Volume 4 (2), 2016, Page-1130-1135
CODEN (USA)-IJPRUR, e-ISSN: 2348-6465

PHS Scientific House
PHARMAHEALTHSCIENCES

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Original Article

Development of UV-Spectrophotometric Method for the Determination of Imatinib Mesylate (ITM) In Bulk and Formulation

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ARTICLE INFO

Received: 13 Apr 2016
Accepted: 28 Apr 2016

ABSTRACT

A simple, rapid, precise and highly selective spectrophotometric method was developed for estimation of imatinib in tablet dosage form.this method, involves the measurement of absorbances of imatinib at the wavelength of 255.20nm. distilled water was used as solvent. linearity was observed in the concentration range of 2-12µg/ml for imatinib. the accuracy of the method was confirmed by recovery studies of tablet dosage forms and was found to be 101.2% for imatinib.the method showed good reproducibility and recovery with%rsd lessthan 6. the lod of imatinib was found to be 0.066µg/ml and loq of imatinib was found to be 0.2µg /ml.thus the proposed method was found to berapid,specific, precise, accurate and cost effective quality control tool for the routine analysis of imatinib in bulk and tablet dosage form.

Keywords: Spectrophotometric, Distilled water, Imitanib.

1. INTRODUCTION

Imatinib is a cancer medication prescribed to treat leukemia and gastrointestinal tumors. It operates by inhibiting proteins associated with cancer cell growth in order to relieve symptoms, prevent the spread of cancer cells, and aid other treatments. Imatinib is one of the newest anticancer drugs in the market and was one of the first drugs to be pushed through Food and Drug Administration's (FDA) fast track designation for approval. The drug is designed to inhibit tyrosine kinases such as Bcr-Abl and is used in the treatment of

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chronic myeloid leukemia (CML) and gastrointestinal stroma tumors. [1, 2]

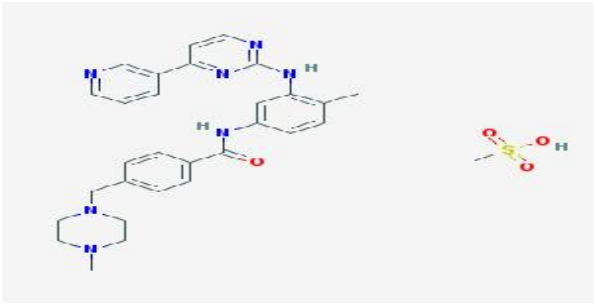

Fig 1: Structure of Imatinib Mesylate

The Chemical name of ImatinibMesylate is 4-4[(4-methyl-1- piperazinyl) methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl] amino] phenyl] – benzamide mono methane sulfonate. It has a molecular formula of C29H31N7O.CH4O3S and a molecular weight of 589.71. It has the structural formula (Fig.1). ImatinibMesylate is a white crystalline powder which in freely soluble is distilled water, 0.1 N Hcl, methanol and sparingly soluble in dimethyl ether [1]. Literature Survey revealed that the drug has been estimated by Liquid chromatography2-9 and Spectrophotometry10 methods in biological fluids like human plasma and rat plasma and HPLC method in pharmaceutical formulations has been reported so far. But no UV-Spectroscopic method was reported for the estimation in bulk and pharmaceutical dosage forms. [3-5]

The aim of present work was to develop and validate a simple, precise, sensitive, specific spectroscopy method for Imatinib Mesylate in its bulk and tablet dosage form. [6]

2. MATERIALS AND METHODS

Instrument

A UV – Visible double beam spectrophotometer (JASCO), model no. V-530 with 10 mm matched quartz cells was used for experiment. All weights were taken on Analytical balance.

Reagents and Standards

ImatinibMesylate reference standard was obtained from KP labs,Hyderabad. The tablets of brand Mitinab(Gleevec) of 400mg were obtained from local pharmacy. The double distilled water was used as solvent for the experiment. [7-10]

Experimental

Preparation of standard stock solutions of ITM Accurately weigh 10 mg of ImatinibMesylate transferred to 10 ml volumetric flasks. It was dissolved in Distilled Water and was shaken manually for 10 min. The volume was made up to the mark with same solvent to obtain final strength 1000 µg/ml.From the stock solutions, 1.0 ml of Imatinib was transferred to 10 ml volumetric flask and the volume was adjusted to the mark with same solvent to obtain strength 100µg/ml. [11, 12]

Determination of λ max From the1st dilution, 1.0 ml of ImatinibMesylate was transferred to 10 ml volumetric flask and the volume was adjusted to the mark with same solvent to obtain Strength 10µg/ml. The solution was scanned in the UV range 200-400 nm. (Figure 2)

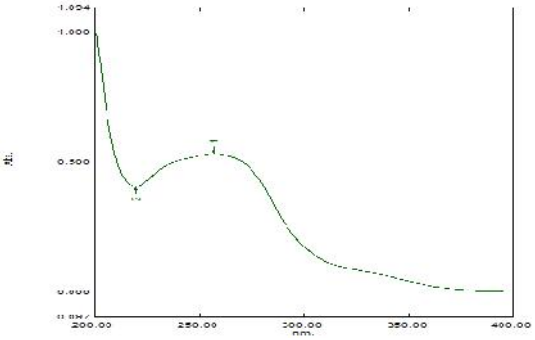

Fig 2: UV Spectrum of ImatinibMesylate in Distilled Water.

LOD and LOQ of Imatinib Mesylate and Imatinib:

The LOD and LOQ of Imatinib Mesylate and Imatinib were determined by using standard deviation of response and slope approach as defined by ICH guidelines and the values are given in the table no-3

$$QL = 10 \times \frac{SD}{S} \qquad DL = 3.3 \times \frac{SD}{S}$$

SD = Standard deviation

S = Slope of the linearity curve

Linearity Studies of Imatinib

Appropriate known volumes of aliquots from 1st dilution were transferred to separate 10 ml volumetric flasks. The volume was adjusted to the mark with Distilled water to a series of concentration in the range of 2-12µg/ml. The solution was scanned in the UV range 200-400 nm.Absorbances of these solutions were recorded at 255.20 nm and Calibration curve was plotted, absorbance vs. concentration and the data is given in the table no-1. [13, 14]

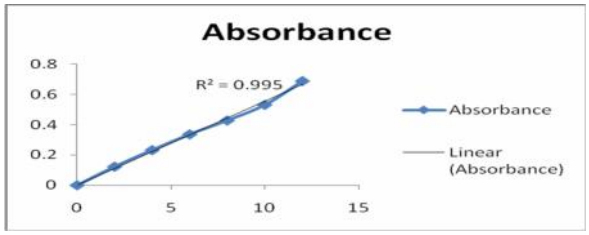

Fig 3: Calibration curve of Imatinib at 255.20nm

Linearity Studies of Imatinib Mesylate

For analysis of commercial formulation, twenty tablets were weighed, average weight determined and crushed into fine powder. An accurately weighed quantity of powder equivalent to 10 mg of ITM was transferred into 10ml volumetric flask containing 10 ml distilled Water, shaken manually for 10 min. and filtered through Whatmannfilter paper no. 45. From the stock solutions, 1.0 ml of Imatinib was transferred to 10 ml volumetric flask and the volume was adjusted to the mark with same solvent to obtain strength 100µg/ml.An appropriate aliquots of 2-12µg/ml werepreprared and absorbance was recorded at 255.20 nm and the data is given in the table no-2. [15, 16]

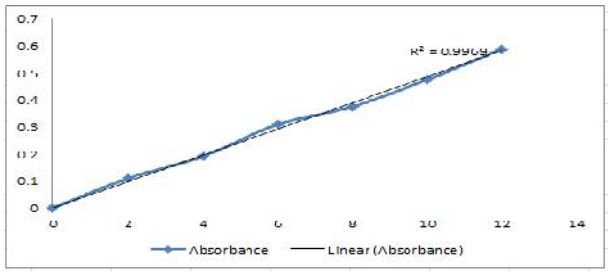

Fig 4: Calibration curve of Imatinib Mesylate at 255.20nm

Validation

The method was validated as per the ICH Q2 (R1) guidelines for linearity, accuracy, precision, LOD and LOQ. [17]

***Validation of Imatinib*:**

Accuracy

The accuracy of an 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 found.

To determine the accuracy, measure the absorbance of all the concentrations at 255.20nm and calculate the concentration found and % concentration using the formula: **y=mx+c**

%Recovery:

To determine the accuracy, recovery studies were carried out three different levels i.e. 80%, 100% and 120%. To the pre- analyzed sample solution a known amount standard drug solution was added at three different levels, absorbance was recorded. The % recovery was then calculated by using formula :

% Recovery = Total amount of drug found – Amount of drug found on pre-analyzed basis/ Amount of pure drug added. [18-20]

Specificity:

Specificity is the ability to assess unequivocally the analyte in the presence of components that may be expected to be present. A major objective of determining specificity is to ensure “peak purity” of the main compound to be determined

Specificity is determined by analyzing 2**µg/ml** concentration repeatedly and measuring the absorbance at 255.20nm wavelength. [21]

Precision:

Precision of the method was studied as intra-day and inter-day precision.

Intraday Precision:

Intra-day precision was determined by analyzing the 4, 6, 10µg/ml for three times in the same day.

*Interday Precision***:**

Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days**.** [22]

***Validation of Imatinib Mesylate*:**

Accuracy:

To determine the accuracy, recovery studies were carried out at 100%. To the pre- analyzed sample solution a known amount standard drug solution was added to the sample and absorbance was recorded.

The % recovery was then calculated by using formula:

% Recovery = Total amount of drug found – Amount of drug found on pre-analyzed basis/ Amount of pure drug added. [23]

Precision of Imatinib mesylate:

Precision studies were performed by preparing the standards three times and measuring the absorbance of drugs at 255.20 nm. Low RSD values indicate that the method is precise.

Specificity:

Specificity was determined by analyzing the absorbance of the concentration of 2µg/ml repeatedly at 255.20nm an

Assay of Imatinib Mesylate:

Twenty tablets containing 400 mg of Imatinibmesylate was accurately weighed to find out the average weight. Tablet powder equivalent to 100 mg of Imatinibmesylate was transferred into 100 mlvolumetric flask, distilled water was added and made up to volume. Then the solution was sonicated for 15 minutes. After sonication, the solution was filtered through whatmann filter paper no.41. From the solution, further dilution was made to bring a final concentration of 10µg/ml with distilled water and used for the analysis. The absorbance was measured at 255.20 nm against the reagent blank and the data obtained were as reported.

***Drug Stability Studies*:**

Photo degradation:

Photo degradation should be carried out at more strenuous conditions than recommended ICH Q1A accelerated testing conditions. The Samples of Imatinibmesylateare exposed to dry heat. Studies may be conducted at higher temperatures for a shorter period and the data obtained were as reported. [20, 24]

ACID and BASIC Degradation:

Transfer 1ml (1000µg/ml. ITM) of above stock solution to10mL.volumetric flask and add 1ml.of 1N HCl/1N NaOH and finally make up the volume with distilled water and kept aside for 24hrs at room temperature. From this transfer 0.6mL.drug solution into 10ml. volumetric flask and neutralize with 1ml.of 1N NaOH/1N HCl the final volume made up to with distilled water to get the concentration of 60µg/ml. The absorbance was measured using above developed methods against blank contain 0.5ml.of 1NHCl and 0.5ml.of 1NNaOH in 10ml.volumetric flask the final volume made up to the mark with distilled water.

3. RESULTS AND DISCUSSION

The direct UV method development for the analysis of Imatinib can be applied for the routine analysis of formulation.

The UV spectroscopic method was found to be rapid,specific,precise,accurateand cost effective quality control tool for the routine analysis of Imatinib in bulk and tablet dosage form. The proposed method was validated as per the ICH guidelines

Imatinib Mesylate is an UV-absorbing molecule with specific chromophores in the structure that absorb at a particular wavelength and this fact was successfully employed for their quantitative determinations using the UV spectroscopic method. The spectral analysis showed the λ max of Imatinib mesylate to be 255.20

nm. The calibration curve was obtained for a series of concentration in the range of 2-12µg/ml. It was found to be linear and hence suitable for the estimation of the drug.

Table 1: Linearity study of Imatinib

S.no	Concentration	Λmax(nm)	Absorbance	Standard deviation	Relative stnadard deviation
1	2µg/ml	255.2	0.122	0.003	2.40%
2	4µg/ml	255.2	0.232	0.0007	0.30%
3	6µg/ml	255.2	0.336	0.001	0.20%
4	8µg/ml	255.2	0.428	0.0007	0.16%
5	10µg/ml	255.2	0.532	0.001	0.18%
6	12µg/ml	255.2	0.69	0.0007	0.10%

Table 2: Accuracy of Imatinib

S.no	% taken	Conc	Λmax(nm)	Absorbance	Sd	Rsd	Conc found(µg/ml)	%conc
1	80%	6.4µg/ml	255.2	0.325	0.001	0.30%	6.5µg/ml	101.50%
2	100%	8.0µg/ml	255.2	0.434	0.001	0.20%	8.6µg/ml	108.50%
3	120%	9.6µg/ml	255.2	0.492	0.001	0.20%	9.8µg/ml	102.50%

Table :3 Precision of Imatinib

S.no	Conc	Λmax(nm)	Intraday Absorbance	Sd	Rsd	Interday Absorbance	Sd	Rsd
1	4µg/ml	255.2	0.246	0.003	1.21%	0.246	0.008	3.25%
2	6µg/ml	255.2	0.33	0.005	1.60%	0.321	0.01	3.10%
3	10µg/ml	255.2	0.526	0.005	0.95%	0.516	0.01	1.93%

Table 4: Assay of Imatinib Mesylate

Sample	Label claim	% Label±SD claim	% RSD
1	400mg	400.02 ± 0.003	0.8

4. CONCLUSION

The precision was measured in terms of repeatability, which was determined by sufficient number of aliquots of a homogeneous sample. The % RSD was found and lie within the range of ± 2.0. This showed that the precision of the method was satisfactory. The results showed that the recovery of Imatinib mesylate by the proposed method was satisfactory.

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Conflict of Interest: None

Source of Funding: Nil