Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

Development and Validation of RP-HPLC Method for Determination of Antidiabetic Drug (Imeglimin HCL) in Bulk and its Dosage Form.

Hemant Chikhale*[1], Yogeshwari Ambekar[2], Saurabh Avhad[3], Laxmikant Borse[4]

[1]Department of Pharmaceutical Chemistry, Sandip Institute of Pharmaceutical Sciences,Affiliated to Savitribai Phule Pune University, Mahiravani, Nashik-422213, MS, India

[2]Department of Post Graduate Study in Quality Assurance, Sandip Institute ofPharmaceutical Sciences, Affiliated to Savitribai Phule Pune University Mahiravani, Nashik-422213, MS, India.

[3]Department of Post Graduate Study in Quality Assurance, Sandip Institute ofPharmaceutical Sciences, Affiliated to Savitribai Phule Pune University Mahiravani, Nashik-422213, MS, India.

[4]Principal and Professor, Sandip Institute of Pharmaceutical Sciences, Affiliated to SavitribaiPhule Pune University, Mahiravani, Nashik-422213, MS, India

Corresponding Author

Name- Prof. Hemant U. Chikhale

Department of Pharmaceutical Chemistry, Sandip Institute of Pharmaceutical Science, Mahiravani Nashik-422213

Affiliated to Savitribai Phule Pune University, Pune,

(Received: 14 April 2024 Revised: 1 May 2024 Accepted: 18 June 2024)

KEYWORDS

validation, RP-HPLC, Antidiabetic, Imeglimin hydrochloride, Accuracy, Linearity.

ABSTRACT:

Background: Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) is used to analyse the Imeglimin hydrochloride (HCL). Accurate and precise analytical methods are crucial for the pharmaceutical analysis of imeglimin HCL, a novel antidiabetic pharmaceutical with promising therapeutic effects.

Objective: To Optimize chromatographic conditions including mobile phase composition, column type, and detection wavelength to achieve good resolution, sensitivity, and selectivity for imeglimin. To Validate the developed RP-HPLC method according to international guidelines (e.g., ICH guidelines).

Method: The method was developed by using Phenomenox, C18 (250 mm X 4.6 mm, 5 µm) column. The mobile phase was adjusted to achieve the highest possible resolution, sensitivity, and peak symmetry. It contains methanol at 0.05 percent TFAA in water at 20% V/V. At a flow rate of 1.0 millimetres / minute, the detection was carried out at 240 nm. The developed method was validated according to ICH guidelines.

Result: To assess the method's performance and reliability, it was validated according to International Conference on Harmonization, or ICH, standards. Specificity, linearity, precision, accuracy, robustness, and system the suitability all within the validation parameters. Imeglimin HCL's linearity was between 1.0 - 15 µg/ml. Imeglimin HCL showed a mean recovery of 99.36%.

Conclusion: Imeglimin HCL in pharmaceutical formulations was successfully evaluated employing the authorized RP-HPLC method, showing the method's suitability for routine quality control. The pharmaceutical industry has a useful tool to ensure the efficacy and quality of formulations containing imeglimin HCL as a result of the suggested method.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

Background

Diabetes type 2 is a metabolic disease that affects millions of people and is considered a major public health concern due to its significant effects on life expectancy and medical costs. In many regions of the world, the prevalence of diabetes is rising as a result of accelerated economic growth and urbanization[1]. Diabetes significantly increases morbidity and early death by affecting a person's quality of life and functional abilities[2]. Concerns have recently been raised over the truth that those under 60 account for over a third of diabetes-related mortality[3]. These changes have been attributed to increased consumption of poor foods and sedentary lifestyles, which have been linked to raised body mass index, or BMI, and fasting plasma glucose[4]. People who have a higher body mass index (BMI) are more prone to type 2 diabetes[5].

Anti-diabetic drugs have been developed to deal with the pathophysiology of type 2 diabetes, but their consumption is restricted because of their negative side effects, including metformin's gastrointestinal side effects, hypoglycaemia caused by sulfonylureas, meglitinides, GLP-1 agonists, and insulin, weight gain caused by sulfonylureas, meglitinides, edema, pancreatitis risk, and urinary tract infections caused by SGLT2 inhibitors[6]. It is clear that none of the anti-diabetic medications now on the market addresses the three aspects of the pathophysiology of type 2 diabetes: elevated glucose synthesis, insulin resistance, and malfunction of the pancreatic b-cells.[6,7]

Imeglimin Hydrochloride, also referred to as Imeglimin, is the first drug in the group of tetrahydroimidazole drugs known as "glimins," and the drug has recently been approved for use as an oral anti-diabetic[8]. Imeglimin mostly acts on the anaerobic cells of mitochondria, and it improves bioenergetics, prevents pancreatic b-cell apoptosis, and protects b-cell action[9-12]. Also, imeglimin decreases excessive sugar production, enhances pancreatic b-cells' insulin-stimulated insulin secretion (GSIS), and increases muscles' intake of glucose.[6,13,14] Chemically Imeglimin Hydrochloride is-(R)-6-imino-N, N,4-trimethyl-1,4,5,6-tetrahydro-1,3,5-triazin-2-amine hydrochloride. Molecular formula is c6h14cln5 with molecular weight of 191.66 g/mol.

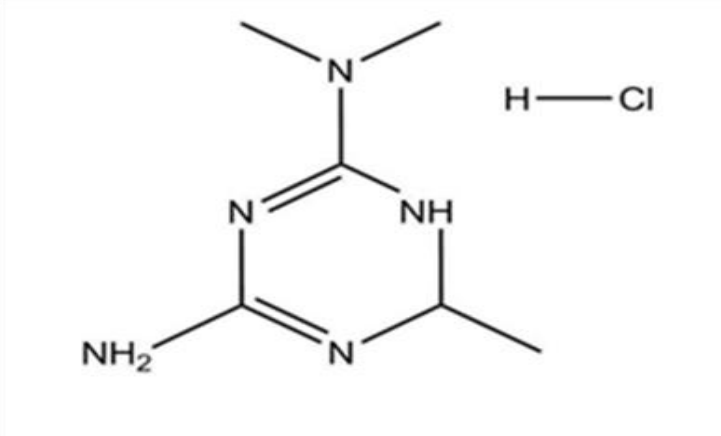


Figure no. 1 Structure of Imeglimin HydrochlorideImeglimin HCL in tablet formulation was determined through the invention and validation of an ultraviolet (UV) spectroscopic method.[15] The aim of the study is to develop an efficient, reliable, rapidly, sensitive, and accurate HPLC method for assessing imeglimin HCL. The criteria used to determine the drug content of the DS in various pharmaceutical commercial products are linearity, precision, precision, limit of quantification (the LOQ), specificity, and limit of detection (LOD).

1. Experimental procedure

1.1. Chemicals and reagents

For this study HPLC grade Acetonitrile and methanol were purchased from Merck, and water from Siddhi Lab India. Marketed preparation of Imeglimin Hydrochloride tablets was purchased from a local pharmacy shop. Gift

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

sample of Imeglimin Hydrochloride was procured from Alkem pharma Limited.

2.2 Instrumentation and chromatographic conditions

The HPLC Binary Gradient System model no 1260 Infinity II used for the method development and validation equipped with UV detector and pump. Analysis and separation have been done on an Phenomenox, C18 column (250 mm X 4.6 mm) 5 µm at 240 nm in 40^0 Celsius column oven temperature. The mobile phase consisted of Methanol: 0.05 % TFAA in Water (20: 80 % V/V), the flow rate was set at 1.0 ml/min in an isocratic mode and the injection volume was set at 20 µl for all samples.

2.3 Preparation of the buffer solution

0.5 ml of Trifluoroacetic acid diluted up to 1000 ml with water.

2. Method Development by RP-HPLC

2.1. Preparation of standard stock solutions for Chromatographic development

Weighed accurately 10 mg Imeglimin HCL and transferred into 20 ml volumetric flask, added 15 ml of water and sonicated to dissolve the standard completely and diluted up to the mark with water (500 PPM). Further diluted 0.8 ml to 20 ml with water (20 PPM).

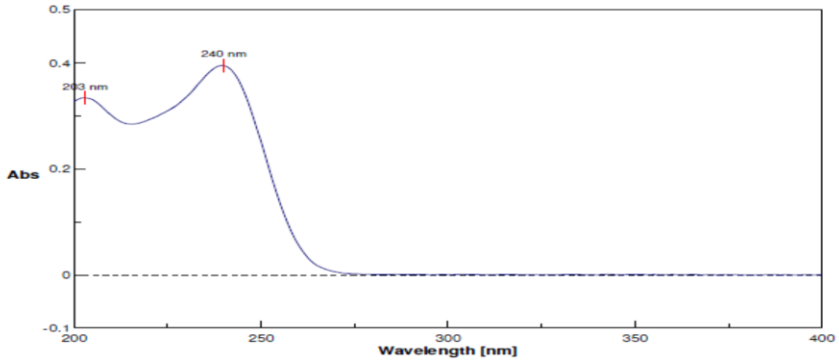
3.2 Sample preparation of Marketed test sample:

Weighed 20 tablets transferred in mortar pestle and crushed to fine powder. Mixed the contents with butter paper uniformly. Weighed the powder material equivalent to 50 mg of Imeglimin HCL and transferred to clean and dried 100 ml of volumetric flask. Added 70 ml of water, sonicated for 10 minutes with intermittent shaking. After 10 minutes allow to cool the solution to room temperature and made volume up to the mark with water. Filtered the solution through suitable 0.45 µ syringe filter discarding 3-5 ml of initial filtrate. Further diluted 0.5 ml of filtered stock solution to 25 ml with water. Injected the resultant solution and chromatograms were recorded and results are recorded.

3.3 Selection of analytical wavelength

Water as a blank and Imeglimin HCL standard solution (20 PPM) was scanned from 400 nm to 200 nm. Absorption maxima was determined for drug. Imeglimin HCL showed maximum absorbance at 240 nm

Figure no. 2 UV spectrum of Imeglimin HCL



3. Method validation

3.1. System suitability

Weighed about 10 mg of Imeglimin HCL **and** transferred in 20 ml volumetric flask, added 15 ml of water, sonicated to dissolve it, made volume up to the mark with water. Pipette out 0.5 ml from standard stock solution and transferred into 25 ml volumetric flask and made volume up to the mark with water. **(10 µ/ml working concentration),** chromatograms were recorded.

4.2 **Specificity:**

Specificity is the ability to access unequivocally the analyte in the presence of components which may be expected to be present. Following solution shall be prepared and injected to prove the specificity nature of

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

the method. (Checked peak purity for standard and test sample solution)

I. Blank (Water as Blank)
II. Placebo
III. Imeglimin HCL Standard solution
IV. Tablet test sample solution

3.2. Linearity and range

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample.

Levels of Linearity were performed from 10% to 150% of working concentration. Each level injected in triplicate and mean area calculated.

Linearity Imeglimin HCl stock solution:

Weighed 10 mg of Imeglimin HCl and dissolved in 10 mL with Water. Further diluted 2.5 ml of stock solution to 50 mL with Water. (50 µg/mL)

Table No.1 Linearity level preparation for HPLC

Sr. No.	Level (%)	mL of stock solution	Diluted to with Water (mL)	Imeglimin HCl Concentration (µg/mL)
1	10	0.20	10	1.00
2	50	1.00	10	5.00
3	100	2.00	10	10.00
4	125	2.50	10	12.50
5	150	3.00	10	15.00

Acceptance criteria: Correlation Coefficient: NLT 0.98

4.2 Accuracy (% recovery)

The accuracy of the analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value of the value found, Accuracy will be conducted in the range from 50 % to 150 % of working concentration. Solution of each accuracy level was prepared in triplicate. Calculated % Recovery for each sample, Mean % recovery for each level and overall recovery and also calculated % RSD for each level and % RSD for overall recovery.

Table No.2 Accuracy sample preparation:

Level (%)	API (mg)	Placebo	Diluted to (mL)	Volume taken (mL)	Diluted to (mL)	Conc (µg/mL)
50	25.2	22.5	100	0.5	25	5.04
	25.0	22.2	100	0.5	25	5.00
	25.3	22.7	100	0.5	25	5.06
100	50.1	22.3	100	0.5	25	10.02
	50.1	22.6	100	0.5	25	10.02

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

	50.3	22.4	100	0.5	25	10.06
150	75.3	22.3	100	0.5	25	15.06
	75.1	22.5	100	0.5	25	15.02
	75.0	22.3	100	0.5	25	15.00

Acceptance criteria: % Recovery for each sample and Mean recovery and overall recovery should be in the range of 98-102%. The Relative Standard Deviation should not be more than 2.0%.

4.3 Precision

Precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous test under the prescribed conditions. Precision is of two types, Repeatability and Intermediate precision.

I.Repeatability:

Preparation of sample solution (6 Samples prepared):

Weighed 20 tablets and calculated average weight and transferred in mortar pestle and crushed to fine powder. Mixed the contents with butter paper uniformly. Weighed the powder material equivalent to 50 mg of Imeglimin HCl and transferred to clean and dried 100 mL of volumetric flask. Added 70 mL of water, sonicate for 10 minutes with intermittent shaking. After 10 minutes allow to cool the solution to room temperature and made volume up to the mark with water. Filtered the solution through suitable 0.45 µ PVDF syringe filter discarding 3-5 mL of initial filtrate. Further dilute 0.5 ml of filtered stock solution to 25 ml with water. (10 mcg of Imeglimin HCl), injected the resultant solution and chromatograms were recorded.

Six samples prepared.

Acceptance criteria: % Assay: 90-110% for each sample and mean assay value.

% RSD for % assay of 6 samples of Intermediate precision**:** NMT 2

4.4 Limit of Detection (LOD) and Limit of Quantitation (LOQ):

Detection limit:

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

Quantitation limit:

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy.

As per ICH Q2R1 guidelines LOD and LOQ was determined by using the approach Based on the Calibration Curve in which residual standard deviation of a regression line was calculated and determined the LOD and LOQ by using following formula:

$LOD = 3.3\ \sigma / S$

$LOQ = 10\ \sigma / S$

Were,

Σ = residual standard deviation of a regression line

S = Slope of regression line

4.5 Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

Determination: Blank and Standard solution were injected under different chromatographic conditions as shown below.

A). Changes in flow rate by ±10%. (± 0.1ml/min)

B). Change in column oven temperature. (± 2^{o}c)

C) Change in wavelength (± 3 nm)

4. Results and discussion

5.1 System Suitability

System suitability is a Pharmacopoeia requirement and is used to verify, whether the chromatographic system is

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

adequate for analysis to be done. The tests were performed by collecting data from Five replicate injection of standard drug solution and the results are recorded.

Table No.3 Results for System Suitability Test of Imeglimin HCL

Sr No.	Standard solution	Area	Asymmetry	Theoretical plates
1	Standard_1	5250741	1.52	6739
2	Standard_2	5267845	1.52	6732
3	Standard_3	5240640	1.52	6759
4	Standard_4	5267894	1.51	6745
5	Standard_5	5237891	1.52	6741
Mean		**5253002**	**1.52**	**6743**
STD Dev		**14390.62020**		
% RSD		**0.27**		

System Suitability Acceptance Criteria:

1. Relative standard deviation of the area of analyte peaks in standard chromatograms should not be more than 2.0 %.

2. Theoretical plates of analyte peak in standard chromatograms should not be less than 2000.

3. Tailing Factor (Asymmetry) of analyte peaks in Standard Chromatograms should be less than 2.0

Discussion: It was observed from the data tabulated above; the method complies with system suitability parameters. Hence, it can be concluded that the chromatographic method is adequate for intended analysis.

5.2 Specificity

Specificity is the ability to access unequivocally the analyte in the presence of components which may be expected to be present. Blank, standard solution prepared and injected to check peak purity.

Table No.4 Results of Specificity.

Description	Observation
Blank	No interference at R.T. of Imeglimin HCL due to blank
Placebo	No interference at R.T. of Imeglimin HCL due to placebo
Standard solution	Peak purity was 0.983
Test Solution	Peak purity was 0.978

5.3 Linearity and Range

Linearity of an analytical method is its ability to elicit test results that are proportional to the concentration of analyte in samples within a given range.

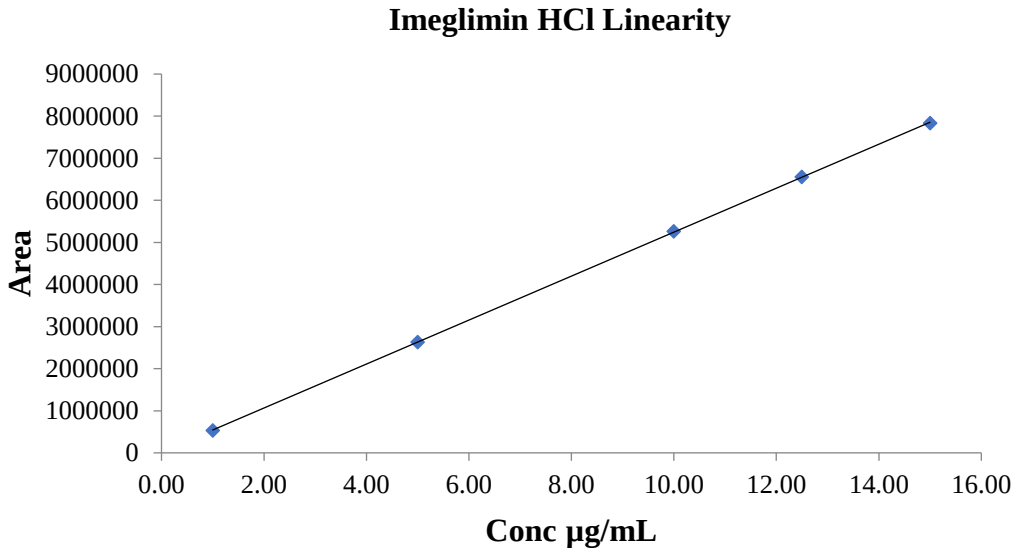
Table No.5 Results of HPLC Linearity Data for Imeglimin HCL:

Level	Conc (µg/ml)	Area	Mean	% RSD
10%	1.00	532478	533050	0.323

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

		534987		
		531684		
50%	5.00	2649647	2636089	0.446
		2629580		
		2629040		
100%	10.00	5261586	5261670	0.230
		5249630		
		5273794		
125%	12.50	6547861	6555180	0.307
		6577945		
		6539734		
150%	15.00	7836984	7838617	0.147
		7827966		
		7850901		

Figure no. 3 Calibration curve of Imeglimin HCL



Discussion:

From the calibration curve (Fig no. 3) it was concluded that the Imeglimin HCL shows linear response in the range of 1.0-15.0 µg /ml. The Regression value was found well within the limit.

5.4 Accuracy (Recovery):

The accuracy of an analytical method is the closeness of test results obtained by that method to the true value. The accuracy of an analytical method is determined by applying the method to analysed samples to which known amounts of analyte have been added.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

Table No.6 Result of Accuracy of Imeglimin HCL

Level	Area	Recovered conc (µg/ml)	Added conc (µg/ml)	% Recovery	Mean Recovery	% RSD
50	2616573	4.98	5.04	98.81	99.61	1.0568
	2647030	5.04	5.00	100.80		
	2636411	5.02	5.06	99.21		
100	5249046	9.99	10.02	99.70	99.24	0.4179
	5204810	9.91	10.02	98.90		
	5234961	9.97	10.06	99.11		
150	7806160	14.86	15.06	98.67	99.22	0.5698
	7826400	14.90	15.02	99.20		
	7864139	14.97	15.00	99.80		

Discussion:

Overall Recovery: 99.36 %

% RSD for Overall Recovery: 0.664.

Recovery of analytical procedure was found well within acceptance criteria at all 3 levels. % Recovery not get hampered by changed in analyte concentration.

5.3 Precision

Precision of an analytical method is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of a homogenous sample. Precision of an analytical method is usually expressed as standard deviation or relative standard deviation. Precision was performed on Test sample.

Table No.7 Result of Intra- day and Inter- Day Precision for Imeglimin HCL:

	Sample	Test Sample (mg)	Area	% Assay
Repeatability	Sample 1	72.6	5265840	99.89
	Sample 2	72.9	5163401	97.54
	Sample 3	72.5	5284970	100.39
	Sample 4	73.2	5243164	98.64
	Sample 5	72.4	5144360	97.85
	Sample 6	72.3	5234254	99.70
	Mean			**99.00**
	STD DEV			**1.166009**
	% RSD			**1.178**
Intermediate precision	Sample 1	72.3	5208103	99.20
	Sample 2	73.1	5190986	97.79

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

(Inter-Day)	Sample 3	72.8	5164090	97.69
	Sample 4	72.2	5237946	99.91
	Sample 5	72.6	5196713	98.57
	Sample 6	72.4	5234678	99.57
	Mean			**98.79**
	STD DEV			**0.926206**
	% RSD			**0.938**
Repeatability Plus Inter-day	**Mean**			**98.895**
	STD DEV			**1.01012**
	% RSD			**1.021**

Discussion:

% Assay: % Assay value for each sample (Individual sample) and mean assay value for precision (6 sample), mean assay value intermediate precision (6 sample), and mean assay value for precision plus intermediate precision sample (12 sample): 90-110%

% RSD: % RSD for precision study samples (6 sample), Intermediate precision study samples (6 sample) and precision plus intermediate precision sample (12 sample): NMT 2.0

5.4 Limit of Detection (LOD) and Limit of Quantitation (LOQ):

Σ = 13643.57666 (Residual standard deviation of a regression line)

S = 522322.4208 (Slope)

Detection limit (LOD):

LOD = 3.3 σ / S

LOD = 3.3 x 13643.57666 / 522322.4208

LOD = 0.086 µg/ml

Quantitation limit (LOQ):

LOQ = 10 σ / S

LOQ = 10 x 13643.57666 / 522322.4208

LOQ = 0.261 µg/ml

5.5 Robustness:

The robustness of an analytical method is a measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

Following changes made under Robustness:

- Change in Wavelength
- Change in flow rate
- Change in column oven temperature

Table No.8 Result of Robustness study:

Change in Parameter	**R.T.**	**Standard area**	**Asymmetry**	**Theoretical plates**
Wavelength by +3 NM (243 NM)	2.78	5106809	1.54	6613
Wavelength by -3 NM (237 NM)	2.80	4896492	1.55	6703
Flow rate by +10% (1.1ml/min)	2.52	4586262	1.56	6586
Flow rate by -10% (0.9ml/min)	3.11	5764850	1.58	6273
Column oven temp by +2ºc (42 ºc)	2.79	5252460	1.54	6813
Column oven temp by -2ºc (38 ºc)	2.79	5268010	1.51	6716

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

Assay

Weighed the powder material equivalent to 50 mg of Imeglimin HCL and transferred to clean and dried 100 ml of volumetric flask. Added 70 ml of water, sonicated for 10 minutes with intermittent shaking. After 10 minutes allow to cool the solution to room temperature and made volume up to the mark with water. Injected the resultant solution and chromatograms were recorded and results are recorded.

Table No.9 Assay results of Imeglyn 500 mg Tablet:

Sample	Area	% Assay	Mean Assay
Sample 1	5236014	99.46	98.93
Sample 2	5201796	98.40	

From the above results, it can be concluded that the assay result is within the limit (90-110%.) For selected marketed test sample and sample can be used for validation.

5. Conclusion

The present paper described the development of simple, sensitive and accurate analytical methods for the determination of Imeglimin Hydrochloride (HCL). The procedure presented here does not need any expensive apparatus; therefore, the proposed method can be used advantageously as a routine method for the determination of Imeglimin Hydrochloride (HCL) in quality control and industry, our method may be applied to the determination the content of the cited drugs in commercial tablets.

6. Abbreviations

RP-HPLC: Reverse Phase High-Performance Liquid Chromatography

HCL: Imeglimin hydrochloride

TFAA: Trifluoroacetic anhydride

ICH: International Conference on Harmonization

BMI: Body mass index

GLP-1: Glucagon- like peptide-1

SGLT2: Sodium- glucose co- transporter

GSIS: Glucose- stimulated insulin secretion

UV: Ultraviolet

LOD: Limit of detection

LOQ: Limit of quantitation

PPM: Parts per million

NLT: Not less than

RSD: Relative standard deviation

NMT: Not more than

R.T.: Retention time

µg/ml: Microgram per millilitre

7. Acknowledgements

Ethics approval and consent to participate: we ensure the originality and integrity of this article.

Consent for publication: We confirm that all individuals featured in this research article have provided explicit consent for using their data, images, or identities.

Availability of data and material: We pledge to make the data and materials underlying this article available upon request, in compliance with the journal's policies and ethical considerations.

Competing Interests: The authors declare no competing interests that could influence the interpretation or presentation of the review article's findings.

Funding: No

References

1. Onyango EM, Onyango BM. The Rise of Noncommunicable Diseases in Kenya: An Examination of the Time Trends and Contribution of the Changes in Diet and Physical Inactivity. Journal of Epidemiology and Global Health. 2018;8(1-2):1.
2. Ramtahal R, Khan C, Maharaj-Khan K, Nallamothu S, Hinds A, Dhanoo A, et al. Prevalence of self-reported sleep duration and sleep habits in type 2 diabetes patients in South Trinidad. J Epidemiol Glob Health. 2015;5: S35–S43.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 675-685 | ISSN:2251-6727

3. Alotaibi A, Perry L, Gholizadeh L, Al-Ganmi A. Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: an overview. J Epidemiol Glob Health. 2017; 7:211–18.
4. Lone S, Lone K, Khan S, Pampori RA. Assessment of metabolic syndrome in Kashmiri population with type 2 diabetes employing the standard criteria's given by WHO, NCEPATP III and IDF. J Epidemiol Glob Health. 2017; 7:235–9.
5. Mahanta TG, Joshi R, Mahanta BN, Xavier D. Prevalence of modifiable cardiovascular risk factors among tea garden and general population in Dibrugarh, Assam, India. J Epidemiol Glob Health. 2013; 3:147–56.
6. Vuylsteke V, Chastain LM, Maggu GA, Brown C. Imeglimin: a potential new multitarget drug for Type 2 diabetes. Drugs R D 2015;15(3):227–32.
7. Doupis J, Baris N, Avramidis K. Imeglimin: a new promising and effective weapon in the treatment of Type 2 Diabetes. Touchreviews Endocrinol 2021;17(2):88– 91.
8. Yanai H, Adachi H, Hakoshima M, Katsuyama H. Glucose-lowering effects of imeglimin and its possible beneficial effects on diabetic complications. Biology (Basel) [Internet]. 2023;12(5).
9. Yanai H, Adachi H, Hakoshima M, Katsuyama H. Glucose-lowering effects of Imeglimin and its possible beneficial effects on Diabetic Complications. Biology (Basel) 2023;12(5):726.
10. Detaille D, Vial G, Borel AL, Cottet-Rouselle C, Hallakou-Bozec S, Bolze S, Fouqueray P, Fontaine E. Imeglimin prevents human endothelial cell death by inhibiting mitochondrial permeability transition without inhibiting mitochondrial respiration. Cell Death Discov 2016; 2:15072.
11. Sanada J, Obata A, Fushimi Y, Kimura T, Shimoda M, Ikeda T, Nogami Y, Obata Y, Yamasaki Y, Nakanishi S, Mune T, Kaku K, Kaneto H. Imeglimin exerts favorable effects on pancreatic b-cells by improving morphology in mitochondria and increasing the number of insulin granules. Sci Rep 2022;12(1):13220.
12. Vial G, Lamarche F, Cottet-Rousselle C, Hallakou-Bozec S, Borel AL, Fontaine E. The mechanism by which imeglimin inhibits gluconeogenesis in rat liver cells. Endocrinol, Diabetes Metabol 2021;4(2): e00211.
13. Yingyue Q, Sugawara K, Takahashi H, Yokoi N, Ohbayashi K, Iwasaki Y, Seino S, Ogawa W. Stimulatory effect of imeglimin on incretin secretion. J Diabetes Investig 2023;14(6):746–55.
14. Hallakou-Bozec S, Kergoat M, Fouqueray P, Bolze S, Moller DE. Imeglimin amplifies glucose-stimulated insulin release from diabetic islets via a distinct mechanism of action. Plos ONE 2021;16(2): e0241651.
15. Tamil Selvan R, Senthilkumar SK, HARI PG, Elakkiya A, Gayatri M, Gokulraj M, Hajima H. A Novel Method Development and Validation of Imeglimin HCL By UV Visible Spectroscopy. International Journal of Pharmaceutical Sciences. 2023 Dec 28;1(12):1.