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Original Article

UV VISIBLE SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF DASATINIB IN BULK AND SOLID DOSAGE FORM

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ABSTRACT

Objective: A new, simple, sensitive, precise, reproducible UV visible spectrophotometric method was developed for the determination of Dasatinib in Tablet dosage form with methanol.

Methods: The method is based on the formation of a colorless complex. The UV spectrum of Dasatinib in methanol showed maximum wavelength at 248 nm. Beer's law is valid in the concentration range of 7-35µg/ml. this method was validated for linearity, accuracy, precision, assay, ruggedness and robustness.

Results: The method has demonstrated excellent linearity over the range of 7-35µg/ml with the regression equation y = 0.0332x+0.0633 and regression coefficient i.e. r^2= 0.9994moreover, the method was found to be highly sensitive with LOD(1.08µg/ml) and LOQ(3.29µg/ml).

Conclusion: Based on the results the proposed method can be successfully applied for the assay of Dasatinib in various tablet dosage forms.

Keywords: Dasatinib, UV visible spectrophotometer, Methanol, Method development and validation

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INTRODUCTION

Dasatinib is an anti-cancer drug. Its IUPAC name is N-(2-chloro-6-methyl phenyl)-2-({6-[4-(2-hydroxyethyl) piperazin-1-yl]-2-methylpyrimidin-4-yl} amino)-1, 3-thiazole-5-carboxamide [1].

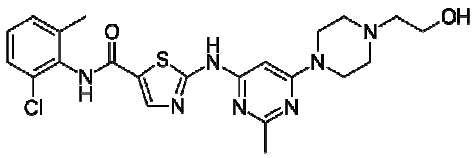

Fig. 1: Structure of dasatinib

Dasatinib's chemical formula is C22H26ClN7O2S and has a molecular weight of 488.005 gm/mol [2]. Dasatinib is poorly soluble in water and freely soluble in acetonitrile, methanol, DMF, DMSO, and in various aqueous buffers. Dasatinib is 96% protein-bound and excreted via hepatic metabolism. Plasma half-life if Dasatinib is estimated to be 3-5 h [3].

Dasatinib is a white to a pale white powder having a melting point of 280°–286 °C. Dasatinib is a tyrosine kinase inhibitor and is a drug of choice for treating chronic myeloid leukemia and acute lymphoblastic leukemia. Dasatinib is the first approved drug to treat patients with CML who are intolerant or resistant to imatinib [4].

Dasatinib inhibits BCR-ABL, EphA2, platelet-derived growth factor receptor, and c-Kit. Additionally, it binds to the other tyrosine and serine/threonine kinases such as the mitogen-activated protein kinases and the receptor tyrosine kinase, discoid in domain receptors. It inhibits the proliferation and kinase activity of BCR-ABL mutant cell lines that are non-reactive to imatinib [5-7].

Kinase inhibitors prevent the growth of tumors by limiting the action of proteins that control cell division, growth and survival. These proteins are usually present in larger quantities in an active form in the cancer cells. By reducing the activity of these proteins, the growth and survival of cancer cells can be inhibited [8].

Dasatinib is available in the market with varying strengths as like 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, and 140 mg [9].

Adverse effects of Dasatinib usually consist of cytopenia, fluid retention, dyspnoea, gastrointestinal disorders, pleural effusions, skin rashes, headache, and fatigue [10].

MATERIALS AND METHODS

UV-visible Spectrophotometry (Systronic 2201), 1 cm quartz cuvette were used for the measurement of absorbance, Weighing Balance (Shimadzu AY220), Sonicator (Oscar Ultrasonicator micro clean-103).

Apparatus used were volumetric flask, pipette, rubber bulb etc.

Chemicals chosen were Dasatinib, methanol and they were taken on an analytical grade basis.

Method development

Preparation of standard stock solution

Standard Dasatinib solution was prepared by dissolving 10 mg of drug in methanol and volume was made up the mark by using methanol (1000µg/ml). It was vortexed for 2 min and sonicated it for 10 min. From the above solution, 1 ml solution was spiked out and diluted up to mark using methanol (100µg/ml). Solution was sonicated for 5 min.

Determination of absorption maxima

Standard stock solution (100µg/ml) was scanned in the range of 200-800 nm for the analysis of the absorption maxima of Dasatinib. The obtained result gives the maximum wavelength.

Procedure for determination of calibration curve

From stock Solution (7, 14, 21, 28, 35) µg/ml solutions were prepared by diluting aliquots of (0.7, 1.4, 2.1, 2.8, 3.5) ml in methanol and volume was made up to the mark using methanol.

Assay of dasatinib

Accurately weighed 10 mg of Dasatinib was dissolved in a sufficient quantity of methanol and the volume was made up to 10 ml by using methanol (1000µg/ml). Vortexed it for 2 min for mixing the solution and sonicated for 10 min.

1 ml solution was spiked out from the drug stock and diluted up to 10 ml using methanol (100µg/ml). Further again 1 ml solution was pipetted out from the above solution was diluted up to 10 ml using methanol (10µg/ml). The obtained result showed the parameters were validated.

RESULTS AND DISCUSSION

The spectral absorption analysis shows the maximum wavelength at 248 nm.

Method validation

By using ICH guidelines, the following Parameters were validated.

Linearity and range

The concentration range of 7-35 µg/ml at 248 nm, the analytical parameter linearity was found to be linear and proportional in the relationship. The regression coefficient was found to be 0.9994. The analytical parameter range is the difference between upper and lower concentration limits. The range was found to be 7-35 µg/ml.

Assay

The absorbance of three dilutions of 10µg/ml of dasatinib tablet was determined and % purity was calculated. The results are as shown in the table.

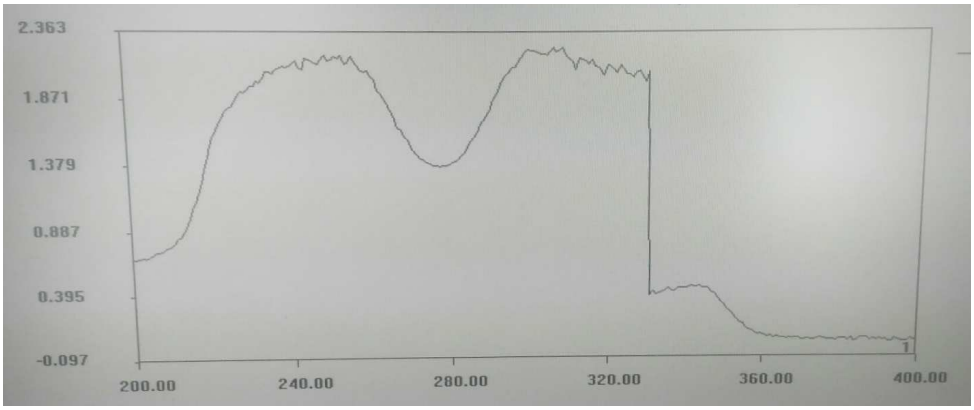

Fig. 2: UV-visible spectra of dasatinib

Table 1: Results of linearity

S. No.	Concentration (µg/ml)	Absorbance
1	7	0.292
2	14	0.529
3	21	0.762
4	28	1.008
5	35	1.216

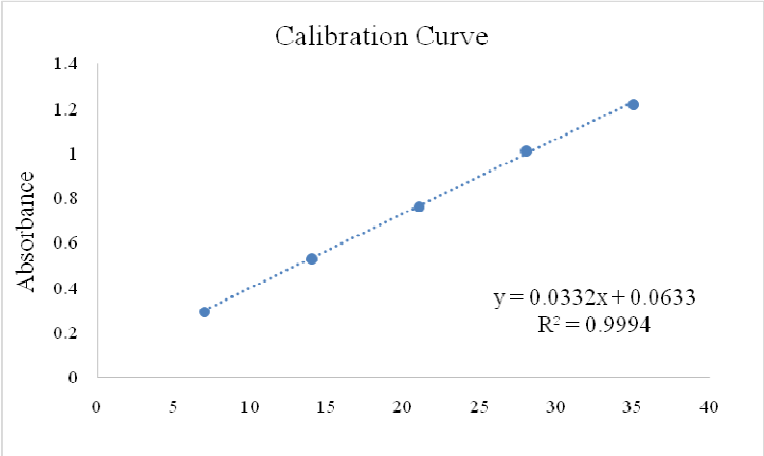

Fig. 3: Calibration curve for dasatinib

Table 2: Assay results of dasatinib

Formulation	Labeled amount	Amount obtained	% recovery
Sprycel 50 mg Tablet	50	49.8	99.6%

Accuracy

The parameter accuracy is the extent to which the experimental results deviates from the expected results and it is a measure of the trueness of the analytical method. Accuracy may be reported as in table 3.

Precision

Intraday and interday precision were performed by using concentration 21µg/ml. The %RSD was found within limit i.e. NMT 2%. Hence the parameter was valid.

Table 3: Accuracy results of dasatinib

Name of drug	Recovery level in %	Concentration	Amount recovered	% recovery with SD
	50	7µg/ml	7.05	100.05±0.25
Dasatinib	100	14µg/ml	14.03	99.03±0.7
	150	21 µg/ml	21.04	100.06±0.04

Table 4: Result for precision (Intra-day)

S. No.	Concentration	Absorbance
1		0.762
2	21(µg/ml)	0.761
3		0.761
4		0.762
5		0.763
6		0.762
	SD	0.000753
	%RSD	0.098811%

Table 5: Result for precision (Inter day)

S. No.	Concentration	Absorbance (Day1)	Absorbance (Day2)
1		0.762	0.761
2	21(µg/ml)	0.761	0.763
3		0.761	0.763
4		0.762	0.761
5		0.763	0.762
		0.762	0.761
	SD	0.000753	0.000983
	% RSD	0.098811%	0.129056%

Robustness

The deliberate change in wavelength i.e. 248 nm and 251 nm and concentration of 10µg/ml in the same environmental condition, gave the reliable results.

Robustness

The change in analyst and laboratories with the same concentration of 10µg/ml gave reproducible results. Hence the parameter was found to be validated.

Table 6: Result for robustness

Wavelength	248 nm	251 nm
Concentration	10 µg/ml	10µg/ml
Absorbance	0.408	0.411
	0.407	0.412
	0.407	0.411
	0.409	0.412
	0.408	0.412
	0.408	0.411
Average	0.407833	0.4115
SD	0.000753	0.000548

Table 7: Result of ruggedness

Concentration	Absorbance (Analyst1)	Absorbance (Analyst2)
	0.408	0.409
10 µg/ml	0.407	0.408
	0.407	0.408
	0.409	0.407
	0.408	0.408
	0.408	0.409
Average	0.407833	0.408167
SD	0.000753	0.000753

Table 8: LOD and LOQ

LOD	1.08µg/ml
LOQ	3.29µg/ml

Limit of detection (LOD) and limit of quantitation (LOQ)

The sensitivity of the developed method was determined in terms of LOD and LOQ and it was calculated using the standard deviation method.

CONCLUSION

An analytical UV Spectrophotometric method was developed and validated thoroughly for the quantitative estimation of Dasatinib in API and tablet dosage form. The above method was found to be easy, producible, simple, accurate, precise, reproducible, rugged.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declare none

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