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# Evaluating Gliclazide Safety and Effectiveness in the Management of Type 2 Diabetes Mellitus

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**Abstract:- Gliclazide is an oral medication used to treat Type 2 diabetes mellitus (T2DM) by reducing blood sugar levels. Being a second-generation sulfonylurea, it functions by promoting the release of insulin from pancreatic beta cells, therefore improving the regulation of blood sugar levels. This study assesses the effectiveness and safety of gliclazide in treating type 2 diabetes mellitus (T2DM), specifically as a second-line treatment after metformin. It also compares the advantages and disadvantages of gliclazide with other oral antidiabetic medications. The study reviews global diabetes guidelines and clinical studies focusing on gliclazide's mechanism of action, pharmacokinetic properties, and clinical outcomes. Gliclazide effectively reduces HbA1c levels, fasting plasma glucose, and postprandial blood glucose, showing comparable or superior efficacy to other sulfonylureas. The mechanism involves stimulating insulin release by binding to the sulfonylurea receptor on pancreatic beta cells. The trial indicated that gliclazide may slow the progression of diabetic retinopathy, particularly in preventing preproliferative stages, compared to other sulfonylureas. Gliclazide also demonstrated a lower incidence of hypoglycemia and weight gain. Gliclazide is an effective and safe second-line treatment for T2DM, providing robust glycemic control and additional benefits in preventing diabetic retinopathy progression. Its favorable safety profile, particularly regarding hypoglycemia and weight gain, supports its use in diabetes management.**

***Keywords:-*** *Gliclazide, Type 2 Diabetes Mellitus, Sulfonylureas, Glycemic Control, Diabetic Retinopathy, Hypoglycemia, Insulin Secretion.*

## I. INTRODUCTION

T2DM is characterized by insulin resistance and impaired insulin secretion, necessitating effective management to prevent complications and improve patient quality of life. While metformin serves as the foundational treatment, alternative oral options include “sulfonylureas (SUs), meglitinides, α-glucosidase inhibitors, thiazolidinediones (TZDs), dipeptidyl peptidase-4 (DPP-4) inhibitors, and sodium glucose transporter-2 receptor (SGLT-2) inhibitors” when metformin is insufficient or contraindicated. The Dutch diabetes management guideline provides explicit recommendations. Gliclazide effectively reduces fasting plasma glucose, postprandial blood glucose, and HbA1c levels, indicating its ability to regulate glucose levels over a period of 8-10 weeks. After undergoing substantial metabolism in the liver, the breakdown products of this substance are eliminated from the body through urine (60-70%) and faeces (10-20%). The IUPAC designation of Gliclazide (C15H21N3O3S) is 1-[(4-methylbenzene) sulfonyl] benzene. The chemical compound is called -3-octahydrocyclopenta[c].The compound depicted in Figure 1 is pyrrol-2-yl urea. The product is commercially promoted under many brand names such as Diamicron, Diamicron MR, Glimicron, and Mylan-Gliclazide. Gliclazide is categorised as a hypoglycemic drug, specifically a sulfonylurea, which is used to treat diabetes [8].

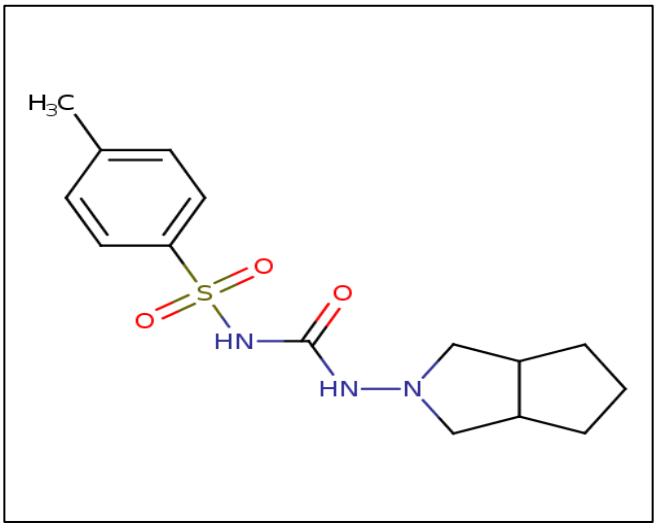


Fig 1 Molecular Structure of Gliclazide

Gliclazide over other SUs due to evidence suggesting its cardiovascular benefits and selectivity for pancreatic SU receptors, minimizing adverse effects on myocardial function compared to non-selective SUs like glibenclamide. Gliclazide's favorable safety profile, reduced hypoglycemic risk, and efficacy in managing glycemic levels make it a preferred choice in T2DM treatment, aligning with various international guidelines that emphasize individualized therapy to achieve optimal outcomes. This table 1 summarizes recommendations from various global diabetes guidelines regarding the use of sulfonylureas, including specific considerations for Gliclazide MR in patients. This review aims to evaluate the efficacy and safety of Gliclazide in the management of T2DM. Specifically, it examines the role of Gliclazide as a second-line treatment option following metformin therapy, comparing its benefits and risks with other oral antidiabetic agents recommended in global diabetes management guidelines.

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Table 1 Recommendations on the use of Sulfonylureas and Gliclazide MR in Patients

| Diabetes Guidelines | Second-Line Treatment Recommendation in Patients with Suboptimal Glucose Control on Metformin | Guideline Information Specific to Gliclazide Modified Release (MR) |
|---|---|---|
| UK (NICE/SIGN) [1] | Add DPP-4i, pioglitazone or SU | GLP-1RAs not recommended |
| South Asian Federation of Endocrine Societies [1] | Add SU as second-line agents of choice | Gliclazide MR or glimepiride are preferred over conventional SU |
| Global (International Diabetes Federation) [2] | Preferred add-on therapies are SU (not glibenclamide/glyburide), DPP-4i or SLGT-2i | Not Applicable |
| Global resource-limited settings (WHO) [2] | Add an SU | Gliclazide is preferred SU if hypoglycaemia is a concern |
| USA/Europe (ADA/EASD) [3] | Add SU as second-line agents if cost is a compelling issue | Reserve SU for fourth-line treatments (after DPP-4i, GLP-1RA, SGLT-2i and/or TZD) if there is a compelling need to minimize hypoglycaemia or weight gain. Gliclazide not licensed in the US for T2DM |

## II. BASICS OF SULFONYLUREAS

Sulfonylureas enhance insulin secretion primarily by stimulating pancreatic beta-cell activity, making them effective when residual beta-cell function exists. Long-term use may also involve extra pancreatic actions. Although hypoglycemia is a potential side effect, it is uncommon and usually indicates excessive dosage, necessitating hospital treatment [4]

Sulfonylureas are recommended for persons who are not obese or when metformin is contraindicated or not well-tolerated. The choice of sulfonylureas is determined by factors such as adverse effects, duration of action, patient age, and renal function. Long-acting medications such as chlorpropamide and glibenclamide have an increased likelihood of causing hypoglycemia, especially in older individuals, and are often not used. It is preferable to use shorter-acting alternatives like gliclazide or tolbutamide. Chlorpropamide, due to its side effect profile, is no longer recommended compared to other sulfonylureas[5].

When diet and sulfonylurea treatment fail, combining sulfonylureas with metformin or acarbose may be considered, though caution is warranted due to potential risks. Combination with thiazolidinediones like pioglitazone or rosiglitazone is another option. Bedtime isophane insulin may also be effective but can lead to weight gain and hypoglycemia.

During intercurrent illness such as myocardial infarction or infection, insulin therapy should temporarily replace sulfonylureas. Before surgery, sulfonylureas should be omitted to prevent perioperative hyperglycemia, necessitating insulin therapy [6]

If symptoms continue after dietary efforts, sulfonylureas should be recommended cautiously due to their potential to cause weight gain. For obese individuals, metformin is the preferable medication. Exercise caution in older individuals and those with mild to moderate liver or kidney dysfunction due to the potential for low blood sugar levels. Short-acting agents metabolized primarily in the liver, such as “tolbutamide, gliquidone, and gliclazide, may be used cautiously in renal impairment with careful glucose monitoring’’ [7] Contraindications include severe hepatic or renal impairment, porphyria, breastfeeding, and pregnancy. Sulfonylureas are also contraindicated in ketoacidosis [7]

Side effects of sulfonylureas, though generally mild and infrequent, may include gastrointestinal disturbances. Chlorpropamide is associated with more side effects due to prolonged action and heightened hypoglycemic risk, particularly with alcohol consumption, and may rarely cause hyponatremia. Allergic reactions, photosensitivity, and rare blood disorders such as anaemia and liver function abnormalities have been reported with various sulfonylureas [8]

In cases of “Maturity-onset diabetes of the young (MODY)”, a monogenic form of diabetes characterized by genetic inheritance patterns and impaired insulin secretion, several subtypes exist, including MODY1, MODY2, MODY3, MODY5, and MODY10. MODY1 and MODY3, which involve mutations in the HNF4A and HNF1A genes respectively, are particularly responsive to sulfonylureas like Gliclazide due to their ability to stimulate insulin secretion in patients with residual beta-cell function. Gliclazide is managed in these specific MODY subtypes by tailoring treatment based on genetic subtype to optimize management and improve patient outcomes.

- *Clinical Pharmacology of Gliclazide*

Gliclazide, a medication belonging to the sulfonylurea class, has a moderate half-life of around 11 hours. It undergoes significant metabolism and only a small portion (4%) is eliminated by the kidneys. The presence of the distinctive azabicyclo-octyl group in the sulfonylurea structure boosts its properties, specifically in activating insulin secretion through the sulfonylurea receptor in β cells and potentially influencing the transport of calcium within cells. Gliclazide specifically enhances the atypical initial release of insulin in individuals with type 2 diabetes and also affects the subsequent phase, resulting in a reduced occurrence of episodes of abnormally low blood sugar levels and weight gain in comparison to some other sulfonylureas. Additionally, it reduces hepatic glucose production, enhances glucose clearance, and decreases platelet adhesion and

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aggregation while increasing fibrinolysis. These actions may help slow the progression of diabetic microangiopathy [9].

➢ *Indication*

Gliclazide is prescribed for the management of hyperglycemia in individuals with gliclazide-responsive diabetes mellitus of stable, moderate, non-ketosis prone, mature onset, or adult type, when proper dietary management and exercise are insufficient or when insulin therapy is not suitable [10].

➢ *Contradiction*

Gliclazide is contraindicated in cases of diabetes accompanied by acidosis, ketosis, or coma, as well as in individuals with a history of recurrent ketoacidosis or coma. Furthermore, it is not recommended for individuals with significant liver or kidney dysfunction. Individuals who have a heightened sensitivity to sulphonylurea agents or who are experiencing an adverse reaction to alcohol should refrain from consuming gliclazide. Additionally, gliclazide is not recommended during pregnancy or breastfeeding, and its use in children has not been established for safety and effectiveness [10].

- **Dose:** The recommended daily dosage is 80 to 320 mg, starting with 160 mg/day [11].
- **Duration:** Patients with diabetes mellitus require life-long therapy [11].
- **Route of Elimination:** Metabolites and conjugates are primarily eliminated by the kidneys (60-70%) and also in the feces (10-20%).
- **Affected Organisms:**Gliclazide affects humans and other mammals.
- **Half-Life:** The half-life of gliclazide is approximately 10.4 hours, with a duration of action between 10-24 hours.
- **Toxicity:** The LD50 for gliclazide is 3000 mg/kg (orally in mice). Accumulation of gliclazide and its metabolites can occur in individuals with severe hepatic and/or renal dysfunction. Symptoms of hypoglycemia include dizziness, lack of energy, drowsiness, headache, and sweating [11].

➢ *Chemical Development*

Both type 1 and type 2 diabetic patients experience the development of microangiopathy and macroangiopathy, which are caused by hyperaggregation and adhesion of platelets, increased fibrin deposition, diminished plasminogen activator, increased blood viscosity, lipid deposition, and atherosclerosis, in addition to hyperglycemia. Gliclazide, which contains a unique azabicyclo-octyl ring, was chosen for its potential hypoglycemic and haemobiological effects [12].

➢ *Physiochemical Properties*

The molecular weight of gliclazide is 323.4, and its chemical formula is 1-(1-azabicyclo[3,3,0]oct-3-yl)-3-(p-tolylsulfonyl)urea. It is an acid of low strength, with a pKa value of 5.8. It has higher solubility in lipids compared to tolbutamide, with a partition coefficient between buffer (pH 7.4) and chloroform exceeding 1000. Its classification as a second-generation sulfonylurea molecule is based on its heterocycle ring [13].

➢ *Mechanism of Action of Gliclazide*

Gliclazide is an oral medication used to treat non-insulin-dependent diabetic mellitus (NIDDM), a condition characterised by high blood sugar levels. Being a member of the sulfonylurea class, it activates pancreatic β cells to secrete insulin, hence enhancing both the release of insulin during periods of fasting and in response to meals. These medications differ in their dosage, absorption rate, length of effect, elimination process, and the specific locations on β cell receptors where they bind. Gliclazide and other sulfonylureas improve the utilisation of glucose in the peripheral tissues, decrease the production of glucose in the liver, and maybe enhance the quantity and responsiveness of insulin receptors. While there is a correlation between this and weight gain, it is not as significant as the correlation with insulin [7]. Consistent meal intake is necessary due to the increased likelihood of hypoglycemia in old, disabled, and malnourished persons.

Sulfonylureas are commonly employed for the treatment of type 2 diabetes mellitus as they promote the secretion of insulin from pancreatic beta cells. Their efficacy is contingent upon the existence of residual beta cell function. The process entails the inhibition of ATP-sensitive potassium (KATP) channels in the beta cell membrane, resulting in depolarization of the membrane, inflow of calcium ions, and subsequent release of insulin [14]. Typically, KATP channels shut down in response to an increase in glucose levels inside the cell. This procedure unfolds in the following manner: Glucose is transported into beta cells through GLUT2 transporters, where it is then phosphorylated by glucokinase. The glucose is metabolised to produce ATP, which leads to the closure of KATP channels, as depicted in Figure 2.

Upon binding to its receptor on the pancreatic beta cell, a sulfonylurea initiates a cascade of actions. Initially, it attaches to the sulfonylurea receptor, resulting in the closure of the KATP channels. The prevention of potassium ion outflow leads to a change in the electrical charge across the cell membrane, causing it to become more positive. Depolarization subsequently activates calcium channels, facilitating the influx of calcium ions into the cell. The elevated intracellular calcium concentration ultimately stimulates the exocytosis of granules carrying insulin, promoting the release of insulin.

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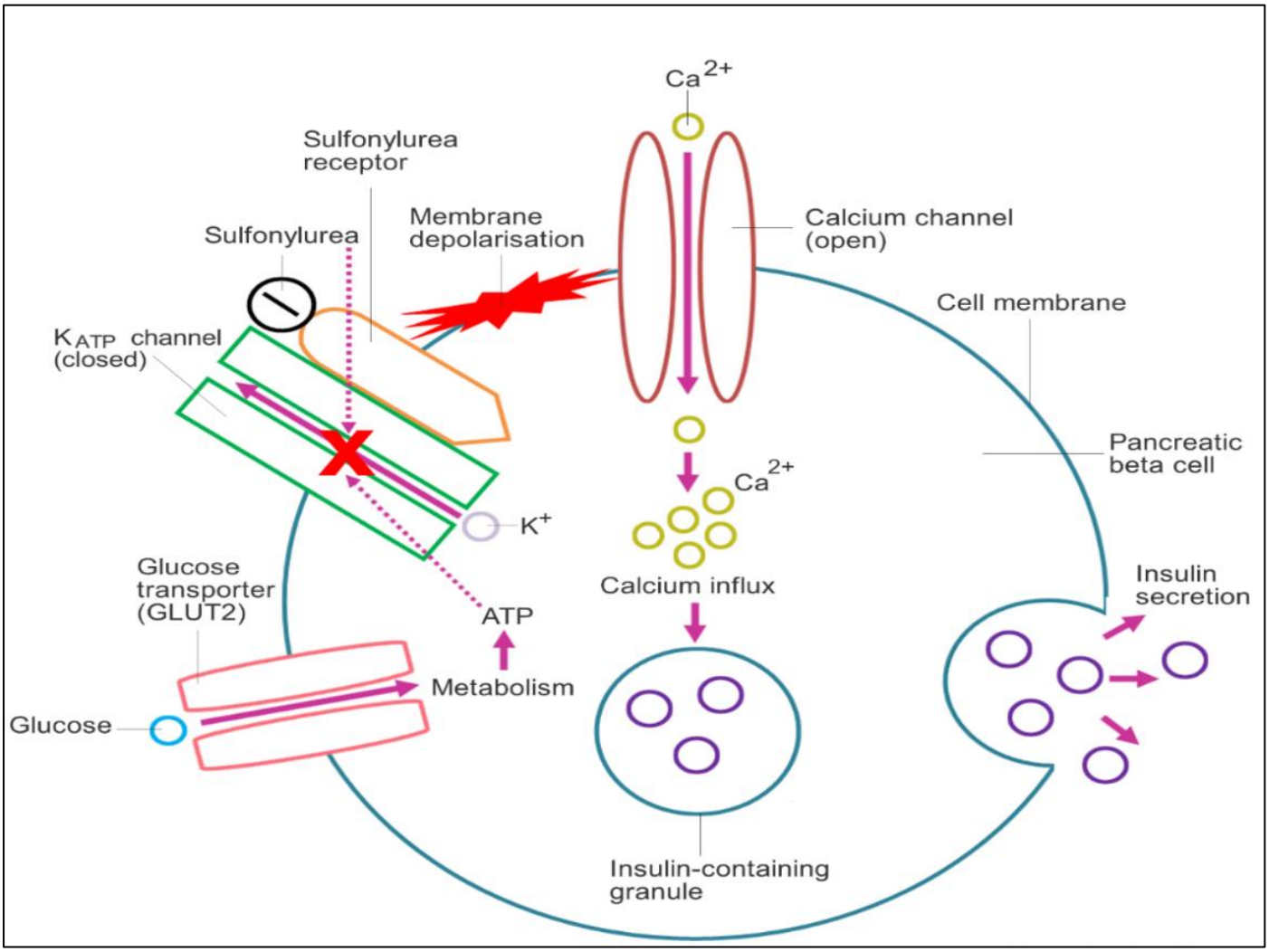


Fig 2 Schematic Representation of Sulfonylureas, Including Gliclazide, and their Site of Action [13].

➢ *The main side effects of Sulfonylureas Include [14]*

- **Hypoglycemia:** More common with long-acting sulfonylureas. Risk factors include increasing age, skipping meals, weight loss, and impaired renal or hepatic function.
- **Gastrointestinal disturbances:** Such as nausea, vomiting, and diarrhea.
- **Weight gain.**

Patients prescribed sulfonylureas should be informed about the potential risk of hypoglycemia. For elderly patients, a short-acting sulfonylurea like tolbutamide is recommended due to its short half-life, whereas long-acting sulfonylureas like glibenclamide should be avoided because of the higher risk of hypoglycaemia [14].

➢ *Sulfonylurea Equivalent Doses / Switching*

When switching between gliclazide MR and gliclazide standard release:

- Gliclazide 80mg standard release is approximately equivalent to gliclazide 30mg MR.
- The manufacturers recommend monitoring blood glucose levels during the switch.

➢ *Pharmacokinetics of Gliclazide*

Gliclazide is well-absorbed from the gastrointestinal tract, achieving peak plasma concentrations within 4 to 6 hours post-administration, with bioavailability nearly unaffected by food. It is extensively bound to plasma proteins, primarily albumin, and metabolized in the liver mainly by CYP2C9 enzymes. The drug's metabolites are primarily excreted in the urine, with a small fraction eliminated unchanged. The elimination half-life of gliclazide ranges from 10 to 12 hours, supporting once or twice-daily dosing, particularly with the modified release formulation as shown in Table 2 [15].

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Table 2 Sulfonylurea Agents and their Pharmacokinetic Properties [13]

| Sulfonylurea | Generation | Pharmacokinetic Properties |
|---|---|---|
| **Gliclazide** | Second | Action duration: 10-24 hours for short-acting sulfonylurea. Half-life (t1/2) is 10-12 hours for regular release and 12-20 hours for modified release. Metabolism: Processed in the liver, Protein binding: High |

➢ *Absorption*

Gliclazide is efficiently absorbed from the gastrointestinal system and reaches its highest levels in the bloodstream about 4 to 6 hours after being taken. Approximately 80% of an oral dose of gliclazide is absorbed by the body, and the highest levels are usually reached within 3 to 4 hours. However, in some cases, individuals may experience a delayed peak at around 8 hours. The maximum plasma levels of the drug, which vary based on the prescribed dose, are roughly 5 µg/ml for an 80 mg dose. These levels can range from 1 to 10 µg/ml and are partly influenced by changes in body weight (correlation coefficient r = -0.684, P< 0.001). The bioavailability of tablets is around 100% and is not influenced by the presence of food, fibre, or guar gum. It is advisable to administer gliclazide up to 30 minutes before meals in order to synchronise the absorption of the medicine and glucose.[14].

➢ *Distribution*

Gliclazide is extensively bound to plasma proteins, primarily albumin, influencing its distribution within the body. Gliclazide, similar to other sulfonylureas, exhibits a high affinity for albumin in plasma, with a binding rate of 95% (range from 85-99%). Although several medicines have the potential to displace gliclazide in laboratory settings, there have been no reported interactions of clinical significance. The volume of distribution is around 19 litres, which is similar to that of other sulfonylureas [14].

➢ *Metabolism*

Gliclazide undergoes extensive hepatic metabolism, predominantly mediated by CYP2C9 enzymes, resulting in the formation of many metabolites that lack pharmacological activity. The compound is metabolised through three primary pathways: oxidation of the tolyl group to form a carboxylic acid, hydroxylation of the azabicyclo-octyl moiety, and glucuronidation [15]. Gliclazide accounts for about 90% of the total radioactivity in plasma, while the metabolites are more soluble in water. None of the minor plasma metabolites, each accounting for less than 1-2%, show any hypoglycemia effects. Gliclazide metabolism does not exhibit genetic variability in debrisoquine phenotyped individuals, unlike tolbutamide [15] .

➢ *Elimination*

The majority of the metabolites are eliminated through the urine, whereas only a little portion of the drug is excreted without undergoing any changes. The elimination half-life of gliclazide varies between 10 and 12 hours, which makes it suitable for once or twice-daily dosage schedules, especially when using the modified release (MR) formulation. Arafa et al. conducted studies on gliclazide and found that radioactivity is expelled quickly and extensively in urine, accounting for 81% of the dose. The remaining amount is removed in faeces within a 48-hour period. Gliclazide has a low renal clearance rate of 0.5 ml/min, which makes it appropriate for individuals with renal failure [15].

➢ *Efficacy of Gliclazide in Glycemic Control*

Gliclazide demonstrates strong efficacy in glycemic control for patients with type 2 diabetes mellitus (T2DM). Numerous studies by Cordiner et al.,[16] consistently show that gliclazide effectively reduces HbA1c levels, fasting plasma glucose, and postprandial blood glucose. It is comparable or superior to other sulfonylureas and demonstrates a lower risk of hypoglycemia. This makes gliclazide a valuable second-line treatment option following metformin therapy, supporting its role in achieving and maintaining target glycemic levels in T2DM patients.

Another randomized controlled trials (RCTs) by Ishaku et al.,[17] have consistently shown that gliclazide effectively reduces HbA1c levels in patients with type 2 diabetes mellitus (T2DM). These studies have demonstrated reductions in HbA1c ranging from 0.8% to 1.5% compared to placebo, highlighting its robust efficacy in achieving target glycemic levels. Comparative studies by Arafa et al.,[13] against other sulfonylureas and oral antidiabetic agents have also shown gliclazide's superiority or comparable efficacy in glycemic control. For instance, modified release (MR) formulations of gliclazide have exhibited superior efficacy over glibenclamide in certain trials.

A meta-analysis by Raza et al.,[18] encompassing nineteen trials with 6,238 patients revealed that gliclazide, compared to other glucose-lowering agents (excluding metformin), achieved a mean reduction in HbA1c of -0.13% (95% CI: -0.25, -0.02, I2 55%). Hypoglycemic events were infrequent, with one severe event reported in 2,387 gliclazide users also on insulin, and a similar incidence of non-severe events compared to other treatments (risk ratio 1.09, 95% CI: 0.20, 5.78, I2 77%). Few studies Tomlinson et al.,[12] evaluated weight changes, and none were designed to assess cardiovascular outcomes.

Three pivotal studies evaluated the efficacy of gliclazide in diet-failed patients with “non-insulin-dependent diabetes mellitus (NIDDM)”. In the first study Polayarapu et al.,[19] involving 224 patients, gliclazide supplementation or substitution for existing therapies led to good glycemic control in 65% of cases, with notable improvements except in those previously treated with glibenclamide. The second study Mim et al.,[11] A study was conducted to examine the effectiveness of several sulphonylureas in controlling diabetes in 112 NIDDM patients over a period of one year. The results showed that glibenclamide and gliclazide were the

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most successful, with 74% and 80% of patients respectively achieving normal HbA1c values. In a study conducted by Pop et al.,[13], over a period of five years and with the participation of 248 patients, it was found that gliclazide had the lowest rate of secondary failure (7%). This rate was much lower than that of glipizide (25.6%), and gliclazide also showed a more favourable trend compared to glibenclamide (17.9%).

These findings underscore gliclazide as a potent hypoglycemic agent with favorable efficacy and a lower incidence of side effects compared to other sulphonylureas. Its sustained efficacy and safety profile position gliclazide as a preferred choice for managing diet-failed NIDDM patients

- *Triple Combination Therapy of Gliclazide (80mg), Metformin (500mg), and Voglibose (0.3 mg) for Managing Type 2 Diabetes Mellitus*

The combination therapy of Gliclazide, Metformin, and Voglibose represents a multifaceted approach to effectively manage type 2 diabetes mellitus (T2DM). By leveraging distinct mechanisms of action, this regimen synergistically targets various aspects of glucose metabolism to achieve optimal glycemic control [20].

This triple therapy combines the insulin secretion stimulation of Gliclazide, the enhanced insulin sensitivity and hepatic glucose reduction effects of Metformin, and Voglibose's inhibition of intestinal alpha-glucosidase enzymes. Together, these actions comprehensively address both fasting and postprandial hyperglycemia throughout the day, thereby improving overall glycemic management [20].

Each component of this triple combination therapy is well-tolerated, with Gliclazide exhibiting a lower risk of hypoglycemia compared to other sulfonylureas. While Metformin may cause gastrointestinal side effects, Voglibose primarily affects the gastrointestinal system, leading to manageable symptoms such as flatulence and abdominal discomfort.

Combining Gliclazide with Metformin and Voglibose minimizes the risk of hypoglycemia associated with sulfonylurea monotherapy, ensuring a balanced approach to diabetes management. Moreover, the convenience of a once- or twice-daily dosing regimen enhances patient adherence compared to managing multiple medications separately, potentially reducing healthcare costs and preventing complications related to inadequate glycemic control[20].

The triple combination of Gliclazide, Metformin, and Voglibose offers a robust therapeutic option for patients with T2DM, particularly those requiring comprehensive glycemic management with minimal hypoglycemic risk. Further research is necessary to establish its long-term efficacy and safety compared to alternative treatments, emphasizing the importance of tailored therapy to achieve and maintain target glycemic levels based on individual patient characteristics and treatment adherence.

- *Safety Profile of Gliclazide*

The safety profile of gliclazide supports its long-term use in managing diabetes, emphasizing the importance of continuous treatment under medical supervision to prevent worsening of the condition if abruptly discontinued. In a study by Shukrath et al.,[21] Gliclazide has demonstrated a lower incidence of hypoglycemia compared to first-generation sulfonylureas, particularly with its modified release formulation. Hypoglycemic events associated with gliclazide are generally mild and infrequent, characterized by symptoms such as dizziness, lack of energy, and sweating.

As suggested by studies Khunti et al.,[22] Weight gain is a common side effect of sulfonylureas, including gliclazide, though it tends to be less pronounced compared to other agents like glibenclamide. Unlike newer agents such as SGLT-2 inhibitors and GLP-1 receptor agonists, which are associated with weight loss, gliclazide does not contribute to weight gain based on findings from the ADVANCE study over a 5-year period.

In terms of cardiovascular safety, evidence from the ADVANCE trial and subsequent analyses suggests that gliclazide does not increase cardiovascular risk and may even provide some protection against cardiovascular events. Further research is needed to fully elucidate its potential nephroprotective effects, which preliminary studies indicate may be linked to its antioxidant properties [23].

Gliclazide, a sulphonylurea hypoglycemic agent, stands out favorably when compared to other drugs of its class. Studies consistently Tomlinson et al.,[23] demonstrate that gliclazide is more effective than other glucose-lowering agents, except metformin, while also exhibiting a lower incidence of side effects and hypoglycemia compared to other sulphonylureas. Moreover, gliclazide maintains its efficacy over extended periods better than other medications within its class.

Studies Kalra et al.,[24] directly comparing gliclazide with other sulphonylureas reveal that it not only offers comparable efficacy but also a more favorable safety profile. The incidence of hypoglycemia associated with gliclazide is notably lower, making it a preferred choice across various clinical scenarios.

In comparison to newer antidiabetic agents like DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors, which provide additional benefits such as weight loss and cardiovascular protection, gliclazide remains a cost-effective and reliable treatment option for many patients with T2DM [25].

The once-daily dosing of gliclazide MR (modified release) further enhances patient adherence and quality of life compared to regimens requiring multiple daily doses. Overall, gliclazide remains an effective and relatively safe option in the management of T2DM, offering significant reductions in HbA1c levels and a reduced risk of hypoglycemia. While newer agents continue to advance diabetes care, the established benefits and affordability of

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gliclazide underscore its ongoing relevance in clinical practice. Further research is warranted to explore its long-term cardiovascular and renal benefits.

## III. CONCLUSION

Gliclazide is a valuable sulfonylurea for managing type 2 diabetes mellitus, particularly when metformin alone is insufficient. It effectively stimulates insulin release, improves first-phase insulin response, and has a favorable safety profile with a lower risk of hypoglycemia compared to other sulfonylureas. Additionally, its potential to prevent the progression of diabetic retinopathy adds to its therapeutic benefits. Overall, gliclazide is a reliable second-line treatment option that can enhance glycemic control while minimizing the risk of adverse effects.

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