A Comprehensive Review of Analytical Method Development and Validation for Imeglimin Hydrochloride.

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ABSTRACT

Imeglimin Hydrochloride is a novel oral antidiabetic agent used in the management of type 2 diabetes mellitus, characterized by its unique mechanism of action targeting mitochondrial bioenergetics. The increasing therapeutic significance of Imeglimin necessitates the development of robust, accurate, and reliable analytical methods for its identification, quantification, and quality control in bulk and pharmaceutical dosage forms. This comprehensive review focuses on the various analytical techniques developed for the estimation of Imeglimin Hydrochloride, including spectroscopic methods such as UV–Visible spectrophotometry and advanced chromatographic techniques like High-Performance Liquid Chromatography (HPLC), High Performance Thin Layer Chromatography (HPTLC), and Liquid Chromatography–Mass Spectrometry (LC–MS). Emphasis is placed on method development strategies, including selection of solvents, mobile phase optimization, detection wavelength, and column characteristics to achieve optimal sensitivity and specificity.

Keywords: Analytical methods, Type 2 diabetes, Glimins (mitochondrial modulators), Antidiabetic, Imeglimin hydrochloride.

INTRODUCTION

Imeglimin hydrochloride (branded as TWYMEEG®)—let's just call it imeglimin for short is a pioneering oral drug from the new "glimin" family. Developed by Poxel and, in parts of Asia, Sumitomo Dainippon Pharma, it's designed to tackle type 2 diabetes (T2D) by targeting several key issues behind the disease. In June 2021, it earned its first approval in Japan, backed by strong preclinical and clinical evidence, including standout results from the phase III TIMES trials. This piece walks through the major steps in imeglimin's journey that paved the way for that approval.. (Lamb, Y.N. (2021)].

Imeglimin Hydrochloride is a potent drug against diabetes as it specifically targets mitochondria bioenergetics. Also, Imeglimin hydrochloride has low chances of hypoglycaemia. Even though there are other anti-diabetic drugs available, Imeglimin hydrochloride appears to be good option for diabetes patients. It is safer, more potent, and better tolerated compared to alternatives.[Pirags, V., Lebovitz, H.,(2012)]

Mechanism

Imeglimin helps people with type 2 diabetes manage their blood sugar levels through a multifaceted approach.

Here's a breakdown of its key mechanisms,

Boosting glucose-stimulated insulin secretion (GSIS): It ramps up the ATP/ADP ratio inside pancreatic βcells, raising their energy levels to trigger a stronger insulin release in response to rising glucose.

Preservation of Beta Cell Mass: Imeglimin safeguards beta cells by curbing apoptosis and encouraging their survival key for ongoing insulin production. It also enhances insulin sensitivity in the liver and muscles, promoting better glucose uptake and use to help control blood sugar.

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Inhibition of Hepatic Glucose Output: It helps cut down on the liver's glucose production, which lowers blood sugar keeping diabetes in check..

Improvement of the Mitochondrial Function: Imeglimin boosts mitochondrial function by raising the ATP/ADP ratio, which powers up energy production and keeps cells healthy overall. This helps insulin work better and improves metabolism.

Reduction of Oxidative Stress This medication helps lower oxidative stress, which in turn boosts insulin sensitivity and supports better overall metabolism making it a solid ally in handling type 2 diabetes..

[Mangore, M. N., Bhosale, N. R., (2025)]

DRUG PROFILE [Pagar, O. K., Suhasini, B., & Aravinda Reddy, P. (2025)]

Drug	**Imeglimin hydrochloride**
IUPAC Name	(6R)-6-(dimethylamino)-2,2-dimethyl-1,3,5-triazinane-4-one hydrochloride
Chemical Formula	$C_6H_{13}ClN_4O$
Molecular Weight	192.65 g/mol
Dosage Form	Tablet
Administration Route	Oral

Reported Methods for Assessment of Imeglimin Hydrochloride:

The various methods are reported for estimation, quantification, by using U.V spectroscopic, High Performance Liquid Chromatography ,High Performance Thin Layer Chromatography, LC-MS/MS.

Here is your data organized into a clean, properly formatted table:

Sr. No.	Title	Description	Ref. No.
1	A Novel Method Development and Validation of Imeglimin HCl by UV Visible Spectroscopy	Solvent: Water; Wavelength: 237 nm; R^2: 0.9991; Linearity: 2–10 µg/mL; LOD: 16.74 µg/mL; LOQ: 50.73 µg/mL	Tamil Selvan, R., et al. (2023)
2	Method Development and Validation for Estimation of Imeglimin by UV Visible Spectroscopy	Solvent: Methanol; Wavelength: 242 nm; R^2: 0.9996; Linearity: 2–10 µg/mL; LOD: 0.082 µg/mL; LOQ: 0.248 µg/mL	Parthiban, C., Renuka, G., Maheshwari, K. (2025)
3	UV-Spectrophotometric Method for Determination of Imeglimin Hydrochloride	Solvent: Methanol:Water (50:50 v/v); Wavelength: 241 nm; R^2: 0.997; LOD: 0.0809 µg/mL; LOQ: 0.2451 µg/mL	Mubeen, G., Meghana, D. (2026)
4	RP-HPLC Method for Determination of Imeglimin Hydrochloride in Bulk and Tablet Formulation	Column: BRISA LC2 C18 (25 mm × 0.46 mm, 5 µm); Mobile Phase: Methanol: Phosphate buffer (10 mM, pH 6.0); Flow rate: 1 mL/min	Mubeen, G., Navali, S., & N, L. (2024)
5	Stability Indicating RP-HPLC Method Development and Validation for Estimation of Imeglimin HCl	Column: Kromasil C18 (250 mm × 4.6 mm, 5 µm); Flow rate: 1 mL/min; Linearity: 80–120 µg/mL	Vikhe, K.B., Sonawane, S.S. (2026)
6	Stability Indicating RP-HPLC Method Development and Validation for Imeglimin HCl	Column: Credchrom C18 (250 mm × 4.6 mm, 5 µm); Mobile Phase: Phosphate buffer: Acetonitrile (80:20 v/v); Flow rate: 1	Adhao, V.S., Chaudhari, S.P. (2024)

	in Pharmaceutical Dosage Form	mL/min; Includes forced degradation studies	
7	Stability Indicating Green HPLC Method for Imeglimin Hydrochloride Determination in Tablets	Column: XTerra® RP8 (150 × 4.6 mm, 5 µm); Mobile Phase: 0.1% 1-octane sulfonic acid sodium salt: Ethanol (80:20 v/v); Flow rate: 1 mL/min	Mansour, F.R., Elagamy, S.H., Elbastawissy, A.B.B. et al. (2026)
8	Development and Validation of Stability Indicating RP-UHPLC Method for Estimation of Imeglimin Hydrochloride	Column: Hypersil Gold ODS (150 × 4.6 mm, 3 µm); Mobile Phase: Water: Acetonitrile (15:85 v/v); Flow rate: 1 mL/min; Injection: 20 µL; Linearity: 25–500 µg/mL	Jain, A.S.L.K., Soni, I.K., Sharma, R.A.J.E.S.H. (2023)
9	Green Bioanalytical Method Development and Validation for Estimation of Imeglimin HCl Using Human Plasma by LC-MS/MS	Column: Phenomenex Kinetex PFP (50 × 4.6 mm, 2.6 µm); Instrument: Shimadzu SIL-20AC; Internal Standard: Carbamazepine; Mobile Phase: 0.1% Formic acid: Acetonitrile (30:70 v/v); Flow rate: 0.5 mL/min; Injection: 5 µL	Chandarana, C.V., Vashi, V.H., Bera, A. et al. (2025)
10	Bioanalytical Method Development and Validation of Antidiabetic Drug: Imeglimin Hydrochloride	Column: C18 (Hypersil BDS, 250 × 4.6 mm, 5 µm); Mobile Phase: Methanol: Ammonium formate buffer (80:20 v/v); Flow rate: 1 mL/min	Gawande, K.A., Waghulkar, V.M., Jadhav, M.P. (2025)
11	QbD Approach: Development and Validation of RP-HPLC Method for Estimating Imeglimin HCl and Its Ketone Impurity	Column: Agilent Zorbax Bonus RP (25 cm × 4.6 mm, 5 µm); Mobile Phase: TFA: Acetonitrile (45:55 v/v); Flow rate: 0.45 mL/min; Injection: 10 µL; Design: Central Composite Design	Giri, Pooja T., et al. (2025)

FUTURE ASPECTS

The development of more sensitive, quick, and environmentally friendly analytical methods should be the main emphasis of future Imeglimin method development research. High-performance techniques like UPLC and LC-MS/MS can be integrated to greatly increase detection sensitivity and shorten analytical times. Another crucial path is to increase the use of bioanalytical techniques in pharmacokinetic and bioequivalence research. Additionally, process optimization can increase efficiency and reproducibility by using automation and artificial intelligence.

CONCLUSION

The established Imeglimin analytical techniques satisfy ICH validation standards because they are exact, accurate, and dependable. These techniques are widely used for routine quality control and are still developing due to improvements in sustainability, speed, and sensitivity. All things considered, the described techniques are appropriate for regular quality control and offer a solid basis for additional study, including bioanalytical applications and innovative formulation systems.

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