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Imeglimin Hydrochloride: A Novel Approach to Type 2 Diabetes Management

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Abstract

Imeglimin hydrochloride is an novel drug evolve for the treatment of type 2 diabetes mellitus. It is characterized by its unique mechanism of action, targeting both pancreatic beta cells and peripheral tissues to improve insulin secretion and sensitivity. Early clinical trials showed promise in reducing blood sugar levels, but further research was needed to determine its safety and effectiveness. Some reported side effects included gastrointestinal symptoms like nausea and diarrhea. The regulatory status of Imeglimin varied by region, and patients were advised to consult with healthcare professionals for the latest information on its availability and use. Validation of imeglimin hydrochloride and its enantiomers, drug release patterns of the nanofibers, comparing its impact with other available drug like metformin, method of action by targeting mitrocondria, pharmacokinetics and therapeutic effect of imeglimin hydrochloride, Imeglimin treatment, both short- and long-term, counteracts the metabolic syndrome's cardiorenal dysfunction, its Potential Ketoacidosis, its solubility and UV-Spectrophotometry. [1]

INTRODUCTION:

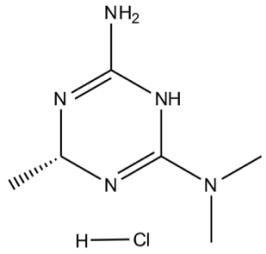
A novel molecule called imeglimin is being developed to treat type 2 diabetes. This medication belongs to the glimin class of glucose-lowering medications, making it the first of its kind in this category. Optimal glucose regulation is necessary in type 2 diabetes to correct anomalies in insulin responsiveness and release. Imeglimin operates through a distinctive mechanism of action, addressing three crucial pathophysiological aspects of type 2 diabetes: greater death of cells, increased hypergluconeogenesis, and decreased muscle tissue absorption of glucose. Recent stage II and phase III studies revealed imeglimin's efficacy for enhancing the level of glycated haemoglobin and fasting blood glucose (FPG) levels, either alone or in conjunction with other sugar-lowering medications.

The rise of diabetes type 2 mellitus (T2DM) in the twenty-first century poses a serious medical, societal, and economic problem. The number of individuals with carbohydrate metabolism problems is growing, particularly among young people. By following the World Diabetes Federation (IDF), The global diabetic population is projected to rise from 463 million in 2019 to reach 700 million by the year 2045. T2DM is typically detected 10 years after the disease manifests itself, and a considerable proportion of people with it already have serious micro- and/or macroangiopathy consequences at the time of diagnosis. Diabetes

complications are connected with a considerable decline in the standard of life and a shorter survival span. Cardiovascular disease is the leading cause of death in diabetes individuals, with microangiopathy-like consequences that result in lack of vision, amputation of limbs, and kidney failure. Early detection is critical. [2]

General profile of imeglimin hydrochloride-
Category- Anti-diabetes Agent
Chemical Name-
(R)-6-imino-N,N,4-trimethyl-1,4,5,6-tetrahydro-1,3,5-triazin-2-amine hydrochloride
Molecular Formula- $C_6H_{14}CLN_5$
Molecular Weight- 191.66 g/mol, pKa- 10.21

Chemical structure



Literature. review

1. Ramalingam et al (2023) work on determine which is the (+) and (-) enantiomer of Formulating imeglimin in its various compositions involves the development of a precise chiral liquid chromatography with tandem mass spectrometry (LC-MS/MS) method to validate its enantiomers. A drug called imeglimin is used to treat type 2 diabetes (T2D). The isocratic mobile phase consisted of methanol and 10 mm ammonium acetate in a 95:5 v/v ratio, flowing at a rate of 0.5 ml/min. The chiral stationary phase employed was reverse phase Chiralpak IG-3 (100 4.6 mm, 3 m). LC-ESI-MS/MS was employed to evaluate the resolution of the (+) and (-) enantiomers for Imeglimin in the positive transition at 155.0 m/z (M+H). The linearity range for both the (+) and (-) enantiomers is 10 to 100 ng/ml. It was found that there was a linear correlation co-efficient (R2) between the (+) and (-) imeglimin enantiomers. The drug's (+) and (-) enantiomers had retention durations of 2.876 and 4.325 minutes, respectively, and the chromatographic analysis took 5 minutes to complete in total. His objective is thus to separate the enantiomers while developing a rapid, sensitive, and inexpensive technique for identifying the (+) and (-) enantiomers in its molecule.[3]

2. Alamer et al (2023) found The global rise in the incidence of type 2 diabetes (T2D) necessitates the urgent development of safe and effective anti-diabetic medications. Imeglimin, a novel tetrahydrotriazene molecule, was recently licenced for use in type 2 diabetes patients in Japan. It has showed promise in decreasing blood glucose levels by enhancing pancreatic beta-cell activity and periphery insulin sensitivity. Nonetheless, it has a number of disadvantages, including poor absorption through the mouth and gastrointestinal (GI) pain. Therefore, the objective of this work was to develop a novel form of imeglimin that could be administered through the buccal canal by incorporating it into electrospun nanofibers. This would prevent the present GI-related side effects and provide an easier way of administration. The nanofiber's diameter, drug release patterns, pharmacological loading (DL), and breakdown were all measured. The nanofibers exhibit a diameter of 361.54 nm and a density (DL) of 23.5 ± 0.2 g/mg of fibers, as indicated by the data. Solid dispersion was confirmed through X-ray diffraction (XRD) data, affirming enhanced drug solubility and release, leading to higher bioavailability. The disintegration rate of the drug-loaded nanofibers was recorded at 21 seconds, indicates that dosage form was suitable for buccal distribution and that the medication would release completely after 30 minutes. The investigation's conclusions indicate that the imeglimin's nanofibers that were produced can be given by buccal administration, which will maximise therapeutic outcomes and improve patient compliance.[4]
3. Hozumi et al (2023) express that imeglimin is a new anti-diabetic medication that is structurally similar to metformin. They evaluated imeglimin's impact on hepatocytes by comparing them to those of metformin to

get insight into its pharmacological features. Utilising an extracellular flow analyzer and a full RNA-sequencing analysis, the effects of imeglimin were examined on the expression of genes in HepG2 cells and on mitochondrial activity in HepG2 cell lines or mouse primary hepatocytes. Examinations were also carried out to assess the impact of the drug on AMPK function in HepG2 cells, mouse primary hepatocytes, and mouse liver. When imeglimin was given to primary hepatocytes from mice or HepG2 cells, it decreased the rate at which oxygen was consumed for ATP generation. Although metformin was more effective in stimulating AMPK in these cells, imeglimin still had some effect. A bolus injection of meglimin increased AMPK in the mice's liver. While metformin and Imeglimin demonstrated similar overall effects on gene transcription in HepG2 cells, Imeglimin specifically enhanced the expression of genes encoding complex I and III mitochondrial respiration proteins, a response not observed with metformin. Those findings imply that imeglimin and metformin have comparable pharmaceutical impacts on mitochondrial respiration, AMPK action, and gene transcription in cultured hepatocytes, but they vary in their effects on the expression of some mitochondrial-related genes.[5]

4. Clemence et al (2020) investigates that imeglimin is a unique oral anti-diabetic medication which targets mitochondrial bioenergetics in the treatment of type 2 diabetes. Several in vitro and in vivo investigations in both animals and humans were conducted to analyse its pharmacokinetics, absorption properties, metabolism, distribution, and elimination. Its ability to cause interactions between drugs was also thoroughly investigated. Imeglimin is a tiny cationic molecule with a low intestinal permeability. Its absorption process includes both passive paracellular absorption and active transport. Drug absorption in vivo was good (50–80%) in a variety of species, but it decreased with dose, most likely because active transport was saturated. Following absorption, meglimin was quickly and extensively distributed throughout internal organs. All animals reported quick distribution to organs can be explained by low plasma protein binding. Both people and animals practically eliminated imeglimin intact from their urine, indicating a low level of metabolism. The drug, in its undisturbed form, was the main substance found circulating in plasma; no human-specific metabolites were found. Compared to creatinine, imeglimin exhibited a higher renal clearance, indicating a quicker rate of urine discharge. There was no evidence that it could stimulate or inhibit cytochrome P450. It was found to act as an inhibitor of OCT1, OCT2, and MATE1, as well as a substrate for OCT1, OCT2, and MATE2-K, a multidrug and toxic extrusion transporter. Clinical drug-drug interaction testing were therefore conducted, which demonstrated the absence of significant interactions with substrate or inhibitor of these transporter.[6]

5. The oral method of administration provides immediate release of the drug with a sustained dose. The am ount of information such as capsule, capsule; Powders, solutions, emulsions and aerosol suspensions have be en used for many years to treat various diseases or chronic conditions. Today the overalls market is the main place where you can find these chemical products. Currently, tablets are the most widely used and most recen tly discovered drug among all types of drugs. Due to its selfcontrol, compactness and simplicity of productio n, as well as ease of management and production. Most prescription oral medications now sold in pharmacies and stores are of the immediaterelease variety, designed to provide immediate release of medication for rapi d absorption. The term "immediaterelease tablet" refers to a tablet that dissolves and releases medication quic kly. Immediate release can be achieved using a suitable diluent or carrier that does not affect the rate of relea se and/or absorption of the drug. The term does not include drugs designed to provide “controlled,” “sustaine d,” “sustained,” “sustained,” or “extended” drug release. Imeglimin is the first drug of the "glimin" class of h ypoglycemic drugs. A new drug to treat type 2 diabetes. It is necessary to know the difference between insuli n secretion and sensitivity to good glycemic control in type 2 diabetes. The unique action of Imeglimin target s three pathophysiological factors in type 2 diabetes: i) excess glucose in the liver, ii) impaired glucose uptak e by sensitive tissues, and iii) dysfunction of pancreatic beta cells. Imeglimin generally increases insulin sens itivity, including the ability to lower blood sugar and improve insulin sensitivity in the liver and skeletal mus cle. It also increases glucose-stimulated insulin secretion (GSIS) and preserves beta cell mass.[7]

6. Sjcrabtree et al (2020) analysis imeglimin is an innovative and pioneering blood-sugar lowering medication, representing a novel class of drugs. It operates through a mitochondrial pathway, facilitating enhanced glucose absorption in skeletal muscles, reducing hepatic glucose production, and enhancing insulin secretion triggered by glucose. A comprehensive review and meta-analysis were conducted on adult patients with type 2 diabetes who participated in randomised controlled clinical trials (RCTs) using imiglimin. Five RCTs were found among the 45 publications that were found, however only three of them could be included

in a metaanalysis (total n=180 participants) because of the format of the data. Imeglimin 1500 mg twice daily as monotherapy or as a supplement to metformin or sitagliptin was associated with lower fasting plasma glucose levels and a reduction in HbA1c of 0.63 percent (95% CI: 0.84 to 0.42; 6.6 mmol/mol, 95% CI: 8.8 to 4.4) compared to placebo, according to a randomeffects model. There were few adverse effects, largely gastrointestinal in nature, and no hypoglycemia. Imeglimin is generally well tolerated and shows promise in HbA1c and fasting plasma glucose, it is concluded.[8]

7. Vuylsteke et al (2015) targeted the imeglimin, a glucose-lowering drug that targets mitochondrial bioenergetics, improves glucose homeostasis and lessens the excess generation of reactive oxygen compounds (ROS). Our study examined the potential preventive effects of this on vascular and left ventricular (LV) dysfunction resulting from the metabolic syndrome. He investigated the impact on left ventricular function of imeglimin given orally for ninety to ninety days at a dose of 150 mg/kg twice a day, LV perfusion of tissues, LV oxidative stress, and vascular function using Zucker fa/fa rats. It results imeglimin treatment for 9 and 90 days reduced the LV end-diastolic pressures and the relationship between LV enddiastolic volume and pressure, enhanced LV tissue perfusion, and reduced LV ROS generation as compared to untreated rats. Imeglimin simultaneously restored mesenteric flow-mediated dilation and acetylcholine-mediated cardiac relaxation. Imeglimin decreased LV mitochondrial production of ROS and enhanced LV performance an hour after dosing, while glucose plasma levels had not yet changed. Treatment with imeglimin for 90 days decreased associated kidney and LV fibrosis and enhanced kidney function. In a rat model of metabolism syndrome, the results show that imeglimin prevented cardiovascular diastolic and vascular dysfunction. It accomplished this by mitigating oxidative stress, increasing nitric oxide (NO) bioavailability, improving myocardial perfusion, and, after a 90-day treatment duration, promoting positive changes in both myocardial and kidney structure. These effects have nothing to do with controlling glucose, at least not entirely.[9]

8. Doupis et al (2021) called imeglimin as a diabetic weapon. A breakthrough medication called imeglimin is currently being developed to treat diabetes with type 2. It may have an effect on three primary pathophysiologic elements of type 2 diabetes: decreased muscle glucose uptake, excessive hepatic gluconeogenesis, and enhanced beta-cell death, according to laboratory research. Imeglimin improves haemoglobin A1 and plasma glucose levels at rest in a manner comparable to that of metformin and sitagliptin, according to preliminary human trials reported within the previous two years. In these earlier human research, there has been a low prevalence of negative effects, particularly hypoglycemia. Although some studies are presently underway, there is currently insufficient long-term evidence to support the safety of imeglimin for the cardiovascular system as well as data on mortality and morbidity. If the FDA approves imegli-min, it could have a considerable impact on a type 2 diabetes treatment strategy.[10]

9. Fouqueray et al (2020) found pharmacokinetics effect of imeglimin. It is a new oral antidiabetic that is first-in-class and is sold in Japan under the trade name TWYMEEG® to treat diabetes type 2 mellitus. Different from every other anti-hyperglycemic classes, it has a unique way of action. Objective to evaluate imeglimin's pharmacokinetics and safety profile in Caucasian and Japanese healthy volunteers. Techniques Following a single dose of 250–8000 mg and numerous doses of 250–2000 mg twice daily in participants who were Caucasian, and following a single dose of 500–6000 mg and multiple doses of 500–2000 mg twice daily in subjects who were Japanese, two randomised placebo-controlled stage 1 clinical investigations were carried out. We measured the concentrations of imeglimin in plasma and urine. It was found the imeglimin doses produced their highest concentrations in Caucasians between 1 and 3.5 hours and in Japanese individuals between 1.5 and 3 hours. The mean elimination half-lives (t1/2) for Caucasian subjects ranged from 9.03 to 20.2 h, whereas those for Japanese subjects ranged from 4.45 to 12 h. The t1/2 were dose-independent. In Caucasians and Japanese, respectively, In the dose range of 250–8000 mg and 500–6000 mg, the dosage-normalized area under a plasma concentration–time curve decreased with dosage, respectively, showing a dosage-dependent but less than dosage-proportional effect in imeglimin exposures. Following multiple doses, there was barely any plasma accumulation, and neither population's pharmacokinetics were impacted by eating. Less than 20% separated the average exposures of Caucasian and Japanese subjects, while there was a trend for Japanese exposures to be a little greater. Imeglimin demonstrated a favourable tolerability and safety profile, with minor gastrointestinal side effects that varied in intensity according on dose.[11]

10. Bozec et al (2020) studied the therapeutic effect of imeglimin and express that imeglimin is a novel oral drug under research that is being used to treat diabetes type 2 (T2D). There is proof of a statistically significant glucose decrease in several key phase III trials, in addition to a usually satisfactory safety and tolerability

profile that does not result in severe hypoglycemia. Imeglimin acts in two different ways: first, it stimulates insulin secretion in response to glucose (GSIS) and maintains cell mass; second, it improves insulin action and may decrease hepatic glucose output while enhancing insulin signalling in the liver and skeletal muscle. Correcting mitochondrial dysfunction, a common underlying component in the aetiology of T2D, may be part of the mechanism underpinning imeglimin, at the cellular and molecular level. Decreased oxygen species that are reactive formation and prevention of permeability of mitochondrial transition pore opening have been observed as a result of the observed rebalancing of respiration chain action. Imeglimin also boosts glucose-stimulated ATP production in islets generated from T2Dafflicted mice and opens the "salvage pathway," which starts the production of NAD+, nicotinamide adenine dinucleotide. NAD+ metabolites play a crucial role as a co-factor in the mitochondria and may also aid in the promotion of GSIS by enhanced Ca++ mobilisation. Imeglimin has demonstrated to maintain the bulk of -cells in animals with T2D. Overall, Imeglimin seems to focus on a critical T2D root cause: faulty cellular energy metabolism. It has been established that this potential mode of action is distinct from those of other significant treatment classes, such as biguanides, sulphonylureas, and glucagon-like peptide-1 receptor agonists.[12]

11. Vial et al (2020) comprehend the process by which imeglimin, a novel oral hypoglycemic medication, reduces hepatic glucose synthesis. Imeglimin and metformin were examined for their effects on rat primary hepatocyte production of glucose, ATP/ADP proportion, utilisation of oxygen rate, mitochondrial redox potential, and membrane potential. He discovered that the ATP/ADP ratio and glucose synthesis were both dose-dependently lowered by imeglimin and metformin. Additionally, they both decreased membrane potential (measured by TMRM fluorescence) and raised mitochondrial redox potential (measured by mitochondrial NAD(P)H fluorescence). It didn't reduce the rate of oxygen consumption in intact cells, in contrast to metformin, which blocks mitochondrial Complex I. When measuring the oxygen consumption of the in situ respiratory chain in relation to NADH concentration, it was observed that metformin reduced both the Vmax and the affinity, indicating uncompetitive inhibition, whereas it reduced the binding ability of NADH for the respiratory chain but had no effect on its Vmax (i.e., competitive inhibition). They come to the conclusion that imeglimin limits the respiratory chain's kinetics without changing its maximal activity. A decrease in the potential of the mitochondrial membrane offsets this kinetic constraint, placing a thermodynamic restriction on ATPase and bringing down the ATP/ADP ratio.[13]

12. Lachaux et al (2020) introduces in a rat model of metabolic syndrome, both the short- and long-term administration of imeglimin counteracts cardiorenal impairment. and express that, It is a glucose-lowering drug that targets mitochondrial bioenergetics, reduces the overproduction of reactive oxygen compounds (ROS) and enhances glucose homeostasis. They looked at whether this had any protective benefits on vascular and left ventricular (LV) dysfunction brought on by the metabolic syndrome. They examined the effects of imeglimin administered orally for 9 or ninety days at a dosage of 150 mg/kg twice a day on LV performance, LV perfusion of tissues, LV oxidative stress, and vascular function using Zucker fa/fa rats. And found Imeglimin treatment for 9 and 90 days reduced LV end-diastolic pressures and the relationship between LV end-diastolic volume and pressure, enhanced LV tissue perfusion, and reduced LV ROS generation as compared to untreated rats. It simultaneously restored mesenteric flow-mediated dilation and acetylcholine-mediated cardiac relaxation. It reduced LV mitochondria ROS production and enhanced LV performance an hour after dosing, while glucose plasma levels had not yet changed. Treatment with imeglimin for 90 days decreased associated kidney and LV fibrosis and enhanced kidney function. In a rat model replicating human metabolic syndrome, Imeglimin demonstrated a reduction in oxidative stress and an increase in nitric oxide (NO) bioavailability, and enhanced myocardial perfusion to prevent metabolism syndrome-related cardiac diastolic dysfunction and vascular dysfunction. These effects are, at least in part, independent of glucose regulation. After 90 days of treatment, myocardial and kidney structure also improved.[14]

13. Theurey et al (2021) compares imeglimin with metformin and express that "By 2040, there will be more than 642 million individuals worldwide who have type 2 diabetes (T2D)" A popular biguanide T2D medication, metformin has been linked to uncommon but serious lactic acidosis episodes, particularly when combined with conditions that predispose to it (such as renal failure or severe surgery). The first drug in a new family of T2D medications with a novel mode of action is imeglimin, a recently licenced drug. Despite not being a biguanide, Imeglimin and Metformin have a chemical moiety and both influence the activity of the mitochondrial complex I, suggesting a plausible explanation for the lactate buildup caused by Metformin. They investigated the possibility that it could cause lacticacidosis in pertinent models of animals and further evaluated variations in significant processes previously recognised to underlie Metformin's actions. Metformin or Imeglimin (30-1000 mg/kg) were abruptly delivered in a canine major surgery model, but only Metformin

caused lactate buildup and pH drops that led to lactic acidosis, which proved lethal at the maximum dose. Metformin or Imeglimin were given to rats with gentamycin induced kidney insufficiency; however, only Metformin elevated lactatemia and H+ concentration with death at higher dosages. Imeglimin and metformin plasma levels were comparable in both models. Mice were administered either Metformin or Imeglimin at a dose of 200 mg/kg on a continuous basis. Acute intraperitoneal glucose load was followed by hyperlactatemia only when metformin was used. Metformin showed greater suppression of mitochondrial complex I activity in ex *vivo* studies compared to Imeglimin, which had just minor effects. Metformin (50-250 M) was shown to be the sole drug that blocked mitochondrial glycerol-3-phosphate dehydrogenase (mGPDH) in isolated rat liver mitochondria exposed to Imeglimin or Metformin. It had lower assessed mGPDH activity than Imeglimin in samples of liver from mice that had received chronic treatment. These results reveal that imeglimin's basic mechanisms of action are different from those of metformin medicine and support the drug's potential benefit for individuals with predisposed illnesses by showing that imeglimin may have a reduced risk of lactic acidosis than metformin.[15]

14. Sanada et al (2022) assessed imeglimin's impact on pancreatic cells. First, the type 2 diabetes db/db mice received a single dosage of imeglimin, which increased insulin release from cells and reduced blood glucose levels. Additionally, islets obtained from nondiabetic db/m mice dramatically increased insulin production in reaction to glucose following a single dose of imeglimin administration. Second, a 4-week chronic therapy with imeglimin improved glycemic control and increased insulin production in diabetic db/db mice during a test for oral glucose tolerance. Imeglimin had positive effects on the shape of the mitochondria in cells and significantly enhanced the quantity of insulin granule in the type 2 diabetes db/db and KK-Ay mice, according to an analysis of electron microscope images. Finally, imeglimin decreased the percentage of cells that died as a result of apoptosis, which was matched by a decrease in the expression of several genes that are involved in apoptosis and inflammatory in cells. It enhances glycemic control by directly improving insulin release in response to glucose from cells, increasing the quantity of insulin granules, and exerting positive effects on the morphology of cell mitochondria, and reducing the death of cells through apoptosis in type 2 diabetic mice.[16]

15. Konkwo et al (2021) explain that the first of the new group of medications called "glimins," imeglimin, was created to treat type 2 diabetes (T2D). This assessment emphasises its mode of action as well as its setting within the T2D treatment industry. Significant impacts on mitochondria, including enhanced mitochondrial bioenergetics, are detailed in preclinical evidence from a variety of animal models. Included in these are adjustments that favour complex II and complex III metabolism, which may act as a catalyst for improved fatty acid oxidation and the reduction in hepatic lipid buildup seen in these mice. Both in *vitro* & in *vivo* studies on imeglimin revealed that it increased muscle glucose absorption while lowering hepatic glucose synthesis. It dramatically increases insulin secretion and reduces beta cell mortality, according to research, however it is yet unknown if its physiologic actions are solely insulin-dependent. Early preclinical investigations have demonstrated enhancements in cardiovascular and kidney function in mice with metabolic syndrome effects that are not provided by the majority of T2D medications currently on the market. Increased insulin secretion, together with lowered fasting plasma glucose levels and haemoglobin A1c, have been observed in human clinical investigations using imeglimin. When used in conjunction with either agent, its observed efficacy was increased and was comparable to that of the already prescribed medications metformin and sitagliptin. It exhibits real promise as a novel method for the treatment of type 2 diabetes with the potential to be used in a bigger, more diverse patient population when taken into account alongside its favourable safety profile found in patients with chronic renal failure.[17]

16. Singh et al (2023) describe Imeglimin is a brand-new oral medication that has just received approval in India for the treatment of type 2 diabetes (T2D). They performed a metaanalysis and reviewing systematically to assess imeglimin's effectiveness in treating type 2 diabetes (T2D) in patients receiving the recommended dose of 1000 mg twice a day (BID). Using the proper keywords and MeSH phrases, A comprehensive search of the PubMed database was conducted until December 20, 2022. At this juncture, all published double-blind, randomized, placebo-controlled studies (RCTs) involving Imeglimin at a dosage of 1000 mg BID were retrieved. In order to determine whether imeglimin 1000 mg BID could lower HbA1c in patients with type 2 diabetes, A meta-analysis was carried out using Comprehensive Meta-Analysis (CMA) software Version 3 from Biostat Inc. in Englewood, New Jersey, USA. Out of the seven Phase 2 studies and three completed trials available up to the specified date, only three double-blind RCTs documented the safety and efficacy of Imeglimin at a dosage of 1000 mg BID compared to placebo. In our meta-analysis utilizing the random-effects model from two monotherapy studies (n=14,360), Imeglimin 1000 mg BID exhibited a significant reduction

in HbA1c (Δ -0.9%, 95% Confidence Interval [CI], -1.1 to -0.74%; P < 0.0001) compared to placebo, with no observed evidence of heterogeneity (I2 = 0%), imeglimin 1000 mg BID dramatically lowered HbA1c, according to a pooled meta-analysis of all three RCTs (n 14 574) (D 0.79%; 95% CI, 1.00 to 0.59%; P 0.0001). It significantly lowers HbA1c in T2D patients with a favourable tolerability profile, according to this meta-analysis. Still, more extensive research is required.[18]

17. Detaille et al (2016) explians that "By blocking the mitochondrial permeability transition without affecting mitochondrial respiration, imeglimin keeps human endothelial cells from dying". The pioneer of a novel class of oral antidiabetic agents, recently concluded its phase 2b trial. Given its demonstrated capability to entirely impede β-cell apoptosis, and recognizing the prominent role of angiopathy in diabetes-related complications, they embarked on a study to explore the protective attributes of Imeglimin against hyperglycemia-triggered demise of human microvascular endothelial cells (HMEC-1). Following exposure to high glucose levels and the oxidising chemical tertbutyl hydroperoxide, these cells underwent a variety of oxidative stress conditions that ultimately, this led to the opening of the mitochondrial permeability transition pore (PTP), the release of cytochrome c, and subsequent cell death. Intriguingly, the administration of Imeglimin fully averted these deleterious events associated with cell death. This protective effect was seen to occur without any appreciable influence on the rate of oxygen consumption, the synthesis of lactate, the cytosolic redox potential, or the phosphate potential. Furthermore, Imeglimin exhibited a remarkable capacity to markedly diminish the generation of reactive oxygen species, primarily achieved by targeted inhibition of reverse electron transfer via complex I within the mitochondrial electron transport chain. In light of our findings, they draw the inference that Imeglimin effectively averts hyperglycemia-induced cell death in HMEC-1 cells by inhibiting the opening of the PTP, while concurrently upholding mitochondrial respiration and cellular energy equilibrium. Given the heightened incidence of both macrovascular and microvascular complications in individuals afflicted with type 2 diabetes, the implications of our results hold substantial promise for therapeutic interventions in this population.[19]

18. Reilhac et al (2021) perform the steps on efficacy and safety of imeglimin to assess the efficacy and safety of Imeglimin as a combination therapy with insulin for a duration of up to 52 weeks in Japanese patients diagnosed with type 2 diabetes, a comprehensive investigation was undertaken. The study employed a double-blind, randomized, parallelgroup phase 3 design across 35 medical centers in Japan. Participants meeting the criteria, For a 16-week period, participants who were at least 20 years old, Individuals diagnosed with type 2 diabetes experiencing insufficient glycemic control despite insulin treatment were randomly allocated in a 1:1 ratio to either the Imeglimin group (1000 mg taken twice daily) or the placebo group, both of which received insulin. A 36-week open-label extension phase ensued, during which time all patients were administered 1000 mg of imeglimin twice a day. The main focus was on assessing changes in the mean glycated haemoglobin (HbA1c) from the beginning to the sixteenth week. According to the results, 108 and 107 patients were allocated to the placebo and imeglimin (1000 mg twice day) groups, respectively. The adjusted mean difference in HbA1c change from baseline at the 16-week point was determined to be -0.60% (with a 95% confidence interval [CI] of -0.80 to -0.40; P < 0.0001) compared to the placebo group. This reduction persisted through 52 weeks, with a mean decrease from baseline of -0.64% (95% CI -0.82 to -0.46). The incidence of adverse events and major adverse events was similar in both treatment groups. The imeglimin and placebo groups likewise saw similar rates of hypoglycemia episodes. Interestingly, all cases of hypoglycemia among patients on imeglimin were classified as mild, and none necessitated external assistance. In conclusion, it demonstrated a significant improvement in HbA1c levels among Japanese patients with inadequately managed type 2 diabetes reliant on insulin therapy. Moreover, its safety profile closely paralleled that of the placebo. The sustained efficacy of imeglimin as an adjunct to insulin persisted over the 52 week duration. This study indicates that it has the potential to serve as a promising novel therapeutic avenue in this patient population when added to insulin regimens.[20]

19. Fauzi et al (2022) express the Preservation effect of imeglimin on pancreatic beta-cell mass . Type 2 diabetes mellitus (T2DM) is adversely affected by a gradual reduction of beta-cell mass (BCM), however BCM measurement has traditionally required an intrusive procedure that only provides cross-sectional data. However, a non-invasive method for measuring BCM over time in living subjects has recently been devised utilising an exendin-4 derivative labelled with indium 111 ([Lys12(111In-BnDTPA-Ahx)] exendin-4 (111In-exendin-4). It is a brand-new anti-diabetic drug that has been shown to enhance mitochondrial function and hence glycemic management and glucose-stimulated insulin secretion (GSIS). It's impact on BCM, however,

is not entirely understood. In prediabetic db/db mice, they investigated the effects of imeglimin on BCM in *vivo* using a non-invasive In-exendin-4 single-photon emission computed tomography/computed tomography (SPECT/CT) method. Type 2 diabetes mellitus (T2DM) is adversely affected by the progressive decrease of b-cell mass (BCM), and BCM evaluation has traditionally needed an intrusive procedure that Imeglimin administration slowed the development of glucose intolerance during the course of the 5-week research, and imeglimin-treated animals had higher BCM levels than control mice, which was in line with the findings of 111In-exendin-4 SPECT/CT scans. Additionally, imeglimin-treated db/db animals showed decreased beta-cell apoptosis and decreased the release of cytosolic cytochrome c protein, according to immunohistochemistry examination. Additionally, the structural strength and efficacy of membrane of the mitochondria in islets treated with imeglimin were found to be improved through electron microscope observation and measurement, respectively. These findings show that suppression of mitochondria-mediated apoptosis slows the progression of BCM loss in prediabetic db/db mice.[21]

20. Bando et al (2022) checked the HbA1c value in patients with type 2 diabetes mellitus (T2DM) undergoing treatment with a combination of dulaglutide and Imeglimin. Recently, imeglimin has been introduced as a novel oral hypoglycemic medication (OHA) called Twymeeg for patients with type 2 diabetic mellitus (T2DM). Its two beneficial processes complement one other to increase insulin secretion and decrease insulin resistance. It is the first OHA for a glimin-containing medication that contains tetrahydrotriazine and possesses a triazine ring. Case presentation the 84-year-old female patient has mild cognitive impairment (MCI) and type 2 diabetes. Her HbA1c was 9.3% a year ago. She started using Dulaglutide 0.75 mg/week, and after six months, her HbA1c level decreased by 1.3%. However, her HbA1c increased once again to 8.5%, at which point she was given Twymeeg 2000 mg per day. In three months, HbA1c dropped from 8.5% to 7.5%.The previous study's combination imeglimin and other agents treatments resulted in mean HbA1c reductions of -0.46%, -0.92%, and -0.12% for single imiglimin, DPP-4i, and GLP-1RA, respectively. Possible explanation for the distinction between the latter two suggests that imeglimin may have a variety of action mechanisms, including one that improves insulin secretion stimulated by glucose (GSIS). She, however, demonstrated an acceptable HbA1c reduction when imeglimin and GLP-1RA were combined. The pathogenesis is unclear, thus further clinical progress monitoring will be necessary.[22]

21. Oda et al (2022) explians intermittently scan continuous glucose monitoring to assess the impact of meglimin on the daily glycemic profile. This represents a novel anti-diabetic medication that enhances glucose-stimulated insulin secretion (GSIS) and improves insulin sensitivity, as demonstrated in various randomized clinical trials, imeglimin has been beneficial for glycemic management in individuals with type 2 diabetes (T2D). Utilizing intermittently scanned continuous glucose monitoring (isCGM), the objective was to assess the safety and short-term impact of Imeglimin on glycemic control. In this retrospective and observational study, 32 patients receiving Imeglimin as part of their regular treatment regimen underwent glucose level evaluations. For a duration exceeding four weeks, the patients were observed starting on the day that imeglimin was started. Aside from gathering information on side effects through interviews, Alterations in glycemic markers, including mean glucose level, coefficient of variation (CV), time in range (TIR), and time above range (TAR), were examined both before and after the administration of Imeglimin. From this result was found (from 159.0 27.5 mg/dL to 141.7 22.1 mg/dL; p 0.001), TIR (from 67.9 17.0% to 79.5 13.3%; p 0.001), and TAR (from 29.4 17.5% to 17.9 13.7%; p 0.001). The 24-hour mean glucose level curves for each of the 32 patients showed a downward shift in relation to the baseline following imeglimin administration. Imeglimin's effectiveness in glycemic management was associated with high mean glucose levels, elevated TAR, decreased TIR, low body mass index, and reduced C-peptide levels. Gastrointestinal issues were the most prevalent side effect observed in patients receiving Imeglimin in combination with insulin or a glinide treatment, with a higher incidence of hypoglycemia. It successfully shifted the daily glucose profile of Japanese patients with type 2 diabetes (T2D) into an acceptable range, indicating a notable improvement in short-term glycemic control. Imeglimin is considered a promising treatment option for individuals with T2D, particularly those with low insulin secretory capacity, a common condition among East Asians with glucose intolerance.[23]

22. Raczynska et al (2023) introduce that Imeglimin has a lesser lithium-cation basicity but a greater proton basicity than metformin. Biguanide-containing medications like metformin, phenformin, and buformin are known to have antihyperglycemic effects. Imeglimin, a dihydro-1,3,5-triazine, has being investigated as a possible novel antidiabetic medication. It can be thought of as a cyclic metformin derivative. Its structure and gas phase basicity towards the lithium cation and the proton have been investigated by quantum-chemical

simulations. Because it can undergo a variety of structural isomeric rearrangements, Twenty-three isomers have been suggested for the neutral molecule in a vacuum at the B3LYP/6-311+G(d,p) level. The G2, G2MP2, and G4 techniques have further verified the remarkable energy stabilities of the four isomers—two main and two minor—that have been chosen. More than 95% of the main isomers match the push-pull biguanide systems, which resemble the neutral metformin systems. There are nonanalogous metformin structures in the minor isomers (<5%). The energetics of protonation and adduct formation with Li+ have been computed in order to investigate the basicity features in the gas phase. The monoprotonated and monolithiated forms of imeglimin were subjected to the same process (beginning with density functional theory, followed by Gn techniques) as the neutral molecule in order to determine the preferred. Imeglimin's proton affinity is greater than 10 kJ mol−1 when compared to metformin; this increase is explained by the presence of an extra >CH−CH3 group. The cyclic version of imeglimin eliminates the chance of a two-imino group chelation action, as is the case with metformin. As a result, imeglimin has a lower affinity for lithium-cations (by around 30 kJ mol−1) than metformin. However, the imino and amino N atoms of imeglimin that are nearby appear to be weakly chelating the lithium cation; The influence of imeglimin's two terminal imino N atoms is less pronounced compared to those of metformin. Lithium-cation basicity falls between tricyclic vinamidine TTT and bicyclic guanidine MTBD. In terms of gas-phase proton basicity, imeglimin is positioned between bicyclic amidine DBU and guanidine TBD. The correlation between electron delocalization in imeglimin's biguanide moiety and isomerism is akin to observations in both the parent biguanide and metformin.[24]

23. Nomoto et al (2022) examine assessing the impact of Imeglimin versus metformin dose escalation on glycemic control in patients with type 2 diabetes receiving low-dose metformin combined with a dipeptidyl peptidase-4 inhibitor. A brand-new anti-hyperglycemic medication called meglimin enhances insulin production and insulin resistance. Phase III clinical trials supported the efficacy of imeglimin on glycemic control, However, there is limited knowledge regarding its performance in routine clinical practice settings, particularly in comparison to metformin. To clarify the effectiveness of Imeglimin in individuals with type 2 diabetes (T2D) undergoing treatment with low-dose metformin and a dipeptidyl peptidase-4 (DPP-4) inhibitor. This is a prospective, multicenter, randomised, open-label, parallel-group study. A randomization process will be used to determine which 70 T2D participants—those whose glycated haemoglobin (HbA1c) level falls between 52 and 85 mmol/mol (7.0% and 9.9%) and Patients who have been treated with a DPP-4 inhibitor in combination with metformin (500–1000 mg/day) for over 12 weeks will be assigned to either receive add-on Imeglimin at 1000 mg twice a day or undergo metformin dose escalation for a duration of 24 weeks. Adverse events will be documented, and baseline and study-ending biochemical assays and physical evaluations will be carried out. The primary outcome is the change in HbA1c after 24 weeks. Secondary objectives include assessing changes in body weight, belly circumference, blood pressure, pulse rate, and other laboratory measurements; side effects; and the correlation between improvements in biological markers, such as glycemic management, and patient background characteristics. This research will provide fresh perspectives on how to include imeglimin in a diabetic treatment plan. This initial randomized controlled trial aims to compare the effectiveness of adding Imeglimin versus escalating metformin dosage in enhancing glycemic control among patients with type 2 diabetes.[25]

24. Hagi et al (2023) work on Imeglimin's safety and effectiveness. Patients with type 2 diabetes mellitus vary widely in their clinical and demographic features, which could have an effect on how they respond to treatment. Based on clinical and demographic factors, In this post-hoc analysis, the efficacy and safety of Imeglimin 1,000 mg twice daily (BID) monotherapy were evaluated in patients with type 2 diabetes. Two 24-week, randomised, double-blind, placebo-controlled investigations involving people with type 2 diabetes were combined into one study. Its results (Safety and the alteration in HbA1c from baseline to week 24, measured by the least squares mean [LSM]) were examined based on subgroups that included clinical features, comorbidities, and demographics. In all patient subgroups analysed, This includes demographics (age, body mass index), clinical characteristics (duration of type 2 diabetes mellitus, chronic kidney disease [CKD] stage, and prior medication use), and comorbidities (hypertension, dyslipidemia, risk of hepatic fibrosis, and liver function parameter status). The difference in LSM change in HbA1c from baseline to week 24 was statistically significant for Imeglimin vs. placebo ($P < 0.05$ for each). Regarding HbA1c, a statistically significant difference from placebo was observed at week four and persisted until week twenty-four. In any patient subgroup, it did not raise any new safety issues. It was shown to be safe and effective in all patient subgroups, regardless of their initial clinical and demographic makeup. the results validate it's effectiveness and safety in a wide range of type 2 diabetic patients.[26]

25. Uchida et al (2023) works on Imeglimin's effects on endothelial function. For diabetic patients, it is a risk factor for cardiovascular disease. They postulated that the novel oral hypoglycemic drug imeglimin would enhance endothelial function. In this trial, patients with type 2 diabetes who were not undergoing insulin therapy and had an HbA1c of 6.5% were administered Imeglimin. Meal tolerance (592 kcal, glucose 75.0g, fat 28.5g) was evaluated both before and three months after the initiation of the medication. Triglycerides, blood glucose, insulin, glucagon, and endothelial function were also assessed. Using flow-mediated dilation, endothelial function was evaluated (FMD). Twelve patients, fifty percent of whom were male, The participants included in the study had a median age of 55.5 years (interquartile range [IQR]: 51.3–66.0). There was no observed difference in fasting Flow-Mediated Dilation (FMD) before or three months after the administration of Imeglimin (from 6.1 [3.9–8.5] to 6.6 [3.9–9.0], p = 0.092). However, a significant enhancement in 2-hour postprandial FMD was noted (from 2.3 [1.9–3.4] to 2.9 [2.4–4.7], p = 0.013) three months after the initiation of Imeglimin. The treatment of imeglimin resulted in significant improvements to the glycemic profile, including an improvement in HbA1c (from 7.2 ± 0.6% to 6.9 ± 0.6%, p = 0.007), fasting glucose (from 138 ± 19 mg/dL to 128 ± 20 mg/dL, p = 0.020), and 2 h postprandial glucose (from 251 ± 47 mg/dL to 215 ± 68 mg/dL, p = 535). A univariate correlation coefficient analysis revealed a negative correlation between the change in 2 h postprandial FMD between before and 3 months afterimeglimin treatment (postprandial FMD) and D2 h postprandial glucose (r = - 0.653, p = 0.021). Three months after imeglimin was administered, postprandial FMD improved in both patients with and without decreased postprandial glucose. The injection of imeglimin improved 2-hour postprandial FMD in this small research. Improved endothelial function may be due to both independent and dependent pathways on glucose regulation.[27]

26. Yamagishi et al (2023) analysis the possible ketoacidosis associated with using metformin and imeglimin together in a patient with type 2 diabetes. After starting metformin in addition to imeglimin medication, a 74-year-old lady with type 2 diabetes mellitus experienced ketoacidosis six days later. Even though they responded to insulin and continued to secrete insulin, there was less chance that ketoacidosis would result from insufficient insulin. Complex I in the mitochondrial respiratory chain is partially inhibited by both imeglimin and metformin. This inhibition causes the mitochondrial respiration process to slow down, which may lead to the suppression of the tricarboxylic acid cycle (TCA cycle). As a result, acetyl-coenzyme A entry into the TCA cycle is limited and eventually directed into ketogenesis. Therefore, it's plausible that the concurrent use of metformin and imeglimin caused the beginning of ketoacidosis.[28]

27. Dubourg et al (2020) propose that Imeglimin, a novel medication belonging to the glimin class of oral antidiabetic drugs, is now being studied to enhance the management of blood sugar levels in individuals diagnosed with type 2 diabetes mellitus. To as certain whether therapeutic and supra-therapeutic doses of imeglimin have any potential electrophysiological effects on cardiac repolarization, a thorough QT study was conducted. The research was planned as a four-period, double-blind, randomised crossover trial with participants who were in good health. The individuals received a single dose of 2250 mg of imeglimin, 6000 mg of imeglimin, 400 mg of moxifloxacin (which acted as an active comparator), and a placebo. 12-Lead Holter electrocardiograms (ECGs) were taken starting an hour before the dose and continuing for at least 24 hours after it was administered. The research was carried out in a single center's controlled inpatient clinical pharmacology unit. None of the imeglimin dosage groups exceeded the regulatory threshold of 10 ms when evaluating the primary endpoint, What was the maximum value of the baseline-adjusted two-sided 90% confidence interval for the placebo-subtracted QTc interval (ΔΔQTcF). Moreover, within the imeglimin cohorts, no QTcF readings above the 500 ms criterion, nor were there any pre-dose to post-dose variations in QTcF over 60 ms. Interestingly, there was no discernible effect of imeglimin administration on heart rate, PR interval, or QRS interval. The 400 mg of moxifloxacin was evaluated for its effects in order to validate the sensitivity of the assay. The study's sensitivity was confirmed when the lower limit of the two-sided 90% confidence interval for ΔΔQTcF exceeded 10.6 ms. As evidenced by test sensitivity and strong confidence levels, our extensive QT study definitively shows that imeglimin doses, whether therapeutic or supra-therapeutic, do not cause QT/QTc prolongation.[29]

28. Okada et al (2023) studied After using imeglimin, commonly known as Twymeeg, an 83-year-old woman with type 2 diabetes (T2D) for 19 years and recent dementia treatment showed clinical improvement. Over the course of four months, she reduced her original HbA1c level of 10.0% to 6.6% while taking 2000 mg of

Twymeeg daily. The patient was treated effectively for neuropsychiatric symptoms related to dementia by concurrently receiving memantine and tiapride. Zinc acetate hydrate, also known as Novelzin, was kept in treatment for dementia and type 2 diabetes. The results of the studies of Imeglimin for Efficacy and Safety (TIMES) 2 and 3 studies indicate that Twymeeg administration was effective. The possible benefit of zinc was taken into consideration, especially in light of Alzheimer's disease and its correlation with low zinc levels (APLZ).[30]

29. Kitakata et al (2021) study Meta-inflammation has been associated with the pathophysiology of heart failure with preserved ejection fraction (HFpEF) in individuals with obesity and diabetes. Elevated levels of inducible nitric oxide synthase (iNOS) expression and disruption of the unfolded protein response (UPR), specifically inositol-requiring enzyme 1aX-box binding protein 1 (IRE1aXbp1s) signaling in the heart, have been identified in connection with HFpEF. They looked into how the pathophysiology of HFpEF was affected by imeglimin, a possible novel type 2 diabetes treatment. For a period of 16 weeks, they induced obesity, impaired glucose tolerance, and heart hypertrophy with fibrosis, fat accumulation, and diastolic dysfunction in wild-type mice by administering a high-fat diet (HFD) along with the nitric oxide synthase (NOS) inhibitor L-NAME. Beginning at 10 weeks, imeglimin treatment improved not only their abnormalities in visceral fat and systemic glucose metabolism, As well as their cardiac abnormalities. They found that imeglimin suppressed the increase in inducible nitric oxide synthase (iNOS) and restored the expression of Xbp1s, E3 ubiquitin ligase STIP1 homology, and U-box-containing protein 1 (STUB1), which is in charge of degrading the direct transcriptional target of Xbp1s, Forkhead box protein O1 (FoxO1). Additionally, it reduced the overactive transcriptional activity of FoxO1, which is implicated in the form development of HFpEF and cardiac adipogenesis and is located downstream of Xbp1s, Glutathione peroxidase 4 (GPX4) safeguards against excessive lipid peroxidation and regulates a distinct form of programmed cell death called ferroptosis, was also made to express again by imeglimin.[31]

30. Nozu et al (2023) works on In irritable bowel syndrome (IBS), the primary symptoms are visceral hypersensitivity and leaky gut, which are mediated by toll-like receptor 4 and corticotropin releasing factor. It has been noted that metformin helps with GI abnormalities. The purpose of this study was to ascertain how the metformin derivative imeglimin affected the function of the gastrointestinal tract in a mouse model of irritable bowel syndrome. It inhibits colonic hyperpermeability and visceral hypersensitivity brought on either LPS or CRF. Naloxone, or compound C, stops these effects. These findings imply that imeglimin may be useful in the treatment of irritable bowel syndrome (IBS) by enhancing the sensitivity of the colonic and visceral barriers that separate AMPK from opioid receptors.[32]

31. Nowak et al (2022) The first medication in the glimin class, which is a novel class of anti-diabetic medications intended to treat patients with type 2 diabetes (T2DM), is imeglimin (IMEG). Report on the drug's chemical makeup and mode of action. The effect of imeglimin are bunique and different from other antidiabetes drugs. It has been shown to be effective in 1 of the 3 main cause of T2DM. it increase gluconeogenesis, insufficient beta cell glucose induced insulin secretion, it increase peripheral insulin resistance. The effects of IMEG on fasting blood glucose FPG and glycosylated hemoglobin HBA1c levels increased after 16 weeks of treatment. People taking IMEG at doses of 1000mg and 1500 mg twice a day had a significant reduction in plasma glucose FPG. This article also describes the pharmacokinetics of IMEG activity, evidence of its effectiveness, results of phase 2 and 3 clinical trails, and adequate use of drug. Our paper appears to suggest that IMEG, with its novel mechanism of action, has the opportunity to improve outcomes for many T2DM patients.[33]

32. Sathawane et al 2023 imeglimin hydrochloride is used in the treatment of type 2 diabetes. A white crystalline powder easily dissolvable in double distilled water, it is associated with diabetes mellitus, a metabolic disorder distinguished by elevated blood sugar levels. To developed a commercial, simple, rapid, accurate and sensitive UV visible method for the bulk detection of imeglimin hydrochloride. The choice of co-solvent is very important, so the solvent and are a under the curve chosen for derivation spectroscopy include double distilled water and the measurement range from 2.5 to 15.0 µg/ml. The maximum absorbance of imeglimin hydrochloride is observed at 239 nm. The area selected from the area under the curve for analysis of imeglimin hydrochloride is in the range of 232 – 245 nm. The method exhibited linearity within the

concentration range of 2.5 to 15.0 µg/ml. double distilled water was chosen to make the heavy test as it was found to be better. The analysis method is derivative spectroscop, measuring the absorbance at 239nm, 250nm and 201nm to extract the zero order, first-order and second-order derivative spectral interface, the concentration range of 2.5- 15.0 µg/ml. recovery for imeglimin hydrochloride ranged from 99% to 101%. The method is measured by linearity, accuracy, precision and limited. This method is simple, practical and effective to detect the presence of imeglimin hydrochloride.[34]

33. Salvi et al (2023) founds the imeglimin is a unique oral medication under investigation that is first of its kind for the cureness of type 2 diabetes. The action mechanism of imeglimin consists of two distinct effects (a) preservation of cell mass and an increase in glucose-stimulated insulin secretion (GSIS) and (b) improvement in insulin action, At the cellular and molecular levels, this could potentially reduce hepatic glucose output and enhance insulin signaling in the liver and skeletal muscle, meglimin may treat mitochondrial dysfunction, a common underlying component in the pathogenesis of Type 2 Diabetes. The observed adjustment in respiratory chain activity, involving the partial inhibition of Complex I and correction of impaired Complex III activity, has been associated with a reduction in reactive oxygen species formation (thus lowering oxidative stress) and the prevention of mitochondrial permeability transition pore opening, which is implicated in averting cell death. For the purpose of estimating imiglimin hydrochloride in bulk and tablets, a straightforward, accurate, and cost-effective RP-HPLC method was created and verified. An optimised approach is required to observe the peak of imeglimin hydrochloride at 14.319 minutes. To reduce the retention duration, further modifications to the mobile phase were necessary, involving a buffer with pH 3.0 and methanol in a ratio of 80:20 (v/v).[35]

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