INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

Development And Validation Of Bosutinib By Using UV – Spectrophotometric Method In Bulk Form

Vardhineedi Shirisha*,R. Parasuraman, M. Poojitha, R. Gayathri, P. Mounika, M. Bheemaji

Department of Pharmaceutical Analysis, Pullareddy Institute of pharmacy, Hydarabad, 502313, India

ARTICLE INFO

Received: 15 May 2024
Accepted: 19 May 2024
Published: 27 May 2024

Keywords:
Bosutinib, UV-Spectroscopy, Methanol, Stability, Validation.

DOI:
10.5281/zenodo.11352665

ABSTRACT

A novel sensitive, accurate and safe UV -Spectrophotometric method was developed for the estimation of anti -cancer drug (bosutinib).The various analytical parameters were validated for the bulk drug according to ICH Q2 guidelines. The proposed method includes two method, Method-A development and validation where methanol were used for all validation studies .As drug is more likely soluble in water it was scanned in the UV where it has shown maximum absorbance at 268nmThe linearity response was observed in the concentration range of 2-12ug/ml,where r2 =0.0996was the regression value the RSD value for method precision was found to be well within acceptance criteria &LOD,LOQ was established for bosutinib further more stability studies for bosutinib were carried out under acidic ,basic andoxidation as per stability assay methods The results of accuracy and recovery studies were carried out by adding specific drug amount(50%,100%,150%)and shown the recovery in range of (96.6%-98.6%).The proposed method was successfully applied for method development,validation and stability studies of bosutinib.

INTRODUCTION

Bosutinib is an antineoplastic agent used for the treatment of chronic, accelerated, or blast phase Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML).

It is chemically 4-[(2,4-dichloro-5-methoxyphenyl) amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl) propoxyl-3-quinoline carbonitrile

Bosutinib is a 7-alkoxy-3-quinolinecarbonitrile that functions as a potent, dual SRC and ABL tyrosine kinase inhibitor indicated for chronic myelogenous leukemia (CML), specifically Philadelphia chromosome-positive (Ph+) CML. Philadelphia chromosome is a hallmark of CML due to the reciprocal translocation t(9; 22) (q34;q11) , resulting in a BCR-ABL fusion protein.The first BCR-ABL inhibitor, imatinib,

***Corresponding Author:** Vardhineedi Shirisha
Address: *Department of Pharmaceutical Analysis, Pullareddy Institute of pharmacy, Hydarabad, 502313, India*
Email : shirishaparasuram7@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

was introduced over a decade ago as a breakthrough in CML management;however, emerging resistance to imatinib poses challenges in achieving remission.4 Second- generation BCR-ABL inhibitors like bosutinib inhibit most resistance-conferring BCR-ABL mutations except V299L and T315, thus providing more therapeutic options for patients.

DRUG PROFILE3

Bosutinib was first approved by the FDA in 2012 for the treatment of adult chronic, accelerated, or blast-phase Ph+ CML with resistance or intolerance to prior therapy. On September 26, 2023, bosutinib was also approved by the FDA for the treatment of pediatric CML that is newly diagnosed or resistant/intolerant to prior therapy.

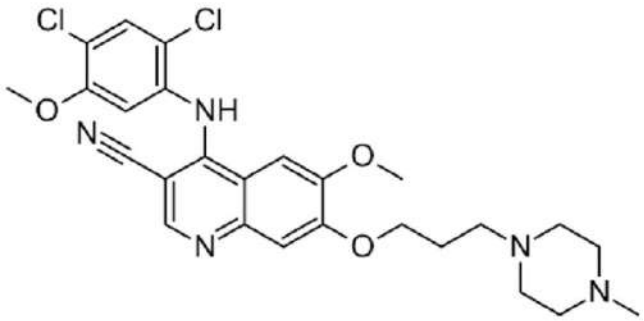

Fig 1: Chemical Structure Of Bosutinibmesylate

IUPAC NAME:

4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl) propoxy]-3-quinolinecarbonitrile.

MOLECULAR FORMULA: C26H29C12N5O3.

MECHANISM OF ACTION:

Bosutinib is a tyrosine kinase inhibitor. Bosutinib inhibits the BCR-ABL kinase that promotes CML; it is also an inhibitor of Src-family kinases including Src, Lyn, and Hck. Bosutinib inhibited 16 of 18 imatinib-resistant forms of BCR-ABL kinase expressed in murine myeloid cell lines. Bosutinib did not inhibit the T315I and V299L mutant cells

USES:

Bosutinib is used to treat a certain type of chronic myeloid leukemia (CML; a type of cancer of the white blood cells)

MATERIALS AND INSTRUMENTS

Materials used:

1. Bosutinib
2. Methanol
3. Acetone
4. Acetonitrile
5. Ethanol
6. Water
7. Di-methyl formamide

Instrument used

Table-1: Instrument

Sr. No	Instrument Name	Model Number	Software	Manufacturer's Name
1	UV Visible Double Beam Spectrophotometer	UV 3000+	UV win Software	T60PG instruments

SOLUBILITY STUDIES AND SELECTION OF SOLVENT:

Table-2: Solubility Studies

Sr. No	Bosutinib Solvent	Solubility parameters
1	Bosutinib+ Methanol	Very soluble
2	Bosutinib+ ethanol	soluble
3	Bosutinib+ Acetone	soluble
4	Bosutinib+ Acetonitrile	Sparingly soluble

5	Bosutinib+ Dimethyl formamide	Sparingly soluble
6	Bosutinib+ Distilled water	Poorly soluble

SELECTION OF SOLVENT:

After Solubility Studies we have selected Methanol as the best solvent, because compared to other solvents Bosutinib was immediately dissolved in methanol

MAXIMUM WAVELENGTH:

λ max: The wavelength at which a substance has its strongest photon absorption (highest point along the spectrums Y- max) .

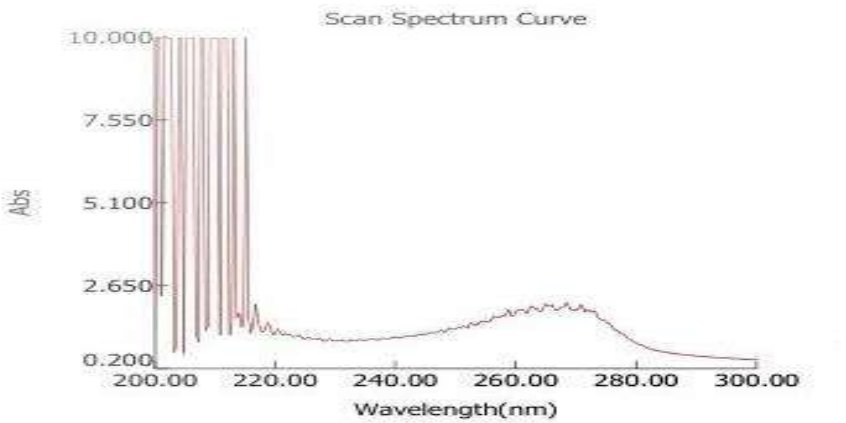

Fig 2: Λ Max Of Bosutinib

Table-3: Linearity

Sr. No	Wavelength	Absorbance
1	268.40	2.140

METHODOLOGY4-17

Method development and validation for the estimation of bosutinib by using UV-spectrophotometer

Preparation of standard solution:

Standard stock 1:

10.0mg of Bosutinib was accurately weighed and transferred to a 10ml volumetric flask. A few ml of methanol was added to dissolve the drug and the volume was made up to the mark with methanol which gives the concentration of 1000µg/ml.

Standard stock II:

1.0ml from standard stock I was pipetted to a 10ml volumetric flask and the volume was made up to the mark with methanol which gives the concentration of 100µg/ml.

VALIDATION OF THE DEVELOPED METHOD:

The developed UV method was validated for precision, linearity, accuracy, LOD, and LOQ.

1. **LINEARITY**

A series of linear concentrations (2 - 12µg / ml) were prepared from standard stock II solutions Appropriate dilutions were made from the aliquot into separate 10 ml volumetric flasks and made up to the volume with methanol. Noted down the absorbance for each of the concentrations (Table no: 9) and a plot of the calibration curve was constructed (shown in Fig.3)

2. **PRECISION**

- The precision of analytical method is defined as the agreement between replicate measures of the same sample.

- The precision was carried out by two methods: Intraday and Interday.

INTRADAY:

The intraday precision was carried by scanning the sample at different times within a day. %RSD is found to be 0.501%

Acceptance criteria: The % RSD for the intraday precision is calculated and the calculated value is within the limits, i.e.≤2%.

INTERDAY:

The interday precision was carried out by scanning the sample at different days with in a week. %RSD is found to be 0.504%

Acceptance criteria: The %RSD for the Interday precision is calculated and the calculated value is within the limits, i.e.,≤2%.

ACCURACY:

Recovery of the spiked standard solution (known concentration) was performed at three different levels (0%, 100%, and 150%) of the sample solution. The % recovery was then calculated from the recorded absorbance values. (Table-7)

LIMIT OF DETECTION:

Least amount of concentration to be detected

Formula: 3.3 x standard deviation/mean

Value found:

1.962µg

LIMIT OF QUANTIFICATION:

Least amount of concentration that is to be quantified

Formula: 10 x standard deviation/mean

Value found:

5.945µg.

DRUG STABILITY STUDIES:

Acid and Base Degradation:

1ml from Standard stock II (100µg/ m l) was pipetted to a 10ml, volumetric flask, and 2ml.of 0.1N HC1/0.IN NaOH was added. After 24hrs neutralize the solution with 2ml of 0.IN NaOH/0.IN HCl the remaining volume were made up to the mark with water (10ug / ml) 2ml each of Appropriate 0.1N HCI and 0.1N NaOH were taken into respective 10ml volumetric flasks and made up to the mark with water. These were used as blank. The absorbance of the acid/base degraded samples was noted applying the calibration developed method.

Oxidation (Hydrogen peroxide):

1ml from Standard stock II (100mg / ml) was pipetted to a 10ml volumetric flask and 2ml of 3% H2O2 was added. After 24hrs the solution is finally made up to the mark with distilled water. The absorbance was measured using the above solution against a blank containing 2ml of 3% H2O2 in a 25ml volumetric flask was kept as blank. The absorbance of the peroxide degraded samples was noted applying the developed method.

RESULT AND DISCUSSION

LINEARITY

Table-4: Calibration Plot Of Bosutinib

Concentration (µg/ml)	Absorbance
2	0.096
4	0.193
6	0.308
8	0.423
10	0.548
12	0.689

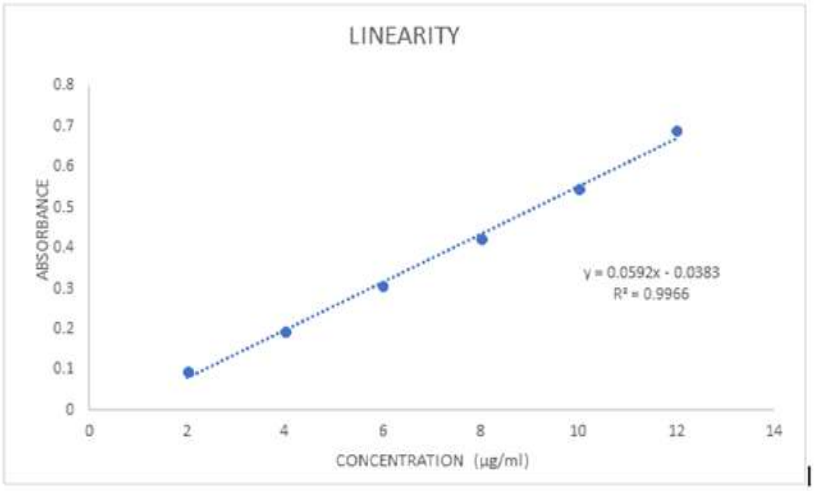

Fig 3: Calibration Graph Of Linearity Study

PRECISION

Table-5: Intraday Precision Studies

Concentration	Absorbance
6µg/ml	0.306
	0.304
	0.303
STDEV	0.001
%RSD	0.501%

Table-6: Interday Precision Studies

Concentration	Absorbance
6µg/ml	0.304
	0.303
	0.301
STDEV	0.001
%RSD	0.504%

ACCURACY

Table-7 Recovery Studies

% of Concentration	Standard Concentration(µg/ml)	Concentration added	Concentration found	% of Recovery	%Mean recovery
50%	6	3+6=9	8.7	96.6	97.83
100%	6	6+6=12	11.8	98.3	
150%	6	9+6=15	14.8	98.6	

STABILITY STUDIES

Table-8: Degradation Studies

Sr. No	Chemical	Absorbance	Concentration found	%Recovery	% Degradation
1	HCl	0.490	8.4	84%	16%

2	NaOH	0.498	8.5	85%	15%
3	H_2O_2	0.482	8.3	83%	17%

SUMMARY

1. Estimation of Bosutinib was achieved by UV Spectroscopy. The linearity was checked in different concentrations and Beer lambert's law obeyed in the concentration range of 2-12µg/ml for bosutinib. The recovery studies were carried to ensure the reproducibility and reliability of the method by adding known amount of bosutinib.
2. This method was carried out by using methanol as solvent.
3. Drug stability studies were also established to evaluate the drug product at different stress conditions of acid, base and oxidation studies.

CONCLUSIONS

1. The method to detect bosutinib by UV - Spectroscopy was established and validated. The results obtained are proved that proposed method is accurate, Precise and rapid for the determination of bosutinib. The developed method can be applied successfully for the determination of bosutinib in bulk form.
2. The development can also be used for the evaluation of stability of bosutinib.

ACKNOOWLEDGEMENT;

The authors are very much thankful to Pullareddy institute of Pharmacy ,Hyderabad, Telangana. For providing necessary facilities and continuous support for this entire research work.

CONFLICT OF INTREST

No conflicts of interest.

REFERENCES:

1. Anik AH, Rahman S, Sarker S. Development of a Dissolution Method Validation Technique Using UV-Spectrophotometry for Bosutinib 500mg Tablet. Oriental Journal of Chemistry. 2022;38(6):1483.
2. PB.Jadhav, GK.Gajare Development and validation of an UV – spectrometric method for estimation bosutinib in bulk and tablet dosage form .International journal of research in pharmacy and chemistry . 2016,6(3),608-612.
3. FDA Approved Drug Products: BOSULIF® (bosutinib) tablets/capsules, for oral use (October 2023
4. Sri RS, Soundarya K. Bhavya Sri, M. Sumakanth. Stability Indicating UV-Spectrophotometric Method Development and its Validation for the Determination of ImatinibMesylate in Bulk and Formulation. Asian Journal of Pharmaceutical Analysis. 2022;12(2):83-6.
5. Ravisankar P, Babu PS, Taslim SM, Kamakshi K, Manasa RL. Development and validation of UV-spectrophotometric method for determination of sorafenib in pharmaceutical dosage form and its degradation behaviour under various stress conditions. Int J Pharm Sci Rev Res. 2019 May 1;56:12-7.
6. RamalingamKalaichevi ,Ekambaramjayachandran , Uv spectrometric estimation of sorafenib in pure and tablet dosage form .journal of pharmacy research 2011,4(10),3705-3706.
7. Dharmendra J Prajapatı, Usmanganı K. Chhalotiya. Minesh D Prajapatı, vol-1, Issue-2, Qualification of newer anticancer drug Enzalutamide by stability RP-LC Method and UV- visible Spectroscopic method in bulk and synthetic mixture Journal of molecular oncology.2017 vol 1 issue 2.
8. Ramurvaturı,T.ManikyaSastry, S.Satyaveni vol-8,Issue-9 2016.Development and validation of a stability indicating HPLC method for the determination of nilotinib hydrochloride in bulk and pharmaceutical

dosage form. International journal of pharmacy and pharmaceutical sciences , ISSN:0975-1491,vol 8 issue 9 , 2016

9. SumantaMondal,SabyasachiBiswal,.Trayambica Acharya Prasenjitmondal, Determination of lapatınıb in bulk and tablet dosage form sung, ultraviolet Spectrophotometric, and RP-HPLC analytical methods. International journal of pharmaceutical investigations,vol-11,issue- 2,April-June 2021;11(2);208-213
10. MonirehHajmalek, Masoumeh GoudarziSolmazGhaffa, Development and validation of a HPLC method for analysis of sunitinib malate. Brazilian journal of pharmaceutical sciences,Vol-52,n-4,oct/dec2016
11. Ankit jam Arvind Gulbake and Sanjay K. Jain Development and Validation of HPLC method for simultaneous estimation of paclitaxel and topotecan, Journal of chromatographic science,2014;52:697-703
12. Uma MaheswariKatari, M .Ajitha, stability indicating method development and validation for determination of daunorubicin and cytarabine, in bulk and pharmaceutical dosage form by RP-HPLC World Journal of pharmaceutical sciences,2022:10(01):41-51.
13. HalahakoonAmilaJeewantha,SlivkinAlekseiIvanovich, Validation of Spectrophotometric method for the estimation of of vincristine and vinblastine, international journal of pharmacy and pharmaceutical sciences vol 9, issue 4, 2017.
14. Varanasi. S.N. Murthy, A Kahini, KE Pravallika, PrameelaKani and SA Rahaman.Development and validation of HPLC method for estimation of Cytarabine& in bulk and pharmaceutical Dosage form,International Journal of Pharmaceutical Sciences and Research, 2013;vol.4(12):4573-4576.
15. SuddaharottyaDey, HIımansuBhusanSamal, P.Monica, Sandeep Reddy, G karthik Method Development and validation for the estimation of Chlorambucil In Bulk and Pharmaceutical dosage form using UV-vis spectrophotometric method.Journal of Pharmacy Research2011,4(9),3244-3246
16. K.Siddappa, PrashantC Hanashetty, Sonu Kumar, B. Mane and NagaBhushanam. s, Development and Validation of Spectrophotometric method for the Determination of Cyclophosphamide in bulk drug and its pharmaceutical dosage form,International Journal of Pharmacy and Pharmaceutical sciences,vol5,issue 4 , 2013..
17. Pooja B-Patel and Paresh, U. Patel, Development and Validation of Spectrophotometric method for Simultaneous Determination of Temozolomide and Capecitabine in synthetic. Mixture,World Journal of Pharmaceutical research, vol 5,issue4, 1042-105

HOW TO CITE: Vardhineedi Shirisha,R. Parasuraman, M. Poojitha, R. Gayathri, P. Mounika, M. Bheemaji, Development And Validation Of Bosutinib By Using UV – Spectrophotometric Method In Bulk Form, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 5, 1544-1550. https://doi.org/10.5281/zenodo.11352665