

Original Article

SPECTROPHOTOMETRIC DETERMINATION OF DASATINIB IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Objective: A new, simple, sensitive, precise and reproducible bioanalytical method was developed for the determination of Dasatinib in pharmaceutical formulations with Chloranilic acid.

Methods: The method is based on formation of violet colored complex. The UV spectrum of Dasatinib in methanol showed λ max at 521 nm. Beer's law is valid in the concentration range of 10-60 μ g/ml. This method was validated for linearity, accuracy, precision, ruggedness and robustness.

Results: The method has demonstrated excellent linearity over the range of 10-60 μ g/ml with regression equation $y = 0.021x - 0.083$ and regression correlation coefficient $r^2 = 0.997$. Moreover, the method was found to be highly sensitive with LOD (2.96 μ g/ml) and LOQ (8.98 μ g/ml).

Conclusion: Based on results the proposed method can be successfully applied for the assay of Dasatinib in various pharmaceutical dosageforms.

Keywords: Dasatinib, Bioanalytical method, Spectrophotometry, Chloranilic acid, Method development, Validation

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INTRODUCTION

Cancer is an abnormal, continuous multiplying of cells. The cells divide uncontrollably and may grow into adjacent tissue or spread to distant parts of the body [1].

Dasatinib is an anticancer agent which is given orally to treat the chronic myeloid leukemia and acute lymphoblastic leukemia. Specifically it is used to treat cases that are Philadelphia chromosome-positive (Ph+). It is classified as a kinase inhibitor. The main action of kinase inhibitors is to prevent the growth of tumors by the action of reducing the activity of proteins that controls growth, cell division and survival. Dasatinib was approved for medical use in the United States in 2006. It is on World Health Organization List of Essentials Medicines, the most effective and safe medicines needed in a health system [2-5].

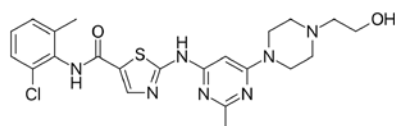


Fig. 1

Structure of dasatinib

The chemical name of Dasatinib is N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl] amino]-5-iazolecarboxamide monohydrate. It has molecular formula of $C_{22}H_{26}ClN_7O_2S$ and molecular weight of 488.01 gm/ml. Dasatinib is white powder and has melting point 280 °-286 °C. The drug substance is soluble in acetonitrile and slightly soluble in methanol [6-8].

The aim of this work is to introduce a simple, precise and rapid procedure for the simultaneous quantitation of the cited drug in pure and pharmaceutical formulation.

MATERIALS AND METHODS

Dasatinib was taken as a gift sample from Microlab, Bengaluru, India. Chloranilic acid, Methanol and Dichloromethane were used were of analytical grade.

Instruments

A UV visible double beam spectrometer [systronics 2201] and Shimadzu 1800-UV spectrophotometer with 1 cm quartz cuvettes was used for all absorbance measurement.

All weights were taken on analytical balance. Sonicator was used for dissolving Dasatinib in methanol.

Experimental

Preparation of chloranilic acid

0.3% (w/v) of Chloranilic acid was dissolved in some amount of methanol (20% of the total volume) and make up the volume using methylene chloride.

Preparation of standard stock solution

Accurately weighed 10 mg of Dasatinib transferred to 100 ml volumetric flask. It was dissolved in methanol and sonicated for 10 min. The volume was made up to mark with methanol to obtain final strength.

Procedure for plotting calibration curve

To a series of 10 ml volumetric flask, 1-6 ml of standard stock solution was pipetted out separately and into each flask 1 ml of 0.3% Chloranilic acid was added. The volume was adjusted using methanol. The produced violet color was measured at wavelength 521 nm against blank solution which was prepared without adding drug in similar manner.

Analysis of dasatinib in pharmaceutical dosage form

20 Tablet containing Dasatinib were weighed. An accurately weighed portion of the powder equivalent to 10 mg of Dasatinib was dissolve in a 100 ml of methanol and mixed for about for 10 min and sonicated for about 15 min then filtered. From formed solution with concentration of 100 μ g/ml seven aliquots were pipetted out into a 100 ml of volumetric flask having concentration 10-60 μ g/ml to each flask and 1 ml of 0.3% Chloranilic acid was added. The volume was made up to mark with methanol. These solutions were analyzed at selected wavelength 521 nm and results were statistically validated.

RESULTS AND DISCUSSION

The absorption spectra shows result of wavelength at 521 nm.

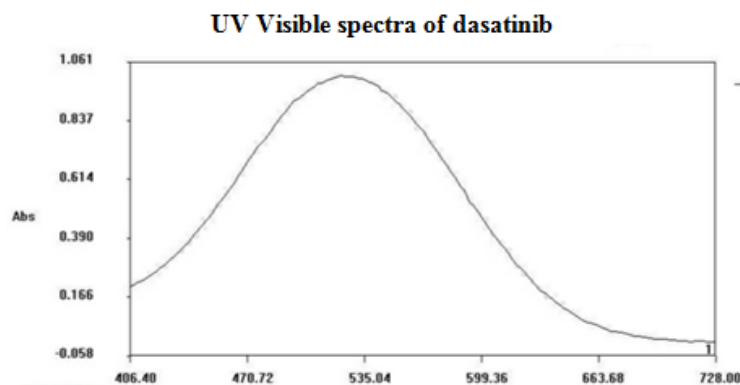


Fig. 2: The proposed method was validated according to ICH Guidelines [9, 10]

Linearity

The linearity was confirmed by taking aliquots of concentration of 10-60 µg/ml and absorbance was measured. It was performed in

single day only. The obtained absorbance shows good regression coefficient at wavelength 521 nm. The slope and intercept values were recorded. The linearity was plotted against absorbance of Dasatinib vs concentration of Dasatinib.

Table 1: Results for linearity

S. No.	Concentration (µg/ml)	Absorbance
1	10	0.107
2	20	0.37
3	30	0.59
4	40	0.8
5	50	1.01
6	60	1.21

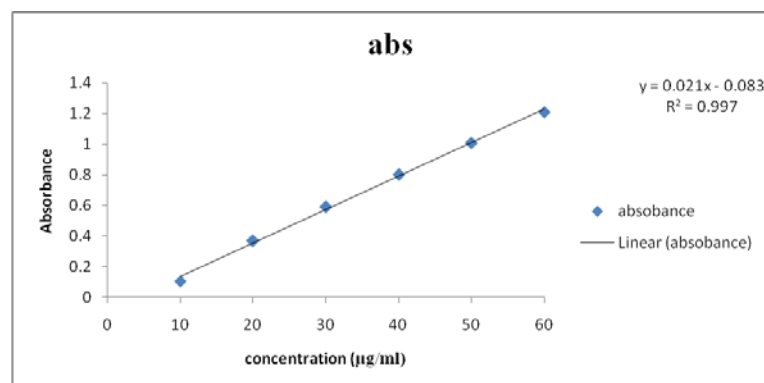


Fig. 3: Calibration curve for dasatinib

Accuracy

The accuracy is parameter of an analytical method which describes the closeness to the test results obtained by that method to the theoretical value. The standard addition method is used to analyze accuracy which is performed by using previously analyzed standard solutions. The percentage relative standard deviation and percentage recovery were analyzed by using standard solutions.

Range

The range is the analytical parameter of interval between lower and upper concentration limit of an analyte i.e. 10-60 µg/ml.

Precision

The precision is performed as inter-day and intra-day. Intra-day precision was performed in one day and inter-day precision was performed in three days. Dasatinib was evaluated at concentration 30 µg/ml. The percentage RSD for intra-day precision was found to be 0.69% and inter-day precision was found to be 0.86%.

Limit of detection (LOD)

The limit of detection (LOD) or lower limit of detection is the lowest quantity of a substance that can be able to distinguish from the absence of that substance with a stated experimental level.

$$\text{LOD} = 3 \text{ Sa/b}$$

Limit of quantitation (LOQ)

The limit of quantitation (LOQ) is the lowest concentration at which the performance of a method or measurement system is acceptable for a specified use.

$$\text{LOQ} = 10 \text{ Sa/b}$$

Ruggedness

The ruggedness is the study of degree of reproducibility of test results obtained by variety of external conditions like different analysts, laboratories, days and reagents. This study shown that there is no any influence of these conditions on test results.

Table 2: Regression analysis of the calibration curve for proposed method

Parameters	Method values
λ max	521 nm
Beer's law	10-60 μ g/ml
Correlation coefficient (r)	0.997
Regression equation (Y = mx+c)	0.021x-0.083
Slope (m)	0.021
Intercept (c)	0.083
LOD(μ g/ml)	2.96
LOQ(μ g/ml)	8.98

Table 3: Result for precision (Intra-day)

S. No.	Concentration (μ g/ml)	Absorbance 1	Absorbance 2	Absorbance 3	%RSD
1	30	0.590	0.589	0.592	
2	30	0.592	0.595	0.583	
3	30	0.591	0.594	0.599	
4	30	0.595	0.592	0.595	
5	30	0.600	0.597	0.594	
6	30	0.597	0.591	0.598	
%RSD		0.64%	0.48%	0.96%	0.69%

Table 4: Result for precision (Inter day)

S. No.	Concentration (μ g/ml)	Day 1	Day 2	Day 3	%RSD
1	30	0.590	0.592	0.598	
2	30	0.592	0.599	0.602	
3	30	0.591	0.609	0.591	
4	30	0.595	0.594	0.593	
5	30	0.600	0.593	0.605	
6	30	0.597	0.597	0.597	
%RSD		0.65%	1.05%	0.88%	0.86%

Table 5: Result for Robustness

Temperature	30 °C	25 °C
Concentration	8 μ g/ml	8 μ g/ml
Absorbance	0.590	0.601
	0.591	0.599
	0.592	0.603
	0.595	0.597
	0.600	0.595
	0.597	0.598
Average	0.594167	0.598833
SD	0.003859	0.002858

Table 6: Result of ruggedness

Concentration	Analyst 1	Analyst 2
8 μ g/ml	0.590	0.598
	0.591	0.594
	0.592	0.599
	0.595	0.591
	0.600	0.601
	0.597	0.592
Average		0.595833
SD		0.00407

Robustness

The robustness is the small but deliberate variations in method parameters such as temperature and stability of analytical solution.

Linearity

Six different concentrations of Dasatinib were prepared and analyzed. Then wavelength was found to be 521 nm. The regression coefficient was found to be 0.997. The absorbance was found in limit i.e. 0-2. Hence the analyzed parameter was found to be validated (table 1).

Precision

Intra-day precision

Intra-day precision was found within limit i.e.30 μ g/ml at 521 nm. The relative standard deviation is less than 2%. Hence the parameter was found to be validated (table 3).

Inter-day precision

Inter-day precision was performed in three days and the obtained results of concentration 30 μ g/ml at 521 nm shown that the relative

standard deviation is less than 2%. Hence the parameter was found to be validated (table 4).

Robustness

The change in concentration i.e. 8 µg/ml and change in temperatures i.e. at 25 °C and 30 °C. And obtained results shown that there is negligible effect on results. The robustness was found to be in limit i.e. the relative standard deviation is less than 2%. Hence the performed parameter was found to be validated (table 5).

Ruggedness

The change in analyst at concentration of 8µg/ml showed that the obtained result does not affected by it (table 6).

Limit of detection

The limit of detection was found to be 2.96 µg/ml (table 2).

Limit of quantification

The limit of quantification was found to be 8.98 µg/ml (table 2).

CONCLUSION

Bioanalytical method was developed and validated thoroughly for quantitative determination of Dasatinib Tablets. The presented method was found to be rugged, simple, accurate, precise, and reproducible and gives an acceptable recovery of the analyte, which can be directly easily applied to the analysis of pharmaceutical Tablets formulation of Dasatinib.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declare none

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