DEVELOPMENT & VALIDATION OF RP-HPLC METHOD FOR QUANTITATIVE ESTIMATION OF DASATINIB AND ITS IMPURITIES IN PHARMACEUTICAL DOSAGE FORM

ABSTRACT

Aim:

The primary objective of the research work is to develop a effective, sensitive, economical and simple reverse phase HPLC method for the separation and quantification of Dasatinib and its impurities are described in tablet formulations.

Study design:

HPLC based quantification studies

Place and Duration of Study:

Department of Chemistry, Acharya Nagarjuna University, Guntur, Andhra Pradesh between April 2021 and August 2022.

Methodology:

Separation and quantification of Dasatinib and its impurities are done by using an Inertsil ODS-3V, 250 x 4.6 mm, 5µm and the mobile phase consists of two Channels A and B. Channel-A: pH 5.80 phosphate buffer : acetonitrile (90:10 v/v) and Channel-B: acetonitrile : water (90:10 v/v). The flow rate is 1.0 ml/min. The column temperature was maintained at 25°C and sample temperature was maintained at 25°C, injection volume 10µL and wavelength fixed at 320nm UV-detection.

Results:

There is no interference of diluent and placebo at Dasatinib and impurities peaks. The elution order and the retention times of impurities and Dasatinib obtained from individual standard preparations and mixed standard preparations are comparable.

The limit of detection (LOD) and limit of quantitation (LOQ) for Dasatinib standard 0.147&0.048µg/mL, impurity-A 0.334&0.110 µg/mL, impurity-C 0.184&0.061 µg/mL, impurity-D 0.136&0.045 µg/mL, impurity-E 0.089&0.029 µg/mL and impurity-F 0.222 & 0.073 µg/mL respectively.

The linearity results for Dasatinib and all the impurities in the specified concentration range are found satisfactory, with a correlation coefficient greater than 0.99.Calibration curve was

plotted and correlation co-efficient for Dasatinib and its impurities found to be 1.000, 0.9999, 0.9912, 1.000, 0.9932 and 0.9922 respectively.

The accuracy studies were shown as %recovery for Dasatinib and its impurities at specification level. The limit of % recovered shown is in the range of 80 and 120% and the results obtained were found to be within the limits. Hence the method was found to be accurate.

The method has validated as per ICH guidelines and all the validation parameters are satisfy the ICH Q2 specification acceptance limits

Conclusion:

The developed LC method was validated with respect to specificity, precision, linearity, ruggedness and robustness. Therefore this method has high probability to adopt in pharmaceutical industry for regular analysis of Dasatinib tablet formulations.

Key words: Dasatinib, determination of related substances, liquid chromatography.

1.0 Introduction

Dasatinib is an inhibitor of multiple tyrosine kinases. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines over expressing BCR-ABL. The chemical name for Dasatinib is N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazole carboxamide. The molecular formula is $C_{22}H_{26}ClN_7O_2S.H_2O$, which corresponds to a formula weight of 506.02 (monohydrate). The anhydrous free base has a molecular weight of 488.01. Dasatinib is a white to off-white powder. The drug substance is soluble in dimethyl sulphoxide and practically insoluble in water and slightly soluble in ethanol and methanol. The molecule structure is shown in **Figure: 1.1**

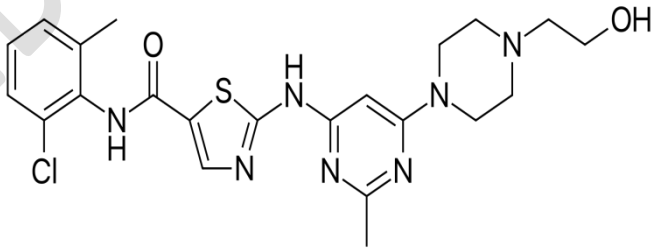

Figure: 1.1 Chemical structure of Dasatinib

A few analytical methods have been reported for quantitative estimation of Dasatinib in pharmaceutical formulations. A thorough literature survey of Dasatinib revealed that very few analytical methods had been reported for estimation of Dasatinib hitherto. Majority of methods for determination of Dasatinib in biological fluids and pharmaceutical dosage forms

includes LC-MS/MS [1-4], LC-MS [5-6], HPTLC-LC [7], HPTLC [8], UPLC-MS [9], HPLC-MS [10], RP-HPLC [11] and UV-Visible Spectrophotometric method [12-13].

The objective of the present work is to develop a stability indicating HPLC method and validated as per ICH [14-18] and Q2 (R1) validation guidelines.

Impurity profiling of active pharmaceutical ingredients (API) in both bulk material and formulations is one of the most challenging tasks. The presence of unwanted or in certain cases unknown chemicals, even in small amounts, may influence not only the therapeutic efficacy but also the safety of the pharmaceutical products. For these reasons, all major international pharmacopoeias have established maximum allowed limits for related compounds for both bulk and formulated APIs. As per the requirements of various regulatory authorities, the impurity profile study of drug substances and drug products has to be carried out using a suitable analytical method in the final product.

2.0 Experimental

2.1 Reagents and chemicals

Potassium dihydrogen orthophosphate, Potassium hydroxide, Orthophosphoric acid, Acetonitrile and methanol was procured from Merck. Water (Milli-Q). All chemicals were of an analytical grade and used as received.

2.2 Instrumentation

Chromatographic separation was achieved by using an Waters e2695, Empower^3 software using, Inertsil ODS-3V, 250 x 4.6 mm, 5µm and the mobile phase consists of two Channels A and B. Channel-A: pH 5.80 phosphate buffer : Acetonitrile (90:10 v/v) and Channel-B: Acetonitrile : water (90:10 v/v). The flow rate is 1.0 ml/min. The column temperature was maintained at 25°C and sample temperature was maintained at 25°C, injection volume 10µL and wavelength fixed at 320nm UV-detection. Retention times of impurities were 9.29 for impurity-D, 10.54 for Impurity-A, 12.76 for Impurity-F, 28.82 for impurity-C, 36.93 for impurity-E and 17.91 for Dasatinib.

2.3 Preparation of solutions:

2.3.1 Preparation of 10% Potassium hydroxide solution:

Weigh about 10.0 g of potassium hydroxide pellets and transfer into a 100 mL volumetric flask and add 60mL of water sonicate to dissolve and makeup the volume with water and mixed well.

2.3.2 Preparation of pH 5.8 Potassium dihydrogen phosphate Buffer solution:

Weighed 2.722 g of Potassium dihydrogen phosphate anhydrous and transferred into a 2000 mL of water and mixed well. Adjusted the pH to 5.81 with 10% potassium hydroxide solution and mixed well. Filtered through 0.45µm membrane filter and sonicated to degas.

2.3.3 Preparation of pH 3.0 Potassium dihydrogen phosphate Buffer solution:

Weighed 1.36368 g of Potassium dihydrogen phosphate and transferred into a 1000 mL of water and mixed well. Adjusted the pH to 3.05 with diluted orthophosphoric acid and mixed well. Filtered through 0.45 µm membrane filter and sonicated to degas.

2.3.4 Preparation of mobile phase-A:

Prepared a mixture of 1800mL of pH 5.8 Potassium dihydrogen phosphate buffer solution and 200mL of acetonitrile in the ratio of 90:10 (% v/v) and sonicated to degas.

2.3.5 Preparation of mobile phase-B:

Prepared a mixture of 1800mL of acetonitrile and 200mL of water in the ratio of 90:10 (%v/v) and sonicated to degas.

2.3.6 Preparation of diluent:

Prepared a mixture of 600mL of pH 3.0 Potassium dihydrogen phosphate Buffer and 1400 mL of methanol in the ratio of 30:70 (%v/v), filtered through 0.45 µm membrane filter and sonicated to degas.

2.3.7 Preparation of impurity stock solution;

Weighed accurately 1.57 mg of Dasatinib Impurity-A and 1.17 mg of Dasatinib Impurity-D, transferred into a 25mL volumetric flask, to it added 15mL of diluent, sonicated for 5 minutes to dissolved, diluted to volume with diluent and mixed well.

2.3.8 Preparation of resolution solution:

Weighed accurately 20.04 mg of Dasatinib working standard and transferred into a 20 mL volumetric flask, to it added 10 mL of diluent sonicate for 5 minutes to dissolved. Added 1.0 mL of Impurity stock solution diluted to volume with diluent and mixed well.

2.3.9 Preparation of standard solution:

Weighaccurately 10.25 mg of Dasatinib working standard in to a10 mL volumetric flask, to it added 5mL of diluent sonicate to dissolved and diluted to volume with diluent and mixed well. Further transferred 2.0mL of this solution into a 100 mL volumetric flask, diluted to volume with diluent and mixed well. Further transferred 5.0 mL of this solution into a 50mL volumetric flask, diluted to volume with diluent and mixed well. (The concentration of the solution contains 0.002 mg/ mL of Dasatinib).

2.4.0 Preparation of sensitivity solution:

Pipette out 5.0mL of above standard solution into a 20mL volumetric flask, diluted to volume with diluent and mixed well.

2.4.1 Preparation of placebo solution:

Weighed accurately 79.74 mg of Dasatinib placebo (equivalent to 25 mg of Dasatinib)into a 25mL volumetric flask, added 15mL of diluent and sonicated for 30minutes with intermediate shaking, maintaining the temperature at 25°C to dissolved and then diluted to the volume with diluent, mixed well. Filtered the solution through 0.45µm PVDF syringe filter PVDF syringe filter.

2.4.2 Preparation of test solution:

Weighed 10 tablets, take average weight and crushed into fine powder. Weighed accurately 105.53 mg (equivalent to 25 mg of Dasatinib) of Dasatinib sample powder, transferred into 25mL volumetric flask, added 15mL of diluent, sonicated for 30 minutes with intermediate shaking, maintaining the temperature at 25°C to dissolved and then diluted to the volume with diluent, mixed well. Filtered the solution through 0.45 µm PVDF syringe filter.

3.0 Method Development:

3.1 Method optimization parameters

An understanding of the nature of API (functionality, acidity, or basicity), the synthetic process, related impurities, the possible degradation pathways and their degradation products are needed for successful method development in reverse-phase HPLC. In addition, successful method development should result a robust, simple and time efficient method that is capable of being utilized in manufacturing setting.

3.2 Selection of wavelength

The sensitivity of the HPLC method depends upon the selection of detection wavelength. An ideal wavelength is one that gives good response for related substances and the drugs to be detected. The wavelength for measurement was selected as 320 nm from the absorption spectrum.

3.3. Selection of stationary phase

Proper selection of the stationary phase depends up on the nature of the sample and chemical profile. The drug selected for the present study was polar compound and could be separated either by normal phase chromatography or reverse phase chromatography. From literature survey, it was found that different C18 columns could be appropriately used for the separation of related substances for Dasatinib.

3.4. Selection of mobile phase

Different mobile phase and stationary phases were employed to develop a suitable LC method for the quantitative determination of impurities in Dasatinib. A number of column chemistries supplied by different manufacturers and different mobile phase composition were tried to get good peak shapes and selectivity for the impurities present in Dasatinib.

Poor peak shape and resolution was observed when Zorbax SB C18 (250mm x 4.6mm, 5µ) and gradient mobile phase programmed of Mobile Phase: A pH 2.80 phosphate buffer and Mobile Phase: B Acetonitrile. There was no proper resolution of impurities and analyte peak and efficiency of the peak is also not achieved and peak interferences are present.

In second attempt made using Inertsil ODS-3V, 250 x 4.6 mm, 5µm column, and gradient mobile phase programmed of Mobile Phase: A pH 5.80 phosphate buffer: acetonitrile and Mobile Phase: B Acetonitrile: water. The resolution of both drug and impurities was achieved. These chromatographic conditions were selected for validation studies.

4.0 Method Validation

4.1 Specificity

Specificity was demonstrated by injected blank solution, placebo solution, standard solution, sample solution, spiked sample and individual impurities and analyzed as per the test method.

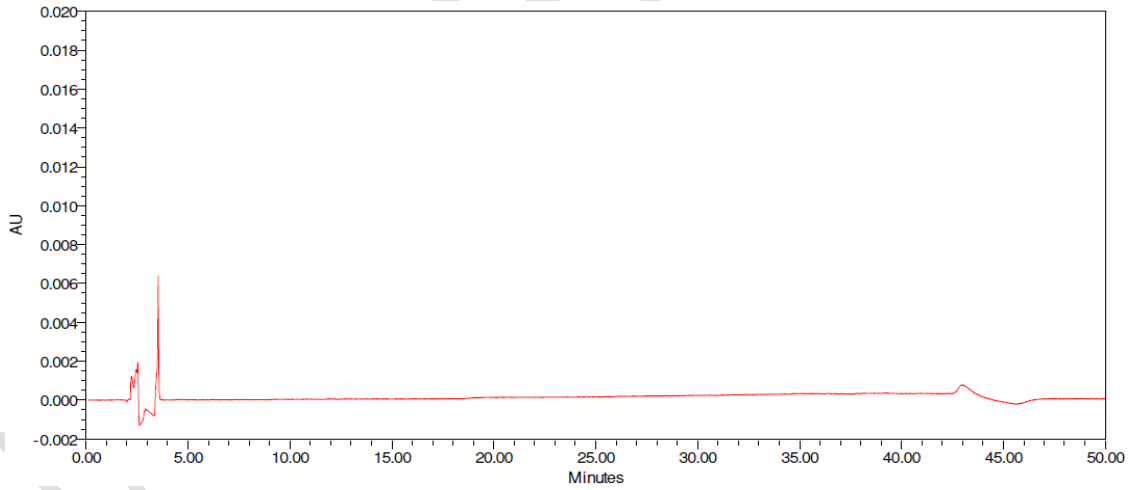

Figure: 1.2 typical chromatogram of Blank

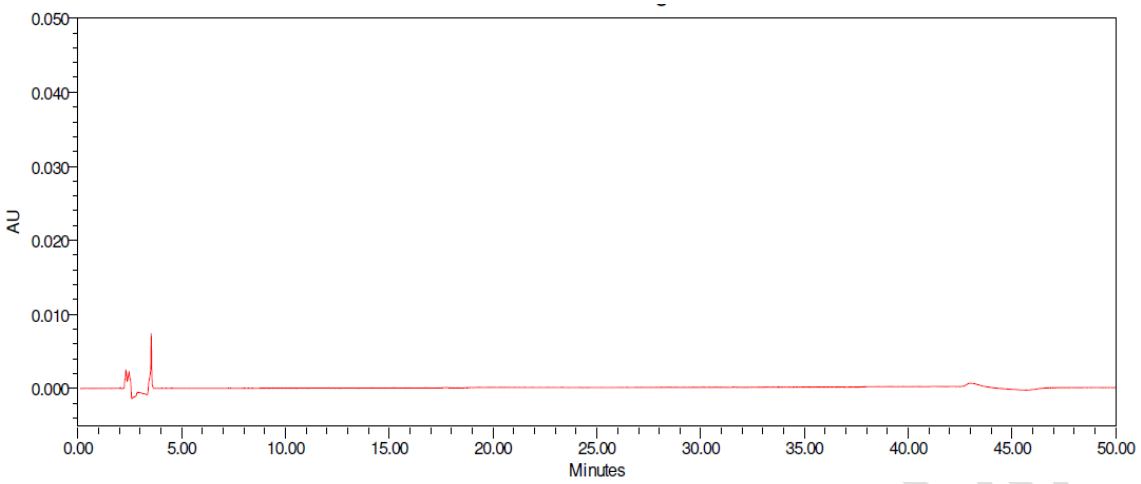

Figure: 1.3 typical chromatogram of Placebo

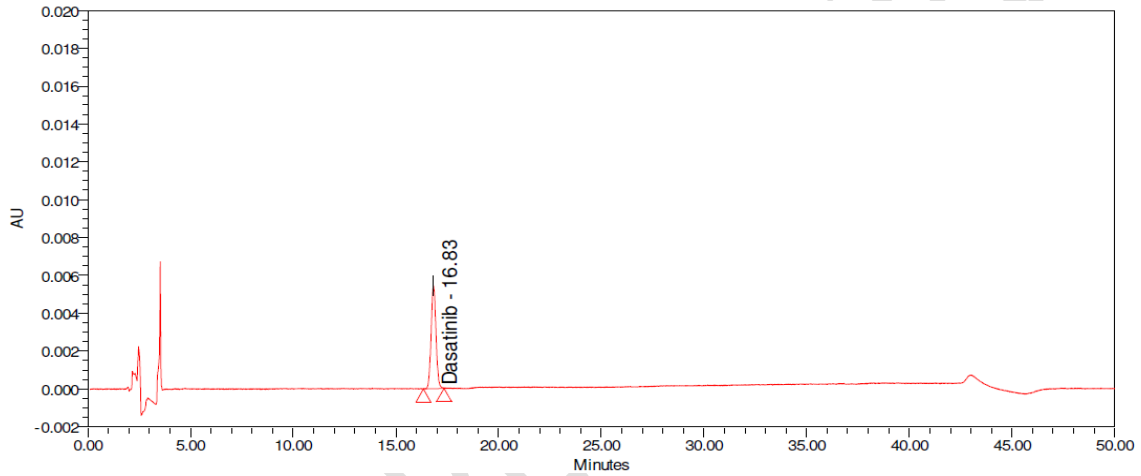

Figure: 1.4 typical chromatogram Diluted Standard

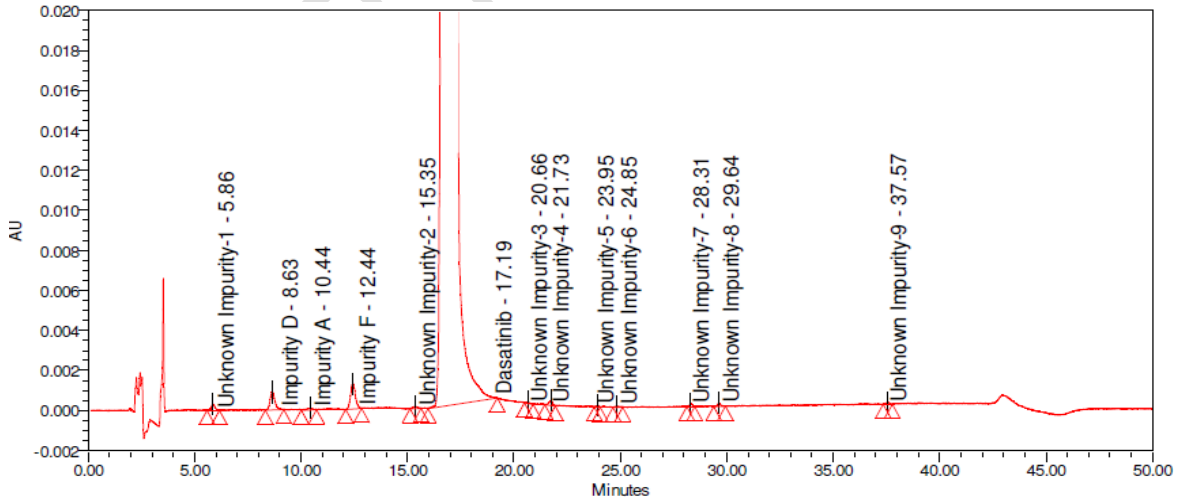

Figure: 1.5 typical chromatogram as such Sample

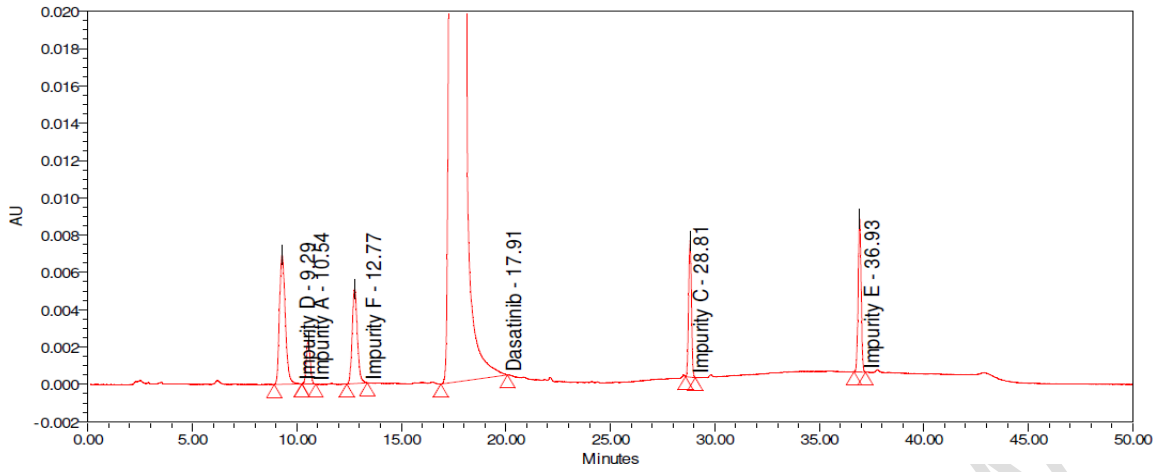

Figure: 1.6 Typical chromatogram Spiked Sample

Table: 1.1 Impurity interference data (Specificity results)

Peak Name	Retention Time	Blank	Placebo
Blank	ND	**NA**	**NA**
Placebo	ND	**NA**	**NA**
Impurity-D	9.29	No	No
Impurity-A	10.54	No	No
Impurity-F	12.77	No	No
Impurity-C	28.81	No	No
Impurity-E	36.93	No	No
Dasatinib	17.91	No	No

It was observed that known impurities are not co eluting with each other and main analyte peak.

4.2 Precision

4.2.1 System Precision:

System precision was demonstrated by prepared standard solution as per the test method and injected for six times into HPLC system. The retention time and area response of analyte peak were recorded.

Table: 1.2 System Precision data for Dasatinib

S.No.	Area response	Retention time
1	79275	17.5
2	79695	17.44
3	79492	17.44
4	79256	17.41
5	79241	17.37
6	80036	17.41
Average	**79499**	**17.43**
% RSD	**0.4**	**0.2**

The %RSD of peak area for Dasatinib was found to be 0.4% which is below 5.0% indicates that the system gives precise result.

4.2.2 Method Precision

Method precision was demonstrated by prepared six samples by spiking of impurities at specification level and analyzed as per the test method. The samples were prepared as per the method and the result for precision study is tabulated in **Table: 1.3.**

Table: 1.3 Results of method precision

S.No.	Sample Details	Impurity (% Recovery)				
		Imp-A	Imp-C	Imp-D	Imp-E	Imp-F
1	Prep-1	87.7	87	108.9	106.1	105.8
2	Prep-2	88.6	85.6	109.4	106.6	109.7
3	Prep-3	87.7	87	108.5	105.6	107.3
4	Prep-4	87.2	85.1	107.5	106.6	109.2
5	Prep-5	87.2	87	107	106.1	106.8
6	Prep-6	88.6	85.6	109.4	107.1	109.2
Avg.		87.8	86.2	108.5	106.4	108
Std. Dev.		0.6346	0.8773	1.0015	0.5244	1.5837
%RSD		0.7	1	0.9	0.5	1.5

The results were well within the limits. From the above results, it is concluded that method is precise.

4.3 Limit of detection (LOD) & Limit of Quantitation (LOQ)

Limit of detection: The worst found signal to noise ratio for each peak was greater than 3 in each injection. All the peaks were detected in all the three injections.

Limit of Quantitation: The worst found signal to noise ratio for each peak was greater than 10 in each injection. All the peaks were detected in all the six injections.

Table: 1.4 LOD & LOQ concentrations and S/N values for Dasatinib and impurities

Name of the Impurity	Concentration in ppm		Signal to noise ratio value	
	LOD	LOQ	LOD	LOQ
Impurity D	0.045	0.136	4	16
Impurity A	0.11	0.334	5	18
Impurity F	0.073	0.222	5	18
Dasatinib	0.048	0.147	5	17
Impurity C	0.061	0.184	4	15
Impurity E	0.029	0.089	3	10

Table: 1.5 LOQ precision for Dasatinib and impurities

S.No.	Name of the solution	Impurity-A	Impurity-B	Impurity-C	Dasatinib
1	LOQ precision-1	2804	8184	3248	5754
2	LOQ precision-2	2729	6994	3306	5457
3	LOQ precision-3	2872	6942	3319	5833
4	LOQ precision-4	2640	6518	3022	6133
5	LOQ precision-5	2607	6518	3384	5865
6	LOQ precision-6	2772	6660	3557	5464
Avg.		2737	6969	3306	5751
Std.Dev.		100.311	629.263	175.085	258.634
%RSD		3.7	9.0	5.3	4.5

The limit of quantitation and limit of detection values obtained for each impurity and Dasatinib are within the acceptance criteria.

4.4 Linearity

The linearity of detector response for analytes was demonstrated by preparing solutions over the range of 0.1%, 0.5% & 1.0% of specification limit with respect to sample concentration. These solutions were injected into the HPLC system and the responses of the same were recorded. A plot of concentration vs. peak area was done. The Coefficient of determination between concentration and response was evaluated. The observations are tabulated below.

Table: 1.6 Linearity for Impurity-A

S.No	Levels	Concentration in ppm	Area response
1	Linearity Level-1	1.05	34397
2	Linearity Level-2	5.07	158475
3	Linearity Level-3	10.05	318434
Correlation coefficient (r)			0.9999
Square root of Correlation coefficient (r^2)			0.9999
Slope			31598.5213
Intercept			94.6559

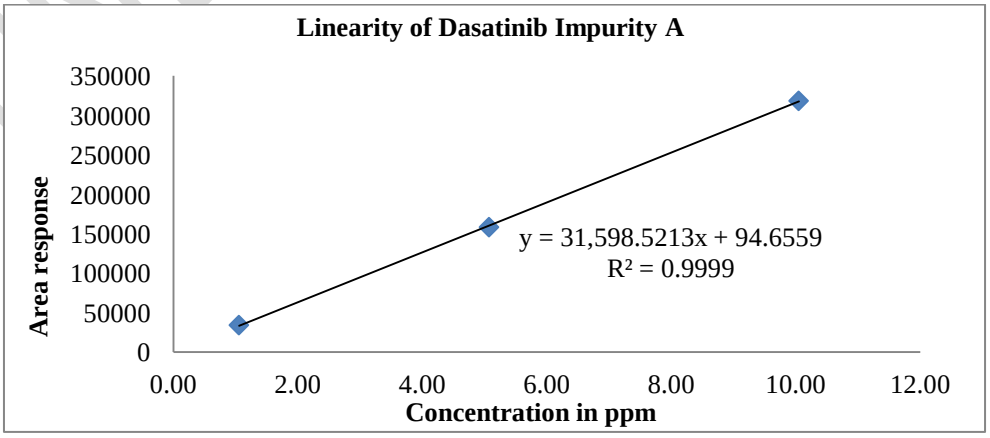

Figure: 1.7 Linearity graph of Impurity-A

Table: 1.7 Linearity for Impurity-C

S.No	Levels	Concentration in ppm	Area response
1	Linearity Level-1	0.99	59938
2	Linearity Level-2	5.02	283491
3	Linearity Level-3	10.04	739911
Correlation coefficient (r)			0.9912
Square root of Correlation coefficient (r^2)			0.9826
Slope			75771.7603
Intercept			-43979.4359
RRF			0.93

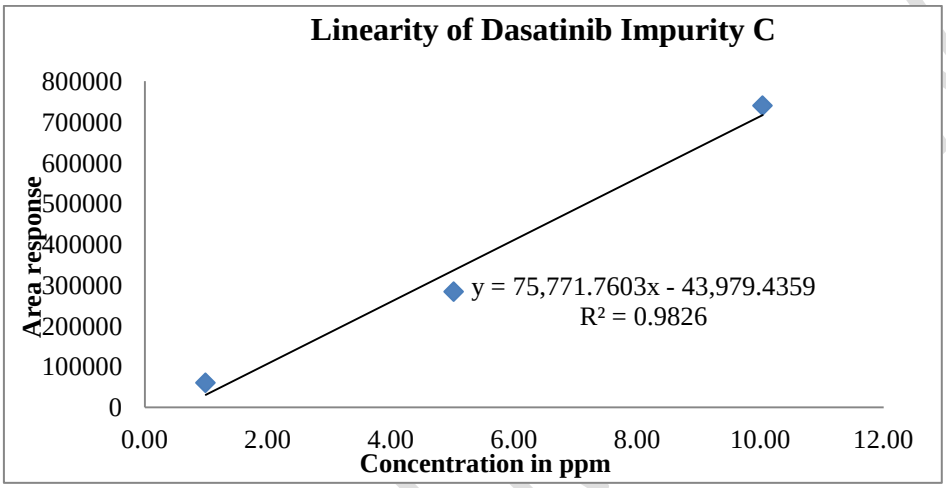

Figure: 1.8 Linearity graph of Impurity-C

Table: 1.8 Linearity for Impurity-D

S.No.	Levels	Concentration in ppm	Area response
1	Linearity Level-1	0.97	109705
2	Linearity Level-2	5.03	548541
3	Linearity Level-3	9.96	1068435
Correlation coefficient (r)			1.0000
Square root of Correlation coefficient (r^2)			1.0000
Slope			106528.5321
Intercept			8792.4080

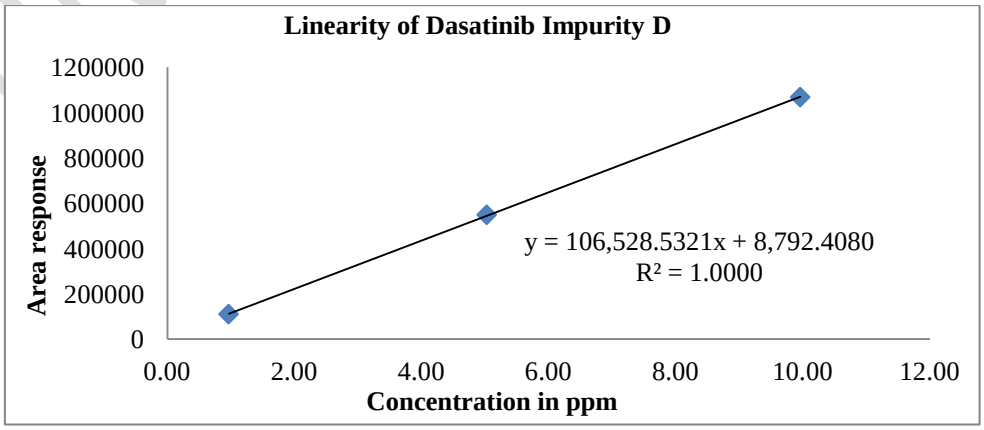

Figure: 1.9 Linearity graph of Impurity-D

Table: 1.9 Linearity for Impurity-E

S.No.	Levels	Concentration in ppm	Area response
1	Linearity Level-1	1.08	91955
2	Linearity Level-2	5.03	336276
3	Linearity Level-3	10.07	816165
Correlation coefficient (r)			0.9932
Square root of Correlation coefficient (r^2)			0.9865
Slope			81217.0878
Intercept			-23278.1964

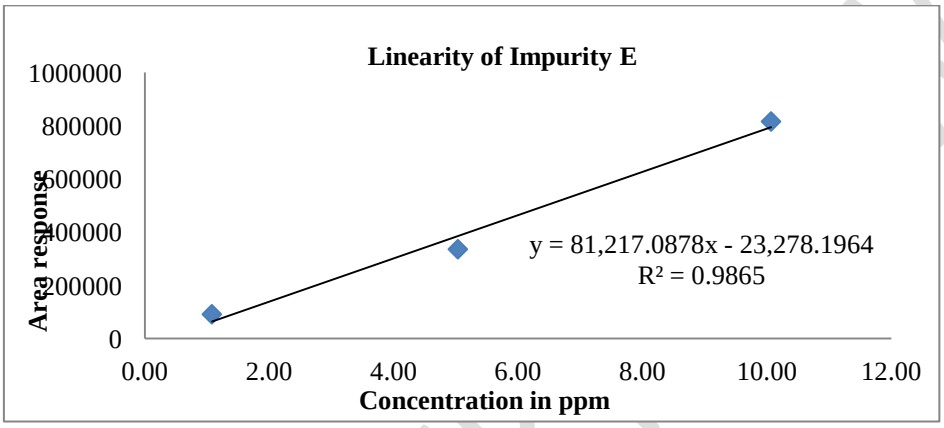

Figure: 1.10 Linearity graph of Impurity-E

Table: 1.10 Linearity for Impurity-F

S.No	Levels	Concentration in ppm	Area response
1	Linearity Level-1	1.03	73030
2	Linearity Level-2	5.05	292265
3	Linearity Level-3	10.01	722404
Correlation coefficient (r)			0.9922
Square root of Correlation coefficient (r^2)			0.9844
Slope			72834.8498
Intercept			-28214.3277

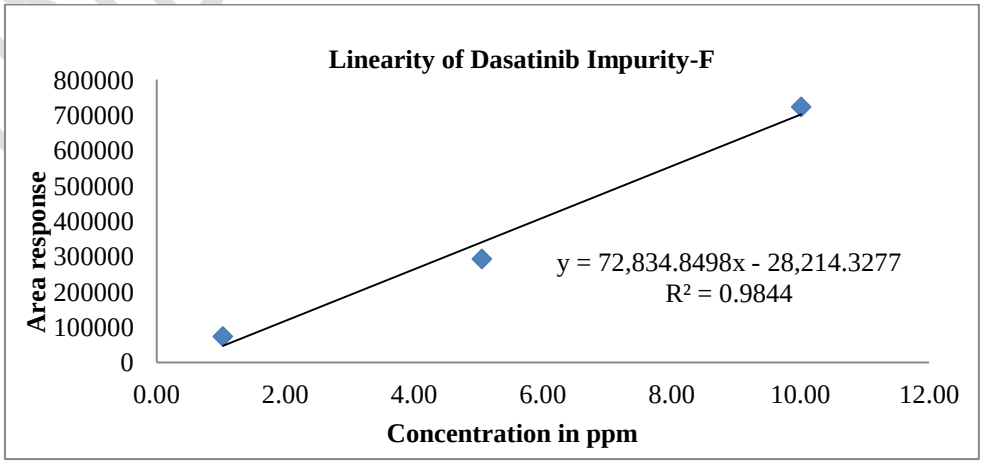

Figure: 1.11 Linearity graph of Impurity-E

Table: 1.11 Linearity for Dasatinib

S.No.	Levels	Concentration in ppm	Area response
1	Linearity Level-1	1.00	75877
2	Linearity Level-2	4.99	402737
3	Linearity Level-3	9.99	808234
Correlation coefficient (r)			1.0000
Square root of Correlation coefficient (r^2)			1.0000
Slope			81460.3539
Intercept			-4980.1967

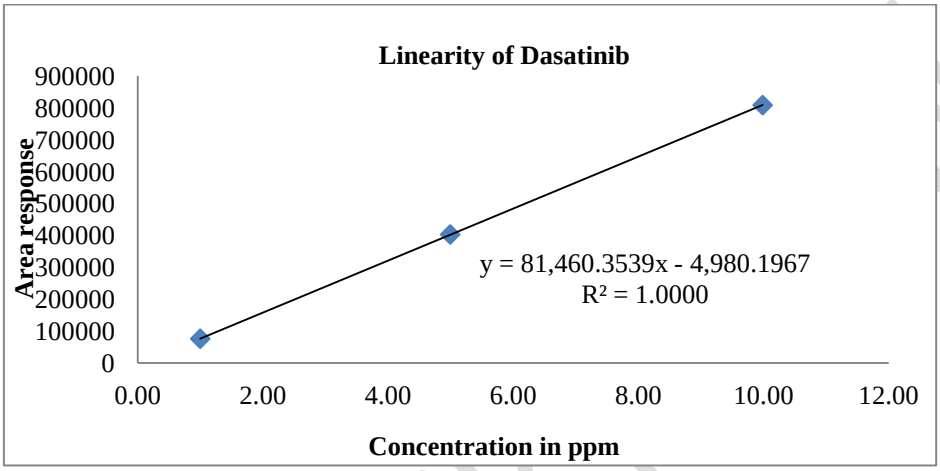

Figure: 1.12 Linearity graph of Dasatinib

The linearity results for Dasatinib and all the impurities in the specified concentration range are found satisfactory, with a correlation coefficient greater than 0.99.

4.5 Accuracy

Recovery of Dasatinib impurities in Dasatinib was performed. The sample was taken and varying amounts of Dasatinib impurities representing LOQ to 150 % of specification level were added to the flasks. The spiked samples were prepared as per the method and the results are tabulated in **Table 1.12.**

Table: 1.12 Accuracy study of Dasatinib

S.No.	Theoretical (%)	% Mean Recovery				
		Imp-A	Imp-C	Imp-D	Imp-E	Imp-F
1	LOQ	99.0	91.2	102.4	88.9	89.4
2	100	84.3	98.0	83.0	82.9	90.7
3	150	84.7	98.3	82.6	83.5	92.3

4.6 Solution stability of analytical solutions:

Standard and sample and spiked sample solutions were kept for 48 hrs at room temperature in transparent bottles in auto sampler and in refrigerator 2-8°C. The stability of standard and sample and spiked sample solutions was determined by comparison of “old” prepared standard solutions with freshly prepared standard solutions.

Table: 1.13 Results for solution stability of standard

Time Interval	%Recovery	
	Room temperature	Refrigerator
Initial	NA	NA
24hrs	98.9	97.6
48hrs	98.5	98.4

Table: 1.14 Results for solution stability of test solution at room temperature

Component	Initial	After 24Hrs	% Difference	After 48Hrs	% Difference
Impurity-A	0.006	0.005	0.001	0.006	0.00
Impurity-C	ND	ND	NA	ND	NA
Impurity-D	0.028	0.027	0.001	0.027	0.01
Impurity-E	ND	ND	NA	ND	NA
Impurity-F	0.04	0.049	0.009	0.062	0.022
Maximum unknown impurity	0.008	0.008	0	0.009	0.001
Total impurities	0.1	0.11	0.01	0.12	0.02

Table: 1.15 Results for solution stability of test solution at refrigerator

Component	Initial	After 24Hrs	% Difference	After 48Hrs	% Difference
Impurity-A	0.006	0.006	0.00	0.006	0.00
Impurity-C	ND	ND	NA	ND	NA
Impurity-D	0.028	0.027	0.001	0.028	0.00
Impurity-E	ND	ND	NA	ND	NA
Impurity-F	0.04	0.029	0.011	0.030	0.010
Maximum unknown impurity	0.008	0.007	0.01	0.007	0.001
Total impurities	0.1	0.09	0.01	0.09	0.01

Table: 1.16 Results for solution stability of spiked sample at room temperature

Component	Initial	After 24Hrs	% Difference	After 48Hrs	% Difference
Impurity-A	0.206	0.205	0.001	0.206	0.001
Impurity-C	0.177	0.176	0.001	0.177	0.000
Impurity-D	0.237	0.239	0.002	0.239	0.002
Impurity-E	0.195	0.195	0.000	0.195	0.00
Impurity-F	0.239	0.245	0.006	0.231	0.008

Table: 1.17 Results for solution stability of spiked sample at refrigerator

Component	Initial	After 24Hrs	% Difference	After 48Hrs	% Difference
Impurity-A	0.206	0.206	0.000	0.205	0.001
Impurity-C	0.177	0.177	0.000	0.176	0.001
Impurity-D	0.237	0.239	0.002	0.239	0.002
Impurity-E	0.195	0.195	0.000	0.194	0.001
Impurity-F	0.239	0.241	0.008	0.238	0.001

5.0 Results & Discussion

A simple, economic, accurate and precise HPLC method was successfully developed. In this method it was carried out by using Inertsil ODS-3V, 250 x 4.6 mm, 5µm column and the mobile phase consists of two Channels A and B. Channel-A: pH 5.80 phosphate buffer : Acetonitrile (90:10 v/v) and Channel-B: Acetonitrile : water (90:10 v/v). The flow rate is 1.0 ml/min. The column temperature was maintained at 25°C and sample temperature was maintained at 25°C, injection volume 10µL and wavelength fixed at 320nm UV-detection. The results obtained were accurate and reproducible. The method developed was statistically validated in terms of selectivity, accuracy, linearity, precision, and stability of solution.

For Selectivity, the chromatograms were recorded for standard and sample solutions of Dasatinib and its related substances. Selectivity studies reveal that the peak is well separated from each other. Therefore the method is selective for the determination of related substances in Dasatinib. There is no interference of diluent and placebo at Dasatinib and impurities peaks. The elution order and the retention times of impurities and Dasatinib obtained from individual standard preparations and mixed standard preparations are comparable.

The limit of detection (LOD) and limit of quantitation (LOQ) for Dasatinib standard 0.147&0.048µg/mL, impurity-A 0.334&0.110 µg/mL, impurity-C 0.184&0.061 µg/mL, impurity-D 0.136&0.045 µg/mL, impurity-E 0.089&0.029 µg/mL and impurity-F 0.222 & 0.073 µg/mL respectively.

The linearity results for Dasatinib and all the impurities in the specified concentration range are found satisfactory, with a correlation coefficient greater than 0.99.Calibration curve was plotted and correlation co-efficient for Dasatinib and its impurities found to be 1.000, 0.9999, 0.9912, 1.000, 0.9932 and 0.9922 respectively.

The accuracy studies were shown as %recovery for Dasatinib and its impurities at specification level. The limit of % recovered shown is in the range of 80 and 120% and the results obtained were found to be within the limits. Hence the method was found to be accurate.

For Precision studies six (6) replicate injections were performed. %RSD was determined from the peak areas of Dasatinib and its impurities. The acceptance limit should be not more than 10, and the results were found to be within the acceptance limits.

6.0. Conclusion

The new HPLC method developed and validated for determination of Dasatinib pharmaceutical dosage forms and assured the satisfactory precision and accuracy and also determining lower concentration of drug in its solid dosage form by RP-HPLC method. The method was found to be simple, accurate, economical and rapid and they can be applied for routine analysis in laboratories and is suitable for the quality control.

Ethical approval

It is not applicable.

Abbreviations

FDA: Food and Drug Administration

API: Active pharmaceutical ingredients

HPLC: High-Performance Liquid Chromatography

RT: Retention Time

LOD: Limit of Detection

LOQ: Limit of Quantification

RRF: Relative Response factor

ICH: International Council on Harmonization

SD: Standard Deviation

RSD: Relative Standard Deviation

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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