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Development of Novel Uv-Spectrophotometric Method for Imeglimin Hydrochloride

Yaminee J. Sathawane, Saurabh Thakare, Abhijit Awachat,M.J. Umekar, R.T.Lohiya

Department of Pharmaceutical Chemistry, Smt. Kishoritai Bhoyar College of Pharmacy, Kamptee.

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ABSTRACT

Introduction: Imeglimin hydrochloride is used to treat type-2 Diabetes mellitus. Imeglimin hydrochloride is a white crystalline powder and freely soluble in double distilled water. Diabetes mellitus is a metabolic condition marked by high blood sugar levels. **Objective**: Develop an economic, simple, rapid, accurate, and precise UV-visible method for Imeglimin hydrochloride in bulk. **Methodology:** Choice of common solvent were essential so, solvent including double distilled water and various concentrations of analyte ranges from 2.5 - 15.0µg/ml were selected for the methods i.e., Derivative Spectroscopic method and Area Under Curve method. Maximum absorbance of Imeglimin hydrochloride was found at 239nm. Area selected for the area under curve method in the range of 232-245nm for the analysis of Imeglimin hydrochloride. Linearity of methods was found under concentration range of 2.5-15µg/ml.**Conclusion:** The double distilled water was chosen as the solvent for the experiment since it has shown better results. The method of analysis is a derivative spectroscopic method to eliminate spectral interface by measuring absorbance's at 239 nm, 250 nm, 201nm for zero order, 1 st order and 2 nd order derivative respectively, having concentrations ranges from 2.5- 15µg/ml. For Imeglimin hydrochloride, percentage recoveries ranged from 99 to 101 %. The evaluation of the method was done by linearity, accuracy, precision, and ruggedness. The result of recovery studies and precision were found to be within limits. The procedure was easy, practical, and acceptable to identify the presence of Imeglimin hydrochloride.

Keywords – Derivative spectrophotometry, Imeglimin hydrochloride , Area Under Curve.

I. INTRODUCTION

Imeglimin, the first a new group of medications called glimin's, is being created to treat type 2 diabetes. Imeglimin hydrochloride, chemically known as (6R)-(+)-4- dimethylamino-2-imino-6-methyl-1, 2, 5, 6-tetrahydro-1, 3, 5-triazine hydrochloride, is a tetrahydrotriazine molecule(1) . Imeglimin was created with the intention of giving patients of type 2 diabetes mellitus a secure, well-tolerated medication that can successfully address the underlying metabolic abnormalities in these individuals

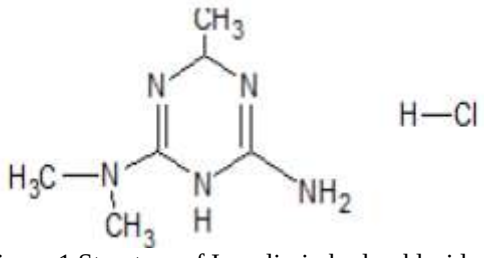

Figure 1 Structure of Imeglimin hydrochloride

There were no reports of severe hypoglycemia, statistically significant glucose decreases, or unfavorable safety and tolerability profiles in a number of critical phase III trials. Imeglimin hydrochloride is interacts with mitochondria to enhance flux via Complex II of the respiratory chain, enhancing ATP synthesis and decreasing reactive oxygen species production . It is an inhibitor of oxidative phosphorylation that also works to improve muscle glucose absorption and restore regular insulin secretion. Imeglimin hydrochloride is the first anti-diabetic drug of this category to receive approval. It is an oral anti-diabetic drug sold under the trade name Twymeeg. Insulin resistance, beta-cell dysfunction, and numerous additional abnormalities that lead to the development of hyperglycemia are pathogenic factors that cause type 2 diabetes.

According to a review of the literature, there was no any techniques for estimating imeglimin in biological matrices. The purpose of the current research was to develop a simple, quick, accurate, economical, precise and reliable UV

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method for measuring the dosage of Imeglimin hydrochloride utilising double distilled water as a solvent.

II. MATERIAL'SANDMETHOD [8], [9], [10]

Chemicals-

Analytical pure sample of Imeglimin hydrochloride (Purity-99.99%) was obtained as a gift sample procured from Ravenbhel Healthcare Private Limited Jammu (India).Used as standard reference material. The solvent used for the proposed method are of analytical grade and highly pure double distilled water.

Instrument-

The present work performed by using a JASCO UV/Visible double beam spectrophotometer(ModelV-630)with1cmmatchedquartzcellsforspectrumand absorbance measurements.

METHOD-

Selection of solvent-

The solubility of Imeglimin hydrochloride was studied under various organic solvent among these it was found that API freely soluble in double distilled water was selected as suitable solvent for proposed method.

Preparation of standard stock solutions[10][11]

According to Indian Pharmacopoeia, 100mg of Imeglimin hydrochloride was weighed separately and dissolved in 50 ml double distilled water, then volume was made upto 100ml with same solvent to get final concentration 1000ug/ml.

Preparation of working standard solution:

10 ml solution was pipette out from standard stock solution and diluted up to 100ml by double distilled water to get the final concentration of 100µg/ml. The solution is used as working standard solution from above solution pipette out 2.5ml, 5ml, 7.5 ml, 10ml, 12.5ml, 15ml diluted to 100ml by double distilled water, having concentration ranges 2.5µg/ml -15 µg/ml respectively.

Method A: Absorbance Maxima Method

Imeglimin hydrochloride is soluble in double distilled water so double distilled was selected throughout study. Working standard solution of different concentrations was scanned in between the range of 200-400 nm and shows maximum absorbance at 239 nm by UV spectrophotometer Jasco UV-1700. The specific absorbance value for Imeglimin hydrochloride was found to be 895.

Method B: Area Under Curve Method

When broad spectra obtained the AUC approach can be used, between the two chosen wavelength 1&2. The processing item for area computation determines the area enclosed by the curve and horizontal axis.By inputting the wavelength across which,the area has to be estimated. The wavelength range was selected on the basis of repeated observations so, as to get linearity between Area Under Curve Vs Concentration[12][13]. Results are shown in Table-2

Method C: Derivative Spectroscopic Method

Multi component analysis uses the analytical method of derivative UV spectrophotometry. It frequently has significant implications for getting quantitative and qualitative orders from spectra. When it comes to qualitative and quantitative analysis, it employs the first or higher derivatives of absorbance in accordance with wavelength for unresolved bands.

The most straightforward technique for derivatizing spectra to increase selectivity is derivative spectroscopy. This approach is utilised when a drug sample demonstrates significant, pointless absorption. It entails converting the natural spectrum to its higher derivatives, first, and second [13].

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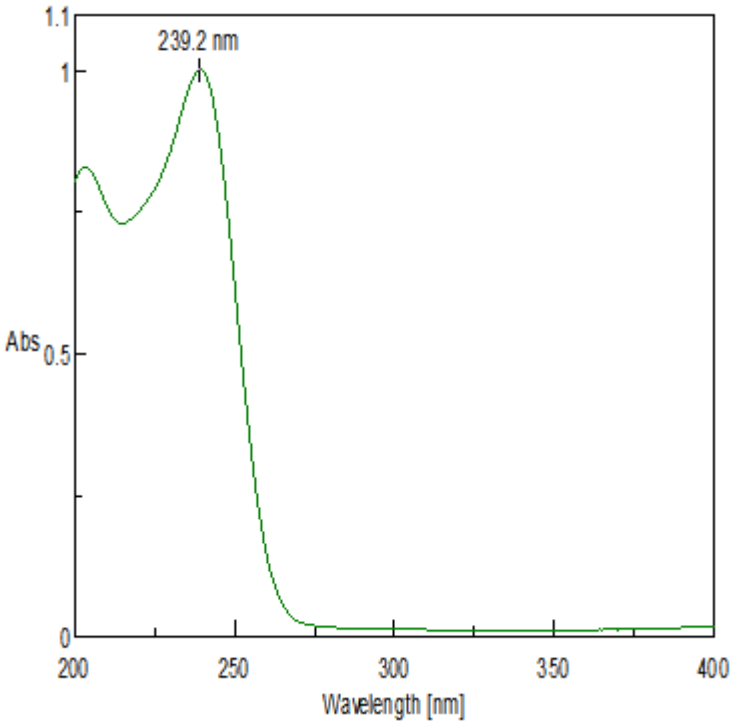

Figure 2UV Spectrum of standard Imeglimin Hydrochloride

Validation data of proposed method [14]-

The developed method was tested for Accuracy, Precision, Ruggedness, robustness and sensitivity.

Linearity [15]-

The linearity was examined by taking ranges of various concentrations of Imeglimin hydrochloride. The Beers- Lamberts was plotted for different concentrations 2.5µg/ml, 5µg/ml,7.5µg/ml, 10µg/ml, 12.5µg/ml, 15µg/ml. The calibration curve was plotted the relationship between the concentration vs. absorbance, found that it was linear results shown in Table-1.

Table 1: Linearity study of Imeglimin Hydrochloride

Sr. no.	Conncentration (µg/ml)	Absorbance
1.	2.5	0.2225
2.	5	0.4292
3.	7.5	0.6864
4.	10	0.9114
5.	12.5	1.1489
6.	15	1.3630
Mean		0.7935
SD		0.3947
Correlation coeffcient		0.999
Slope		0.231

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Table 2: Area under curve of Imeglimin Hydrochloride

Sr. No.	Concentration(µg/ml)	Absorbance
1	**2.5**	0.2083
2	**5**	0.4459
3	**7.5**	0.6356
4	**10**	0.8433
5	**12.5**	1.0034
6	**15**	1.2587
Mean		0.7325
Standard Deviation		0.3485
Correlation Coefficient		0.9996
Slope		0.208

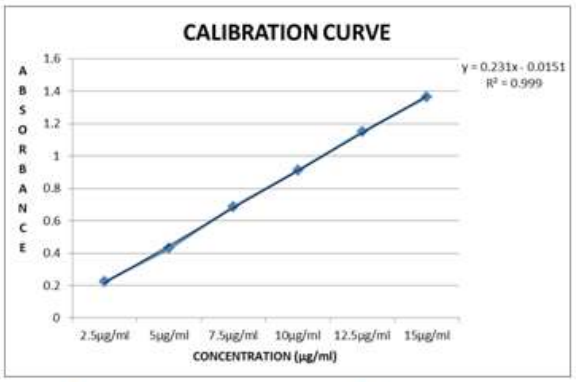

Figure3.Calibration curve of Imeglimin Hydrochloride

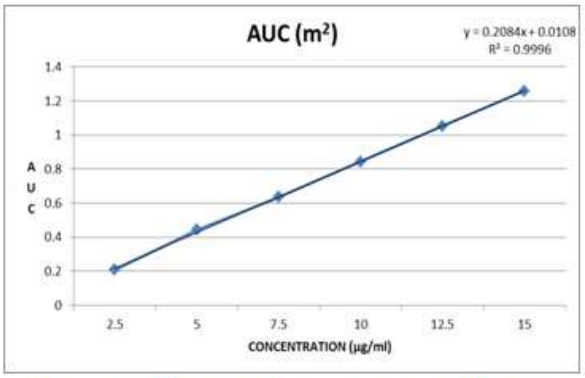

Figure4.Area under curve Vs concentration of Imeglimin Hydrochloride

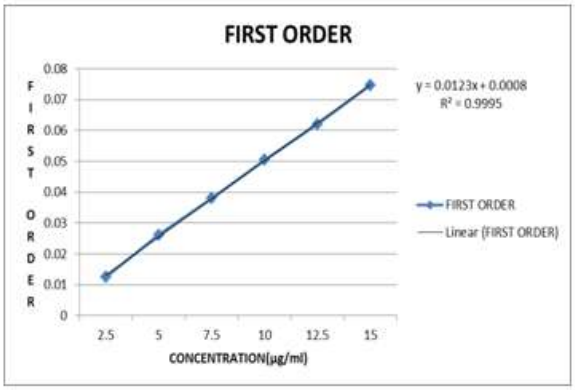

Figure 5 First Order of Imeglimin Hydrochloride

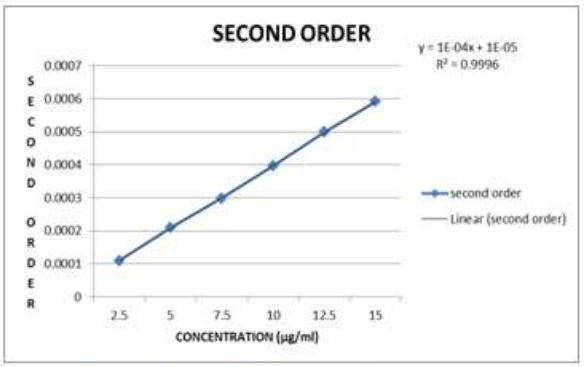

Figure 6 Second Order of Imeglimin Hydrochloride

Accuracy

The accuracy of an analytical method is closeness of test results to true value.The accuracystudy was performed by placebo method[16],bytaking3different concentrations of thesample solution prepared by procedures given in the methods from dilutions used linearity.Resultsarewithin the rangeit ensures that results wereaccurate [17][18].

Precision [19], [20], [21], [22]

The closeness of agreement between a set of measurements obtained from multiple sampling of the same homogenous sample under specified conditions is expressed as the analytical procedure's precision. Standard deviation or coefficient of variation are used to express the %RSD for Repeatability, Intraday and Interday precision were calculated and mentioned in Table 3 and Table 4

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Table- 2 Result of Recovery (Placebo spike method)

Range relative to theoretical concentration	%Recovery			
	1st value	2nd value	3rd value	Mean
80%	99.81	99.54	99.50	99.61
100%	99.80	99.70	99.42	99.64
120%	99.71	98.51	99.42	99.21
Mean assay		99.48		
Standard Deviation		0.39		
No. of Determinant		9		
Minimum		98.51		
Maximum		99.81		

Table -3 Intraday Precision results for Imeglimin Hydrochloride

Sr.no.	Concentration (µg/ml)	Absorbance-1 11.00Am	Absorbance-2 1.00 Pm	Absorbance -3 3.00 Pm
1	10	0.9114	0.9116	0.9113
2	10	0.9113	0.9114	0.9112
3	10	0.9117	0.9113	0.9111
4	10	0.9113	0.9115	0.9115
5	10	0.9115	0.9113	0.9112
6	10	0.9112	0.9112	0.9111
Average		0.9114	0.9114	0.9112
SD		0.000163	0.000134	0.000137
RSD		0.000179	0.000147	0.000151
%RSD		0.0179	0.0147	0.0151

Table-4 Interday Precision Results for Imeglimin Hydrochloride

Interday Precision for Imeglimin hydrochloride(n=6)				
Sr. no.	Concentration(µg/ml)	Day-1	Day-2	Day-3
1	10	0.9117	0.9118	0.9111
2	10	0.9112	0.9113	0.9117
3	10	0.9111	0.9115	0.9119
4	10	0.9115	0.9118	0.9116
5	10	0.9116	0.9114	0.9115
6	10	0.9114	0.9116	0.9114
Average		0.9114	0.9115	0.9115
SD		0.000171	0.000189	0.000249
RSD		0.000187	0.000206	0.000273
%RSD		0.01873	0.02068	0.02736

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Formulae-

Standard Deviation= $\sqrt{\sum (xi - \mu)^2}$ / $N - 1$

Where,

x=Valuein sampledistribution

μ=Samplemean

N=Numberofsamples

Relative Standard Deviation = SD/Mean

Where,

SD= Standard Deviation

Table -4 Statistical Validation for Ruggedness

Sr.no.	Parameter	Set-1	Set-2
1	System	Schimadzu(UV-1700)	Jasco(V-630)
1	Day	Tuesday	Wednesday
2	Date	19/10/2022	20/10/2022
3	Time	10.30am	1.00am
4	Laboratory	Analysis	Analysis
5	Analyst	Y.J.Sathawane	S.A.Thakare
6	Sample	10µg/ml	10µg/ml
7	Absorbance	0.9114	0.9118

Table -5 Readings for ruggedness at different wavelengths

Sr. no.	Setno.	Wavelength(nm)	Concentration(µg/ml)	Absorbance	Mean	SD	RSD	%RSD	Average %RSD
1	I	239	10	0.9112	0.9112	0.0001	0.0137	1.37	1.59
2		239	10	0.9117					
3		239	10	0.9114					
4	II	240	10	0.9114	0.9117	0.0001	0.0179	1.79	
5		240	10	0.9118					
6		240	10	0.9116					
7	III	241	10	0.9112	0.9114	0.0001	0.0163	1.63	
8		241	10	0.9116					
9		241	10	0.9114					

Ruggedness-

Ruggedness of the method was evaluated by applying same developed procedure to 10µg/mlsolution of Imeglimin hydrochloride by using the same instrument by different analysts ondifferent days under same conditions [1-19]. Results are mentioned in Table:4

III. RESULTS AND DISSCUSION-

Various solvents of different compositions were tried to provide sufficient selectivity towardsthe drugs. To optimize the UV parameters, several conditions were tried to achieve a goodabsorptionand peak shape for Imeglimin hydrochloride. Distilled water components resulted in better sensitivity.

The method described in this paper offer a simple, economic, quick and precise way to analyse Imeglimin hydrochloride using UV Spectrophotometry. For the study of Imeglimin hydrochloride, the 239 nm wavelength was chosen. Imeglimin hydrochloride absorbance ranged from 0.2225 to 1.3630. Selected methods as in concentration range of 2.5-15 µg /ml, linearity was seen. Using the corresponding absorptivity value, the drug concentration measure at 239nm.

The relationship between absorbance and concentration was found to be linear for area under

curve method and derivative spectroscopic method. The Imeglimin hydrochloride calibration curve displayed linearity in the concentration range of 2.5-15 µg/ml. The magnitude of the correlation coefficients supported the linearity of the calibration curve. Correlation coefficient for Imeglimin hydrochloride was found to be 0. 999.By carrying out experiments under same conditions on various days, by various analysts, using various instruments, and at various times, robustness was assessed

IV. CONCLUSION

The results of evaluation parameters shows that the UV spectrophotometric methods were found to be accurate, precise and sensitive. Because of cost-effectiveness and minimal maintenance, the present UV spectrophotometric methods can be preferred at small scale industries, successfully applied and suggested for the quantitative analysis of Imeglimin hydrochloride for QC, where economy and time are essential and to assure therapeutic efficacy.

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