RESEARCH PAPER

Imeglimin in Type 2 Diabetes Mellitus: Pharmacological Advances, Clinical Efficacy, and Analytical Perspectives

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Abstract
Imeglimin is an innovative oral antidiabetic agent that represents a significant advancement in the treatment of Type 2 diabetes mellitus (T2DM). Distinguished by its unique mitochondrial-targeting mechanism, Imeglimin improves mitochondrial function to enhance insulin sensitivity, reduce hepatic glucose production, and preserve pancreatic β-cell function. Clinical trials have demonstrated its efficacy in lowering HbA1c levels with a favorable safety profile and minimal adverse effects. In addition to its pharmacological benefits, various analytical methods, including High-Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC), have been developed for the accurate quantification and pharmacokinetic evaluation of Imeglimin, supporting its clinical application and therapeutic monitoring. While promising, potential drug-drug interactions, particularly with metformin and sulfonylureas, necessitate careful clinical consideration. Overall, Imeglimin offers a novel and effective option for patients with T2DM inadequately controlled by existing therapies. Continued research is essential to elucidate its long-term benefits, optimize combination regimens, and refine analytical techniques to support personalized diabetes management.

Keywords: Imeglimin, Type 2 Diabetes Mellitus, Mitochondrial Dysfunction, Insulin Sensitivity, Analytical Method Development, Drug-Drug Interactions
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1.Introduction

1.1. Current Scenario

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic dis order characterized by insulin
resistance and inadequate insulin secretion. As the number of people with T2DM around the world grows, we need new ways to treat it right away. Imeglimin is a promising new drug for diabetes because it works in a unique way and has many benefits[1]. Imeglimin is a new oral medication that belongs to the “glimin” class. It was made to treat the complicated nature of type-2 diabetes mellitus(Giruzzi et al., 2021). Its mechanism of action is unique, concentrating on mitochondrial bioenergetics. Imeglimin improves the function of mitochondria, increases insulin secretion, and reduces oxidative stress. It also stops beta-cell apoptosis by improving the structure of mitochondria and the membrane potential of beta-cell[3]. These two effects make Imeglimin a promising treatment for people with type 2 diabetes mellitus[4].

2. Experimental

Material and methods

A comprehensive review of scientific literature published from January 2000 to May 2025 was performed across prominent databases, including PubMed, Scopus, Web of Science, and Google Scholar. We chose published English-language papers that focused on Imeglimin's pharmacology, clinical efficacy, safety, drug interactions, and critical characterization. We only included studies that were preclinical, clinical trials, systematic reviews, and meta-analyses. We did not include conference abstracts or publications in standard languages other than English.
The analysis also talks about developing analytical methods for Imeglimin, including High-Performance Liquid Chromatography, Gas Chromatography, and the steps that need to be taken to prepare samples. These methods were evaluated for their suitability in pharmacokinetic and bioavailability stuides.
The information on mechanism of action, clinical outcomes, toxicity, drug interactions, and analytical profiles were critically analyzed. We utilized defined tools to make sure

that the methodological quality of clinical studies was credible. This integrated approach offers a comprehensive and evidence-based knowledge of Imeglimin's function in the treatment of Type 2 diabetes mellitus.

Review of the analytical profile of Imeglimin

Drug Profile and Pharmacokinetics

Imeglimin The chemical formula for imeglimin is C6H13N5, and it has a molecular weight of 155.205 g/mol. Its unique structure contributes to its pharmacological properties(Shrivastava et al.,). **Table 1.** shows the drug profile of Imeglimin with details. Imeglimin Chemical Structure is shown in **Fig 1**. Its unique structure makes it work as a drug. It has a great half-life for taking twice a day and is very bioavailable when taken by mouth. It is quickly absorbed, reaching peak plasma levels within 1-2 hours after administration[6] as shown in **Table 2.** The drug's effects depend on the dose, and at therapeutic doses, it greatly improves glycaemic control[7]. The pharmacodynamic properties of imeglimin render it appropriate for use as both a monotherapy and in combination with other antidiabetic agents[8]. Imeglimin is available in oral tablet form and is typically administered twice daily. The prescribed starting dose is 500 mg, it can be titrated based on patient response and tolerability [9].

Table 1. Imeglimin drug profile

Parameter	Details
Chemical Structure	Tetrahydrotriazine
Pharmacokinetics	Good oral bioavailability, suitable half-life
Common Side Effects	Nausea, Diarrhea, Vomiting
Serious Side Effects	Lactic acidosis (rare)
Drug Interactions	Low potential, no significant interactions with metformin or sitagliptin

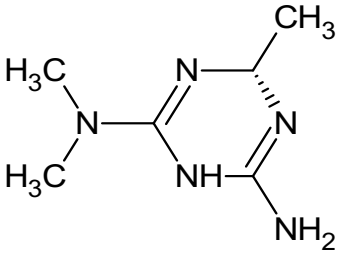

Fig 1. Imeglimin Chemical Structure

Table 2: Pharmacokinetic Parameters of Imeglimin

Parameter	Value
Oral Bioavailability	High
Peak Plasma Concentration	1-2 hours
Half-life	appropriate for twice-daily administration

Pharmacological Profile

Imeglimin's mechanism of action is multifactorial[10], targeting various aspects of glucose metabolism and mitochondrial function as shown in **Fig 2.**

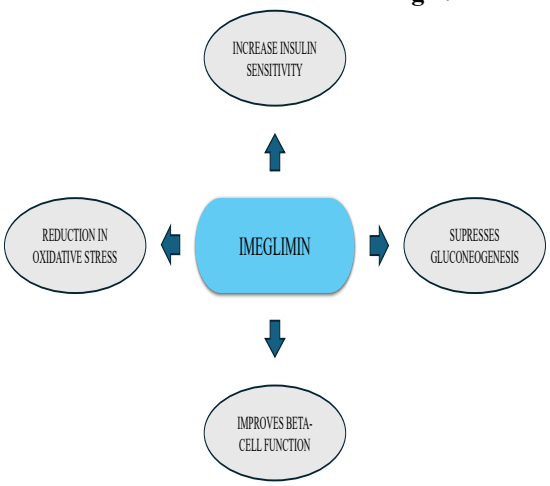

Fig 2. Pharmacological Action

Mitochondrial Bioenergetics:

Imeglimin enhances mitochondrial function by increasing ATP production and improving the ATP/ADP ratio. This improvement in mitochondrial bioenergetics helps in better energy use and glucose metabolism[11], Imeglimin improves the function of pancreatic β-cells by enhancing the mitochondrial structure and increasing insulin granule numbers. Healthier mitochondria result in improved energy production, which is essential for cell function[12]. Additionally, the greater number of insulin granules ensures more effective regulation of blood glucose levels through an increased supply for release[13]. Imeglimin works by inhibiting oxidative phosphorylation in the liver, which in turn reduces gluconeogenesis[14] and helps to reduce blood glucose levels in people with type 2 diabetes. In addition, Imeglimin also enhances glucose absorption in muscle cells and regulates insulin secretion, contributing to improved glucose control[15]as shown in **Fig. 3.**

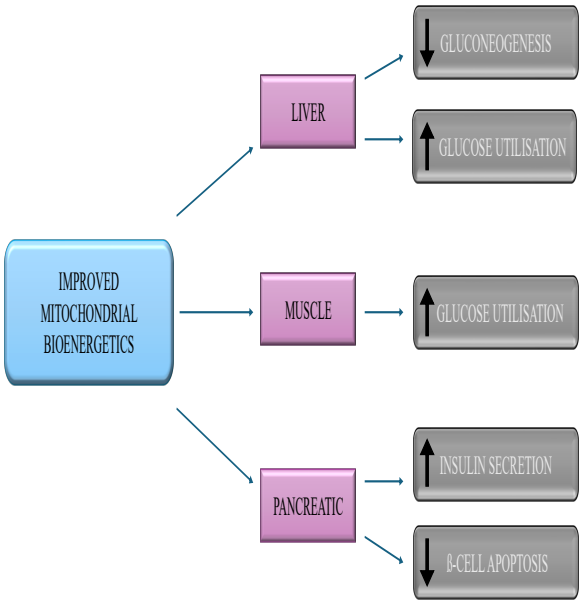

Fig 3. Mitochondrial

Bioenergetics

Imeglimin effectively enhances the efficiency of the mitoch ondrial respiratory chain, a
crucial process for cellular energy production. This chain w hich is located in the inner side of the mitochondrial membrane consists of several complexes (complexes 1 to 4) that aid in the electron transfer from nutrients. This electron transfer creates a proton gradient across the membrane, which ATP synthase (complex 5) then uses to generate ATP through oxidative phosphorylation by optimizing the mitochondrial respiratory chain's function, Imeglimin increases ATP production, the main energy source for cells(Mima et al., 2022)

Imeglimin modulates the mitochondrial permeability transition pore, a channel that can open in response to increased calcium levels and oxidative stress. When the mPTP opens, it can cause a decrease in mitochondrial membrane potential, trigger the release of pro-apoptotic factors, and cell death. By regulating the mPTP, Imeglimin helps maintain mitochondrial integrity and function, reducing the formation of reactive oxygen species (ROS) and preventing oxidative stress-induced cellular damage[17]. This guarding effect is crucial for preserving the health of pancreatic β-cells and other tissues affected by diabetes[18].

Fatty Acid Oxidation

Imeglimin enhances the mitochondrial capacity to oxidize fatty acids by favoring complex II substrate oxidation. Fatty acid oxidation is a critical process for energy production[19], especially in tissues like muscle and liver. By improving this process, Imeglimin helps increase the efficiency of energy production and reduces the accumulation of lipids in tissues, which can contribute to insulin resistance. Enhanced fatty acid oxidation also supports better glucose metabolism and overall glycemic control.

Reduction of Reactive Oxygen Species (ROS)

Imeglimin decreases the overproduction of ROS, which are highly reactive molecules that can cause significant cellular damage. Excessive ROS production is often linked to mitochondrial dysfunction and is a major contributor to oxidative stress. By lowering ROS levels, Imeglimin protects β-cells and endothelial cells from oxidative stress-induced apoptosis (programmed cell death)[20]. This protection helps to preserve the function of cells and delays the advancement of diabetes-related complications, such as cardiovascular disease and neuropathy.

Glucose-stimulated ATP Synthesis

Imeglimin promotes glucose-stimulated ATP synthesis, which is crucial for the release of insulin. In pancreatic β-cells, the increase in ATP levels in response to glucose triggers the secretion of insulin[21]. By enhancing ATP production, Imeglimin improves the capability of β-cell to release insulin when the glucose levels rise, thereby aiding in better glycemic control[22]. This mechanism is particularly important for individuals with type 2 diabetes, who often have impaired insulin secretion.

Activation of NAD+ Synthesis

Imeglimin kickstarts the "salvage pathway," which triggers the production of Nicotinamide adenine dinucleotide (NAD+). NAD+ is a coenzyme essential for various metabolic actions like energy metabolism, repairing the DNA, and cell communication by enhancing NAD+ levels, Imeglimin supports improved mitochondrial function and overall cellular health. Enhanced NAD+ synthesis also contributes to better glucose metabolism and insulin sensitivity, further supporting the control of type 2 diabetes.

Insulin Release Enhancement:

It amplifies glucose-stimulated insulin release by boosting nicotinamide phosphoribosyl transferase (NAMPT) activity[23], leading to higher NAD levels and enhanced calcium mobilization within pancreatic beta cells[24]. Imeglimin boosts cADPR production, which in turn activate s TRP channels. This activation allows calcium ions to flow into the cell, and the resulting calcium influx is crucial as it activates the release of insulin from pancreatic beta cells[25].

Amplification of Glucose Stimulated Insulin Secretion (GSIS)

Imeglimin substantially amplifies insulin release in response to glucose levels[26]. This means that in the presence of glucose, Imeglimin enhances the ability of β-cells to release insulin. This is crucial for maintaining proper blood glucose levels, especially after meals[27].

Imeglimin's increase in NAD+ levels also contributes to the mobilization of calcium within β-cells. Calcium is a critical second messenger in the insulin secretion pathway. When glucose enters β-cells, it triggers the chain reaction leading to an inflow of calcium, which then stimulates the exocytosis

of insulin granules. By enhancing calcium mobilization, Imeglimin boosts insulin secretion[28].

Glucose Homeostasis

Imeglimin improves the sensitivity of insulin in both the liver and skeletal muscle[29]. It reduces hepatic glucose production and increases glucose uptake in muscle tissues, thereby aiding in better glucose homeostasis[30].

By blocking the mitochondrial permeability transition pore (mPTP), Imeglimin reduces oxidative stress and prevents endothelial cell death. This action helps maintain vascular health and reduce diabetes-related complications[31].

Drug-Drug and Food-Drug Interaction

Imeglimin has a low risk of drug-drug interactions, which makes it a good choice for combination therapy with other antidiabetic agents: There have been no clinically significant interactions reported between imeglimin and metformin, so they can be safely taken together. This combination can provide synergistic benefits in glycemic control[32]. Imeglimin also helps to reduce the risk of lactic acidosis as compared to metformin[33]. Imeglimin has a low risk of interacting with other drugs. It doesn't show clinically important interactions with drugs that are often given together, like statins, antihypertensives, and anticoagulants. The pharmacokinetics of imeglimin stay the same whether you eat or not, so you can take it with or without food. This flexibility is good for patients, especially those who don't eat regularly or who want to take their medicine when it's most convenient for them, without having to worry about when they eat.

Safety and tolerability

Imeglimin is generally well accepted by patients, meaning that most people do not experience severe or intolerable side effects[34]. Clinical studies have demonstrated that its safety profile is analogous to that of a placebo, which is an inert substance employed as a control in the evaluation of new pharmaceuticals[35]. The most common side effects are mild stomach problems, like feeling sick or like you might throw up, and having bowel movements that are loose, watery, or happen a lot.These side effects are usually mild to moderate and depend on the dose, which means they are more likely to happen at higher doses. However, these symptoms often lessen over time as the body adjusts to the medication. lThere have been no major severe side effects linked to Imeglimin in clinical trials. This means that most people who take Imeglimin don't have any serious health problems.

New Diabetes Therapies

Managing diabetes mellitus, particularly type 2 diabetes, is complex and demands innovative solutions(Kaneko et al., 2021). Here are some reasons why we need the new drugs: People with type 2 diabetes have a number of problems, including less sensitive insulin, less insulin secretion, and more glucose being made in the liver[37]. Most of the time, current treatments only deal with one or two of these problems, which may not be enough to keep blood sugar levels under control. Effective diabetes management is essential to avoid long-term complications which can be achieved by the Imeglimin and decrease disease, nerve damage, kidney disease, and eye problems[38]. New medications can offer better blood sugar control and potentially lower the risk of these complications[39].

Overcoming Limitations of Existing Therapies

Some diabetes medications have problems, like causing low blood sugar, weight gain, or stomach problems. Over time, some patients may become less responsive to certain medications, which makes them less effective9. Clinical trials demonstrate that Imeglimin is well tolerated, exhibiting a safety profile akin to that of a placebo. Most patients have very few side effects, which shows that it could be a very effective treatment for type 2 diabetes. This positions Imeglimin as a promising, safe long-term management option for the disease diabetes10. Some treatments require multiple daily doses or injections, which can be inconvenient for patients. When Imeglimin is used alongside other antidiabetic medications, such as sitagliptin, it does not cause significant changes in the levels of these drugs in the body49. This indicates that Imeglimin can be safely combined with other diabetes treatments without increasing the risk of adverse effects[40].

Comparative Study of Imeglimin with Other Antidiabetic Drugs

Imeglimin vs. Metformin

Imeglimin is as effective as metformin in lowering HbA1c levels[41], which is a key indicator of long-term blood sugar control. Clinical trials have demonstrated that Imeglimin effectively reduces both HbA1c and fasting blood glucose levels, similar to metformin [42].Metformin primarily works by reducing glucose production in the liver and enhancing insulin sensitivity. Imeglimin, however, has a dual mechanism it boosts insulin secretion and improves mitochondrial function, aiding the body in using glucose more efficiently. Both drugs are generally considered safe, but Imeglimin tends to cause fewer gastrointestinal side effects compared to metformin[43].

Imeglimin vs. Sitagliptin

In lowering HbA1c levels, imeglimin has been as effective as sitagliptin, a DPP-4 inhibitor. Imeglimin works better to control blood sugar levels when taken with sitagliptin[44]. Sitagliptin stops the enzyme DPP-4 from working, which raises incretin levels and makes insulin secretion better. Imeglimin, on the other hand, works in a different way to boost both insulin production and insulin sensitivity. Both Imeglimin and sitagliptin are safe to use and don't have a high risk of causing low blood sugar. Imeglimin's dual mechanism, on the other hand, may have more metabolic benefits.

Imeglimin as add-on therapy

Patients who took Imeglimin along with sitagliptin therapy had much lower HbA1c levels than those who took a placebo. This shows that Imeglimin could make current diabetes treatments work better[45]. Researchers have also looked into using imeglimin with metformin. The combination worked better than metformin alone to control blood sugar, and it didn't significantly raise the risk of side effects[46]. In people with type 2 diabetes, imeglimin has done an amazing job of lowering HbA1c levels and body weight[47]. Imeglimin significantly lowers HbA1c, indicating better long-term blood sugar control, and aids in

weight reduction[48]. EquMet helps keep blood sugar levels stable and improves overall glycemic control. This is especially helpful for older patients who don't always eat the same way[49].

Clinical Applications

Imeglimin is primarily indicated for the management of T2DM as an adjunct to diet and exercise. It can be used in patients who are inadequately controlled on metformin or other antidiabetic agents[50]. Ongoing research explores its potential benefits in other metabolic disorders and conditions characterized by mitochondrial dysfunction[51].Several clinical trials have been conducted to evaluate the efficacy and safety of Imeglimin:

Trial 1: Imeglimin Monotherapy: A 24-week, randomized, double-blind, placebo-controlled trial involving 400 patients with T2DM[52]. The primary endpoint of the study was to measure the change in HbA1c levels from the baseline[53].

Trial 2: Imeglimin in Combination with Metformin: A 24-week, randomized, double-blind, placebo-controlled trial involving 300 patients with T2DM inadequately controlled on metformin[54]. The primary endpoint was the change in HbA1c from baseline.

Trial 3: Long-Term Safety and Efficacy: A 52-week, open-label extension study involving 200 patients with T2DM. The primary endpoint was the long-term safety and tolerability of Imeglimin[55]. The study confirmed the favorable safety profile of Imeglimin with sustained glycaemic control over one year.

Several clinical trials are underway to explore the long-term efficacy and safety of Imeglimin(Mima et al., 2023)(as shown in **Table 3.)** .These studies aim to evaluate its impact on cardiovascular and renal outcomes in patients with T2DM[57].

Table 3: Clinical trial outcomes

Trial	Primary Endpoint	Outcome
Imeglimin Monotherapy	HbA1c Reduction	-0.6% vs. placebo
Imeglimin vs. Metformin	Glycaemic Control	Favorable safety profile; sustained glycaemic control vs. metformin alone
Long-Term Safety and Efficacy	Safety and Tolerability	Favorable safety profile; sustained glycaemic control

Phase 2 and 3 trials have demonstrated that Imeglimin is well tolerated over extended periods. The most common side effects were gastrointestinal, but these were generally mild and temporary[58].Imeglimin does not typically cause hypoglycemia (dangerously low blood sugar levels), which is a significant benefit[59]**.**Imeglimin monotherapy was well tolerated in Ja panese patients with T2D and significantly improved glycaemic co ntrol without a notable increase in hyperglycaemic events compared to placebo[60].Imeglimin's unique mechanism of action makes it a promising candidate for combination therapies. Research is ongoing to assess its efficacy with other antidiabetic agents, including GLP-1 receptor agonists and SGLT2 inhibitors.

Advantages, Limitations and Future Research Directions:

Future studies may look into how Imeglimin can be used to treat other metabolic disorders and how it might help people with conditions that cause problems with mitochondria[61]. Additionally, studies on its long-term safety and efficacy will provide valuable insights into its role in diabetes management(Bando et al., 2024). Imeglimin exhibits distinctive anti-inflammatory properties on microglial cells in mice subjected to elevated glucose concentrations. This happens when ULK1 is turned on, which then stops the TXNIP-NLRP3 pathway that causes inflammation[63] responsible for inflammation.

Dual Mechanism of Action: Imeglimin enhances both insulin secretion and insulin sensitivity, this helps the body use glucose more efficiently and keep blood sugar levels under control[64]. Efficacy: Clinical trials have shown that Imeglimin is an effective treatment for type 2 diabetes because it lowers HbA1c and fasting blood glucose levels by a lot[65]. Safety Profile: Compared to some other diabetes drugs, like metformin, imeglimin has fewer side effects on the stomach. It also has a low chance of making your blood sugar too low[66]. Add-On Therapy: Imeglimin can be used with other diabetes medications like metformin and sitagliptin[67], providing additional benefits in controlling blood sugar without significantly increasing the risk of side effects also the Imeglimin helps to treat depressive state[68]. No Major Drug Interactions: Imeglimin doesn't change the way other commonly used antidiabetic drugs work in the body very much, so it's a safe choice for combination therapy[69]. Investigating the use of Imeglimin in combination with other hypoglycemic agents could provide valuable insights into optimizing treatment strategies[70]. Studies should focus on discovering synergistic effects when Imeglimin is administered in conjunction with other medications, including metformin, sulfonylureas, or novel agents such as GLP-1 receptor agonists and SGLT2 inhibitors. This could help make personalized treatment plans that improve blood sugar control while reducing side effects[66]. Imeglimin has a lot of potential clinical uses, especially for people who don't eat regularly or need to take their medicine at different times. Future studies should look at how well and safely it works in different groups of patients, such as those with different levels of kidney and liver damage, older people, and people with other health[71], elderly patients, and individuals with comorbid conditions[72]. Understanding how Imeglimin performs in these subgroups is crucial for expanding its clinical use. ImpactEffect on healthcare costs and quality of life: As research goes on, Imeglimin could become an important part of personalized diabetes care. This could lower healthcare costs and make patients' lives better. Studies should evaluate the impact of Imeglimin on health-related quality of life (HRQoL) measures, patient adherence, and overall treatment satisfaction. Additionally, economic analyses should evaluate the cost-effectiveness of Imeglimin compared to

other treatment options, considering factors such as reduced hospitalizations and complications. New Trends and Technologies: Improvements in digital health technologies and precision medicine may make Imeglimin even more useful as a treatment. Precision medicine methods could help find groups of patients who are most likely to benefit from Imeglimin by looking at their genetic, phenotypic, and metabolic profiles. Digital health tools, like continuous glucose monitoring (CGM) and telemedicine, could help doctors keep an eye on and treat patients who are taking Imeglimin more effectively. Creating Imeglimin electrospun nanofiber as a buccal antidiabetic[73,74]. Ongoing and Future Clinical Trials: Addressing these research gaps will require ongoing and future clinical trials. Large-scale, multicentre trials with diverse patient populations are needed to validate the findings from earlier studies and provide robust evidence for clinical guidelines. Additionally, real-world evidence from observational studies and registries will complement clinical trial data, offering insights into the practical use of Imeglimin in routine clinical practice[75]. Possibility of Managing Diabetic Complications: In addition to glycemic control, the therapeutic potential of Imeglimin for diabetic complications warrants investigation. PreclinicalPreclinical studies indicate that Imeglimin may positively influence mitochondrial function and oxidative stress, potentially offering protective effects against complications such as diabetic nephropathy, neuropathy, and retinopathy. Subsequent research ought to examine these prospective advantages in clinical environments. In patients with moderate to severe renal impairment, Imeglimin's clearance is diminished, necessitating dosage modifications and continuous surveillance of kidney function[76]. Insufficient long-term data Short-term studies show promise, but there isn't much long-term data on how safe and effective Imeglimin is. More research is needed to fully understand what it will do in the long run. Gastrointestinal side effects, while less common than with certain other medications, Imeglimin may still induce gastrointestinal disturbances such as nausea and diarrhea, particularly at elevated doses. Imeglimin is a newer drug, so it might not be as easy to find as older antidiabetic drugs. This could make it harder for some patients to get. Some patients and healthcare systems may want to think about the fact that newer drugs like Imeglimin can be more expensive than older, generic drugs like metformin, which might be a consideration for some patients and healthcare systems. Future perspectives the existing research on Imeglimin has demonstrated its effectiveness and safety in treating type 2 diabetes. However, several areas need further exploration to fully harness its therapeutic potential[77].

Analytical Profile

Sample preparation

Imeglimin hydrochloride has been developed into immediate-release tablets. The formulation process involved using super-disintegrants like Croscarmellose sodium and optimizing the amount of PVPK-30 to minimize disintegration time. Microcrystalline cellulose served as the diluent, polyvinylpyrrolidone (K-30) as the binder, and colloidal silicon dioxide as the glidant[78].

In-Vitro drug release of the drug was performed using the United States Pharmacopeia Device 2(Paddle) at 37°C ± 0.5°C and 50 rpm. Hydrochloric acid 0.1N was used as the dissolving medium. The percentage of the drug released at various times was measured using UV technology. The formulation labeled as Preliminary F6 showed the best performance, with all measurements within the acceptable range of pharmacopeial specifications[79].Imeglimin is quickly absorbed and mainly distributed to organs and tissues, its half-life is 9.03 - 20.2 hours[80]. It has low plasma protein binding, facilitating its rapid distribution[81]. Imeglimin is eliminated in unchanged form from the urine which signifies minimal metabolism. It is a substrate of multidrug and toxic compound extrusion (MATE) 2-K and an OCT1, OCT2, and MATE1 inhibitor. Clinical studies have confirmed that Imeglimin has a low potential for drug-drug interactions[82].

To prepare dilutions of Imeglimin for experimental purposes, follow these steps:

Solvent Selection: Distilled water or 0.1N Sodium Hydroxide (NaOH) can be used as solvents for preparing Imeglimin solutions. Distilled water is suitable for general purposes, while 0.1N NaOH is used when a basic environment is required(Navali et al., 2024).

Preparation Process: Dissolve Imeglimin in the chosen solvent to prepare a stock solution. For instance, to prepare a 100 mg/mL stock solution, dissolve 100 mg of Imeglimin in 1 mL of distilled water or 0.1N NaOH.

Serial Dilutions: To achieve the desired concentrations, perform serial dilutions. For example, to prepare a 10 mg/mL solution from a 100 mg/mL stock solution, mix 1 mL of the stock solution with 9 mL of the solvent.

Continue this process to achieve further dilutions as needed. For instance, to prepare a 1 mg/mL solution, take 1 mL of the 10 mg/mL solution and mix it with 9 mL of the solvent[84].

Mixing and Storage: Thoroughly mixing at each dilution step to achieve uniform concentration. If available, use a vortex mixer.

Store the diluted solutions at appropriate conditions, typically at 4°C, and use them within a specified timeframe to ensure stability.

Methods based on Spectrophotometry and Chromatography

It is crucial to develop reliable analytical methods to ensure the drug's quality, efficacy, and safety in pharmaceutical formulations. These analytical methods are essential for ensuring that Imeglimin meets the required quality standards and remains effective for patients with type 2 diabetes. The development details are also shown in **Table 4.**

1.6.1. RP-HPLC Method: Researchers created a Reverse Phase high-performance liquid Chromatography method to identify Imeglimin hydrochloride in its bulk and dosage forms[85]. They optimized the conditions such as the mobile phase ratio of acetonitrile and wate (85:15, v/v), the type of column (Hypersil Gold ODS end capped column, 150x4.6 mm, 3 µm), and the detection wavelength (237 nm) for optimal resolution, sensitivity, and selectivity[85].

1.6.2. HPTLC Method: Another technique employed is high-performance thin-layer chromatography (HPTLC) to detect Imeglimin hydrochloride in bulk and tablet forms. The mobile phase, consisting of methanol, chloroform, and ammonia solution in a 7:2:1 ratio (v/v/v), was optimized for resolution and validated for accuracy, precision, and linearity.

1.6.3. UV-Visible Spectroscopy: A method using UV-visible spectroscopy was developed to determine imeglimin hydrochloride in tablet formulations. Utilizing distilled water as the solvent and a detection wavelength of 237nm, this method exhibited good linearity within a 210µg/mL concentration range and adhered to validation guidelines (Selvan et al., 2023).

Table 4: Method Development

Method	Method Development	Ratio (v/v)	Column	Detection Wavelength	Concentration Range
RP-HPLC	Acetonitrile / Water	85:15	Hypersil Gold ODS (150 × 4.6 mm, 3 µm)	237 nm	Not specified
HPTLC	Methanol / Chloroform / Ammonia	7:2:1	Not applicable	Not applicable	Not specified
UV-Visible Spectroscopy	Distilled Water	Not applicable	Not applicable	237 nm	2–10 µg/mL
HPLC	Acetonitrile / Water	70:30	C18 Column (250 × 4.6 mm, 5 µm)	254 nm	0.1–10 µg/mL

3. Result and Discussion

Imeglimin, is a first-in-class tetrahydrotriazine compound that has shown promising results in managing Type 2 Diabetes Mellitus (T2DM) in different phases of clinical trials. Its distinctive dual mechanism—focusing on mitochondrial bioenergetics and enhancing both insulin sensitivity and secretion—presents a novel approach that sets it apart from current therapies. Clinical data have demonstrated substantial decreases in HbA1c levels, yielding beneficial effects on fasting plasma glucose and postprandial regulation, especially when administered in conjunction with metformin, DPP-4 inhibitors, or insulin. Beyond glycemic control, Imeglimin has shown cardiometabolic benefits and a well-tolerated safety profile, with low risk of hypoglycemia or weight gain. The drug also exhibits antioxidant and anti-inflammatory properties, suggesting potential roles in protecting pancreatic β-cells and endothelial function. From an analytical standpoint, robust and validated methods such as HPLC, LC-MS/MS, and stability-indicating assays have been developed for quantifying Imeglimin in biological samples and formulations. These methods make sure that pharmacokinetic testing and quality control are done correctly during development. The pharmacological versatility, clinical efficacy, and reliable analytical profiling of Imeglimin collectively endorse its incorporation into contemporary treatment protocols for T2DM, particularly in patients exhibiting elevated cardiovascular and metabolic risk profiles.

4. Conclusion

Imeglimin is a new and promising way to treat type 2 diabetes. Its multifaceted mechanism of action—encompassing the enhancement of mitochondrial function, the improvement of insulin sensitivity, and the preservation of β-cell function—addresses various aspects of T2DM pathophysiology. This all-around approach not only helps keep blood sugar levels in check, but it may also help protect against complications related to diabetes. Imeglimin is safe for a wide range of patients, including those with irregular eating patterns or other health problems, because it has few side effects and its pharmacokinetics stay the same no matter what you eat. Its ability to be used with other hypoglycemic drugs, like metformin, sulfonylureas, GLP-1 receptor agonists, and SGLT2 inhibitors, shows how flexible and useful it is for managing diabetes in a way that works for each person. Continued research and clinical trials will yield more profound insights into the long-term efficacy and safety of Imeglimin, especially regarding its effects on cardiovascular outcomes, diabetic complications, and overall quality of life. Real-world evidence derived from observational studies will augment clinical trial data, providing pragmatic insights into its application in standard clinical practice. Beyond diabetes, Imeglimin's potential benefits in other metabolic disorders, such as non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome, are areas of active investigation. Its ability to improve mitochondrial function and reduce oxidative stress may have broader therapeutic implications, making it a valuable candidate for addressing various metabolic dysfunctions. In summary, Imeglimin represents a significant advancement in the treatment of T2DM. Continued research and clinical exploration will be essential in fully realizing its potential and integrating it into clinical practice. By addressing the multifaceted nature of T2DM and offering a flexible, safe, and effective treatment option, Imeglimin holds promise for improving patient outcomes and advancing the field of diabetes care.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

M.Y and R.C.: Writing - Original Draft, G.K.: Conceptualization, K.N: Review & Editing Preparation, Preparation, R.B.: Editing Preparation, R.K.: Data Curation.

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