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Research Article

A Novel Method Development and Validation of Imeglimin HCl By UV-Visible Spectroscopy

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ABSTRACT

The development and validation of a UV spectroscopy method for determining Imeglimin Hydrochloride in tablet formulation. The method utilized distilled water as a solvent and a detection wavelength of 237 nm. It was validated following ICH guidelines and demonstrated good linearity within a concentration range of 2-10 µg/mL (r2=0.9991). The method exhibited precision with low RSD values (<2%) and sensitivity with LOD and LOQ values of 16.74 µg/mL and 50.73 µg/mL, respectively. The method also showed good recovery values, indicating the absence of interferences. It was successfully applied for the determination of Imeglimin Hydrochloride in tablets. In conclusion, the UV spectrophotometric methods developed and validated in this study were found to be accurate, precise, and sensitive. Their cost-effectiveness and minimal maintenance make them suitable for use in small-scale industries where economy and time are crucial for quality control and therapeutic efficacy assurance.

INTRODUCTION

Type 2 diabetes is the most common type of diabetes and is characterized by high levels of glucose (sugar) in the blood. Although some symptoms may be similar, it is a different condition to type 1 diabetes. Unlike people with type 1 diabetes, most people with type 2 diabetes still produce insulin. However, it is either not enough to deal with all the glucose that is in their blood or their cells are unable to recognize the insulin and use it properly (this is called insulin resistance).Type 2 diabetes usually affects people who are middle-aged or older, and obesity is by far

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the biggest risk factor. In the past two decades, the condition has become more prevalent in younger people, including children, mainly because of the rising rates of obesity in children. Imeglimin Hydrochloride drug was approved by Central Drugs Standard Control Organization (CDSCO) on January 6, 2023. Imeglimin Hydrochloride (IGH) is Anti-Diabetes drug with remarkable effectiveness and good safety for the treatment of Type 2 diabetes.[1]

ULTRAVIOLET – VISIBLE ABSORPTION SPECTROSCOPY

The technique of Ultraviolet- visible (UV/VIS) spectrophotometry is one of the most frequently employed in pharmaceutical analysis. It involves the measurement of absorption of electromagnetic radiation absorbed by a substance in solution. The wavelength range of UV radiation starts at the blue end of visible light (about 400 nm) and ends at approximately 200 nm for spectrometers operated in air. The radiation has sufficient energy to excite valence electrons in many atoms and molecules; consequently, UV radiation is involved with electronic excitation. Absorption of light in both the UV & visible region of the electromagnetic spectrum occurs when the energy of the light matches that required to induce in the molecule an electronic transition and its associated vibrational and rotational transitions. When beam of light is passed through a transparent cell containing a solution of an absorbing substance, reduction of intensity of light may occur. In that a part of light may get reflected, refracted, absorbed, scattered and some may get transmitted.[2]

INSTRUMENTATION

Source of light:

The best source of light is the one which is more stable, more intense and which gives range of spectrum from 180nm- 360nm (upto 400).

The different source available are

- Hydrogen discharge lamp
- Deuterium lamp
- Xenon discharge lamp
- Mercury lamp

Monochromators:

Monochromators are better and more efficient than filters in convert a polychromatic light or heterochromatic light into monochromatic light.

- Entrance slit (to get narrow source)
- Collimator (to render light parallel)
- Grating or prism (to disperse radiation)
- Collimator (to perform the images of entrance slit)
- Exit slit (to fall on sample cells)

Two types of Monochromators

1. Prism
2. Grating

Sample cell:

The design of sample cells is similar to that used in colorimetry except that it is made up of Quartz, Quartz cells only must be used in UV spectroscopy since glass cells will absorb uv radiation. The path length of the cells is 10mm or 1cm.

Solvents:

Solvent plays an important role in spectra, since compound peak could be obscured by solvent peak. The solvent for a sample is selected in such a way that the solvent neither absorbs the region of measurement nor affects the absorption of the sample.

Detectors:

Although any one of the detectors used in colorimetry can be used photomultiplier tube are mainly used, since the cost of such uv spectrophotometers are high and more accurate measurements are to be made.

Recorders:

Recorders as in colorimetry are used. [3&4]

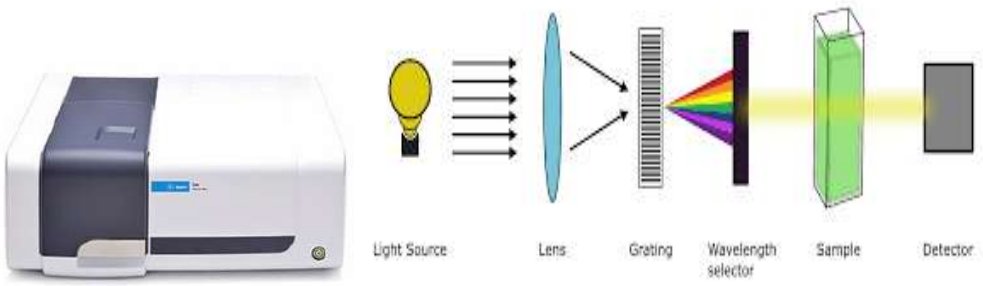


Figure 1: UV Instrumentation

Validation

According to ICH and FDA guidelines, Validation defined as an act of proving that any procedures, process, equipment, materials, activity or system performs as expected under a given set of conditions. Basically, validation is proving that the performance is as intended when extended to an analytical procedure, depending upon the application, it means that a method works reproducibly, when carried out by some different persons, in same or different laboratories using different reagents, different equipments etc. According to U. S. FDA defines the term "Validation is a process of establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce meeting, its predetermined specifications and quality attributes". According to USP, "Validation of an analytical method is the process by which it is established by laboratory studies that the performance characteristic of the method meets the requirements for the intended in analytical applications.

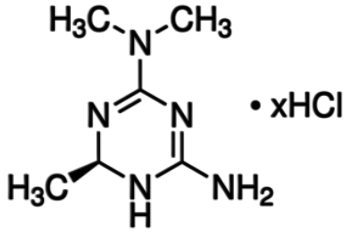
Validation Parameters (ICH)

Typical validation characteristics which should be considered are

1. Accuracy
2. Precision
   - Repeatability
   - Intermediate precision
3. Specificity
4. Linearity
5. Detection limit
6. Quantitation limit
7. Range
8. Robustness
9. Ruggedness [5]

DRUG PROFILE:

Structure



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

Mechanism of action:

Imeglimin's mechanism of action involves two distinct effects: (a) an increase in glucose stimulated insulin secretion (GSIS) and preservation of -cell mass; and (b) an improvement in insulin action, with the potential to reduce hepatic glucose output and enhance insulin signaling in both the liver and skeletal muscle.

Pharmacological action: It is an oxidative phosphorylation blocker that acts to inhibit hepatic gluconeogenesis, increase muscle glucose uptake, and restore normal insulin secretion. It is the first approved drug of this class of antidiabetic medication.[9]

MATERIALS AND METHODS

Materials

Chemicals

Analytical pure sample of Imeglimin hydrochloride (Purity-99.99%) was obtained as a gift sample procured from Exceed pharmaceutics, Gujarat, India. Used as standard reference material. The solvent used for the proposed method are of analytical grade and distilled water.

Marketed formulation

Brand name	Labeled amount	Source
Imeglyn	500mg	Zydus Healthcare Limited, India.

Apparatus and glassware's

100ml volumetric flasks,10ml volumetric flasks, beakers, glass rod etc.

Instrument

UV spectrophotometer	LABOHOLIC-5131 Uv-Visible Spectrophotometer
Sonicator	Ultra Sonicator
Analytical balance	Digital Analytical Balance

Methods

Selection of solvent

SOLVENTS	IMEGLIMIN HYDROCHLORIDE
Water	Freely soluble
Methanol	Soluble
Acetonitrile	Soluble
0.1M NaOH	Sparingly soluble
Acetone	Soluble
Chloroform	Slightly soluble

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

Preparation of standard stock solutions

According to Indian Pharmacopoeia,100mg of Imeglimin hydrochloride was weighed separately and dissolved in 50 ml distilled water, then volume was made up to 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 distilled water to get the final concentration of 100µg/ml. The solution is used as working standard solution from above solution pipette out 2ml, 4ml, 6 ml, 8ml, 10ml diluted to 100ml by distilled water, having concentration ranges 2µg/ml -10 µg/ml respectively

RESULTS AND DISCUSSION

Development And Validated Uv Spectroscopic Method for The Determination of Imeglimin Hydrochloride

Selection of solvent

Solubility of drug was checked in different solvents like, acetonitrile, methanol, water etc. and UV- spectra of drug in these solvents were recorded. Solubility of the drug and response was higher with minimum interference in distilled water and hence selected as diluent for further studies.

Selection of wavelength

The λmax of Imeglimin Hydrochloride (237 nm) was selected as the detection wavelength, Figure 2.

Wavelength	Absorbance
237	0.488

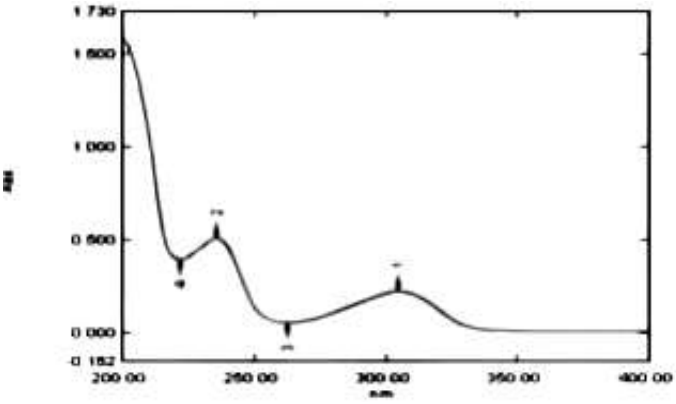


FIGURE 2: UV Spectrum of Imeglimin Hydrochloride (10 µg/mL).

Validation Parameters

LOD & LOQ:

LOD and LOQ values were found to be 16.74 µg/mL and 50.73 µg/mL for Imeglimin Hydrochloride.

Linearity

The calibration curve was linear over a concentration range of 2-10 µg/mL for Imeglimin Hydrochloride, Figure 3. The calibration data is given in the Table 1.

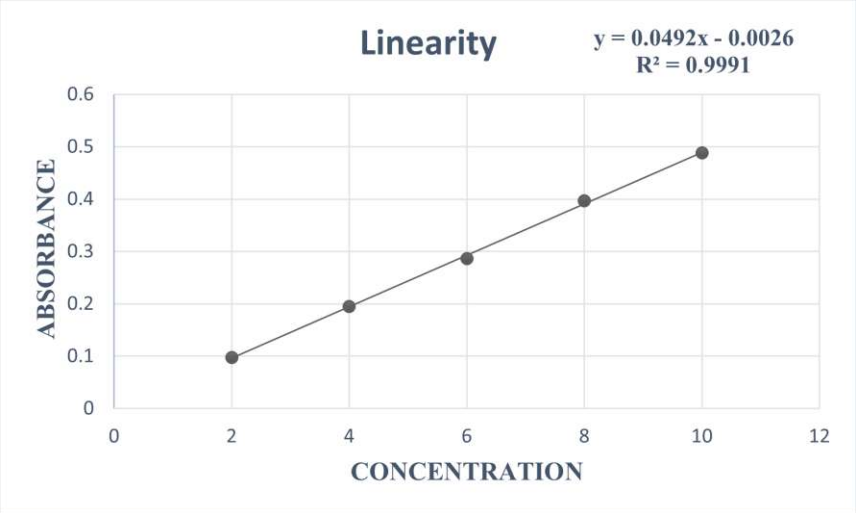


FIGURE 3: Calibration curve of Imeglimin Hydrochloride (2-10 µg/mL).

Table 1: Calibration data of Imeglimin Hydrochloride

Concentration (µg/mL)	Absorbance	Intercept	SE of Intercept	Concentration (µg/mL)	Absorbance	Intercept
2	0.097	-0026	0.111634	0.24962	16.74283	50.73586
4	0.195					
6	0.286					
8	0.397					
10	0.488					

Accuracy:

In order to demonstrate the accuracy of the proposed methods, recovery studies were conducted for pre-analyzed sample formulation by standard addition method at 80,100, and 120% levels. The results of recovery studies are given in the Table 2

Table 2: Recovery data of Imeglimin Hydrochloride

Level	Recovery (%)	RSD (%)*
80%	99.61	0.24
100%	99.64	
120%	99.21	

*Average of three determinations

Precision:

The % RSD values were within the limits for repeatability, intraday precision and interday precision, which indicates that the developed method is precise, Table 3 - 5.

Table 3: Interday precision data of Imeglimin Hydrochloride

Concentration (µg/mL)	Absorbance	RSD (%)
6	0.286	0.35

	0.285	
	0.287	
8	0.397	0.38
	0.400	
	0.399	
10	0.488	0.12
	0.489	
	0.488	

Table 4: Intraday precision data of Imeglimin Hydrochloride

Concentration (µg/mL)	Absorbance	RSD (%)
6	0.286	1.43
	0.281	
	0.278	
8	0.397	1.89
	0.390	
	0.405	
10	0.488	0.8
	0.494	
	0.486	

Table 5: Repeatability data of Imeglimin Hydrochloride

Concentration (µg/mL)	Absorbance	RSD (%)
10	0.488	0.12
	0.489	
	0.488	
	0.487	
	0.486	
	0.488	

Table 6: Ruggedness data of Imeglimin Hydrochloride (10 µg/mL)

Analysts	Absorbance	RSD (%)
Analysts – 1	0.488	1.31
	0.501	
	0.494	
Analysts – 1	0.495	1.19
	0.486	
	0.497	
Analysts – 1	0.487	1.47
	0.499	
	0.486	

Table 7: Robustness data of Imeglimin Hydrochloride (10 µg/mL).

Wavelength	Absorbance	RSD (%)
236	0.486	1.23
	0.480	
	0.492	

237	0.488	0.93
	0.485	
	0.494	
238	0.477	0.43
	0.476	
	0.480	

Assay of marketed formulation

The developed method was successfully applied to formulation. The UV spectrum of the formulation is shown in Figure 4. The results of the formulation studies are given Table 8.

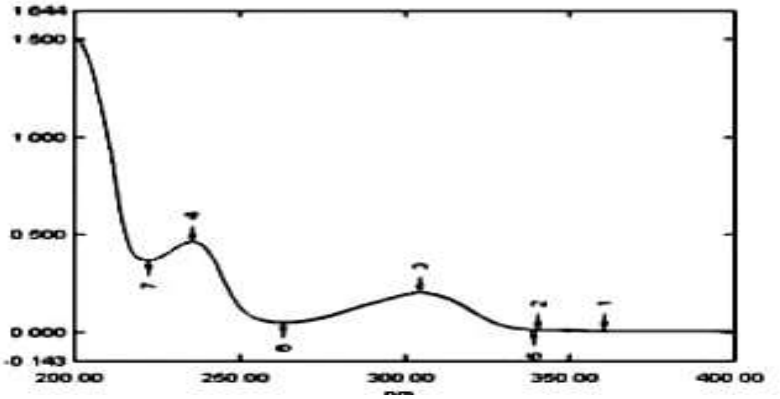


FIGURE 4: UV Spectrum of formulation

Table 8: Results of formulation.

Drug	Amount of drug (mg/tablet)		%Label claim*	RSD (%)
	Labeled	Estimated		
Imeglimin Hydrochloride	500	496.5	99.3	0.40

*Average of three determinations

SUMMARY AND CONCLUSION

SUMMARY

A validated UV spectroscopy method was developed for the determination of Imeglimin Hydrochloride. Distilled water was selected as a solvent and detection wavelength was selected as 237 nm. The method was validated as per ICH guidelines. Linearity was found over a concentration range of 2-10 µg/mL (r2=0.9991). Low RSD (<2%) values shows that the developed method is precise. LOD and LOQ values were found to be 16.74 µg/mL and 50.73 µg/mL. Good recovery values show that the method is free from interferences. This method was successfully applied for the determination of Imeglimin Hydrochloride in tablets.

CONCLUSION

An attempt has been made to develop validated analytical methods for the determination of newer Anti-Diabetes drug, Imeglimin Hydrochloride from tablet formulation. The developed methods were validated according to ICH guidelines. 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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