**IMEGLIMIN: A REVIEW**

Jayakrishnan B

1Professor, Department of Medicine, Educare Institute of Dental Science Malappuram Safe Care Clinics, Tirur, Kerala, India.

**Abstract**

**Background:** Imeglimin is an oral antidiabetic drug. Approved for use in Japan in June 2021. It is an oxidative phosphorylation blocker that inhibits hepatic gluconeogenesis, increases glucose uptake into muscle, and restores normal insulin secretion. It is the first approved drug in this class of antidiabetic agents. This review provides a general overview of imeglimin, including mechanism of action, and key studies in the clinical development program of this promising compound. In contrast to a systematic review, this paper aims to present the compound under study in a comprehensive and narrative manner to the medical community. Our assessment summarizes current knowledge gaps and highlights the need for future research.

**INTRODUCTION**

Imeglimin is an oral antidiabetic drug. Approved for use in Japan in June 2021. It is an oxidative phosphorylation blocker that inhibits hepatic gluconeogenesis, increases glucose uptake into muscle, and restores normal insulin secretion. It is the first approved drug in this class of antidiabetic agents.[1] Type 2 diabetes (T2DM) is a widespread disease that affects more than 380 million people worldwide and is projected to affect more than 590 million people worldwide by 2035. Addressing this global problem requires enormous amounts of time, effort, and funding that many organizations, including private and public agencies, have devoted to treatment, prevention, and education. Despite our best efforts, the prevalence of type 2 diabetes continues to rise, especially given an aging population, rising obesity rates, and an increase in at-risk ethnic groups. Furthermore, the physiological and progressive nature of diabetes requires a combination of lifestyle modifications and pharmacotherapy to achieve and maintain long-term glycemic control. The major physiological defects of type 2 diabetes include excessive hepatic glucose production, decreased peripheral glucose uptake by insulin-sensitive tissues, and insufficient insulin secretion. This article introduces a potential new pharmacological agent, imeglimin, and reviews its basic and clinical activities in comparison with other widely used drugs.

![Figure 1: Structure of Imeglimin](image1)

**Mechanism of action:** Imeglimin exhibits a unique mechanism of action that targets the three major pathophysiological components of type 2 diabetes: impaired glucose uptake by muscle tissue, excessive hepatic gluconeogenesis, and increased β-cell apoptosis. The use of imeglimin to improve fasting glycated hemoglobin (HbA1c) and plasma glucose (FPG) levels, either as monotherapy or in combination with other hypoglycemic agents, has been shown to improve type 2 diabetes mellitus at all stages of the disease spectrum. It is a promising candidate for treatment. For the sake of brevity, this review will focus on the effects of imeglimin on HbA1c and FPG.

![Figure 2: Proposed model for mechanism of Imeglimin action in islet of beta cells.](image2)
showed a statistically significant increase in muscle from streptozotocin diabetic rats, imeglinin with control. the maximum dose given (2 mmol/L), compared dose of 0.5 mmol/L with up to a 3.3-fold increase at the maximum dose given (2 mmol/L), compared with control. In vivo, in soleus and gastrocnemius muscle from streptozotocin diabetic rats, imeglinin showed a statistically significant increase in glucose uptake even at the lowest dose (25 mg/kg), restoring the uptake to normal for diabetic rats at 50 mg/kg and 100 mg/kg. There are various proposed molecular pathways for the action of imeglinin on insulin sensitivity, even though they are not fully understood. One proposed way is the increase in Akt (protein kinase B) phosphorylation, which passes the insulin signal transduction; another possible pathway might include glucose transporter-4 expression and the regulation of insulin receptor substrate phosphorylation.

Metformin is the first-line agent in the treatment of type 2 diabetes, mainly due to its safety, efficacy and low cost. It does not cause hypoglycaemia, and offers an effective reduction in HbA1c as a monotherapy or in combination with other oral glucose-lowering agents. However, in some patients, the use of metformin is limited, mostly due to its gastrointestinal side effects. There are several phase II and phase III studies that demonstrate the effectiveness of imeglinin as an alternative option.

The mechanisms by which imeglinin improves insulin sensitivity and β-cell function are not yet fully understood. The examination of imeglinin’s effect on inflammatory responses, glucagon secretion and mitochondrial function may reveal other pharmacological aspects that demonstrate the potential of this promising new molecule. So far, only a few large, phase III clinical trials have been conducted to evaluate the efficacy of imeglinin as monotherapy or in combination with other approved antidiabetic agents. So far, imeglinin has exhibited a good safety profile in most of the recent clinical trials; it has shown a lower frequency of gastrointestinal adverse effects than metformin, while demonstrating a similar efficacy on glycaemic control, both as a monotherapy and in combination with other antidiabetic medications.

In patients with moderate hepatic impairment, imeglinin administration was well tolerated. Although the increase on maximum plasma concentration in these individuals was not reported as clinically significant, more research needs to be conducted in order to examine the safety profile on individuals with severe hepatic impairment.

**CONCLUSION**

This review presents a general overview of imeglinin, including its mechanism of action, and the most important studies in the clinical development programme of this promising agent. In contrast with a systematic review, this paper aims to introduce this under-development agent to the medical community in a comprehensive, narrative way. However, the appraisal of the most relevant research about this topic summarizes the current lack of knowledge and demonstrates the need for future research.
In both TIMES 2 and TIMES 3, the adverse events were similar to previous clinical trials; overall, the safety profile of imeglimin was favourable and the adverse event incidence was similar to that of a placebo. Hypoglycaemic events reported during TIMES 3 were mild, and the number of patients receiving imeglimin who experienced hypoglycaemia was similar to the placebo group.

REFERENCES