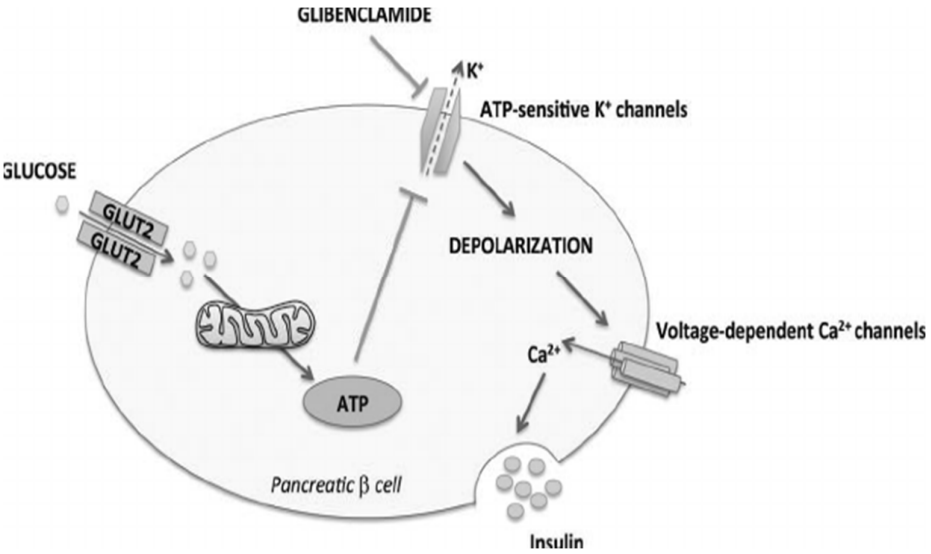
(Table 1.1) Pharmacokinetic properties [9]

BCS classification	Class II
C_{max}	682 ± 196
T_{max}	105 ± 36
T_{half}	135 ± 10



(Fig 1.1) Mechanism of action of drug

(Table1.4) Dosage of Glibenclamide [7]

Stage of patient	Conventional dosage
Initial dosage for untreated patient	2.5 – 5 mg daily
Initial dosage for patient shifting from other anti-diabetic drugs	2.5 - 5 mg daily
Initial dosage for patients transfer from insulin	1.25- 5 mg daily
Titration and maintenance dosage	1.25 – 20 mg daily

(Table 1.5) Interaction of Glibenclamide with drug.[7]

Sr. No.	Drug	Interaction	Observation
1	ACE inhibitors	Enhance hypoglycaemic effects	loss of glycaemic control
2	β-Adrenergic blocking agents	Impaired glucose tolerance	If concomitant therapy is necessary, a β_1-selective adrenergic blocking agent may be preferred
3	Chloramphenicol	Enhance hypoglycaemic effects	loss of glycaemic control
4	Clarithromycin	hypoglycaemic effects	loss of glycaemic control when clarithromycin is initiated or discontinued
5	Diuretics	exacerbate diabetes mellitus	loss of glycaemic control
6	Fluoxetine	Enhance hypoglycaemic effects	loss of glycaemic control when fluoxetine is initiated or discontinued
7	NSAIAs	Possible displacement from plasma proteins	loss of glycaemic control when NSAIAs are initiated or discontinued
8	Phenylbutazone	Enhance hypoglycaemic effects	Monitor blood glucose control
9	Revamping	exacerbate diabetes mellitus	loss of glycaemic control
10	Sulphonamides	Possible displacement from plasma proteins	adverse effects