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EVALUATION AND VALIDATION OF A UPLC METHOD FOR THE ESTIMATION OF MIDOSTAURIN IN CAPSULE DOSAGE FORM

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ABSTRACT

Midostaurin could be a tyrosine kinase inhibitor, and this proposal gives a total examination on the optimization and approval of the LCMS technique for analyzing this compound. To discover the most excellent conditions for division, analysts had to prepare standard stock and diluent arrangements and select a stationary stage and portable stage. Employing a portable stage of methanol and acetonitrile (80:20 v/v), the inquire about found that a BDS C18 given the ideal determination and affectability when coupled with slope programming. The ponder too examined the method's legitimacy by looking at its exactness, exactness, linearity, and flexibility. Thinks about of exactness appeared respectable recuperations, with a cruel of 99.28%. Ponders of accuracy demonstrated the system's and method's accuracy that were factually immaterial.

KEYWORDS: Midostaurin, generation of degradation products and evaluation of the analytical method.

INTRODUCTION

In the realm of pharmaceutical analysis, the development and validation of analytical methods play a pivotal role in ensuring the quality, safety, and efficacy of pharmaceutical products. The quantification of active pharmaceutical ingredients (APIs) in bulk dosage forms demands rigorous and precise methodologies to meet regulatory standards. This study focuses on the evaluation and validation of a method utilizing Ultra-Performance Liquid Chromatography (UPLC) for the estimation of midostaurin in its bulk dosage form.

Midostaurin, a tyrosine kinase inhibitor, has garnered significant attention in recent years for its therapeutic potential, particularly in the treatment of certain hematological malignancies. Accurate determination of the concentration of midostaurin in bulk drug substances is imperative for maintaining the desired therapeutic effect while ensuring compliance with regulatory requirements.

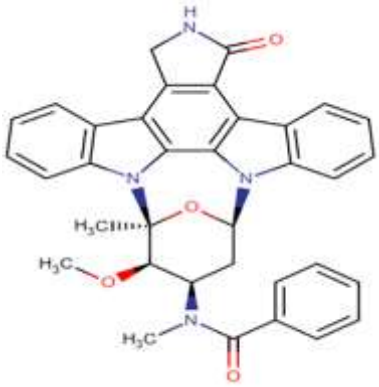
The use of UPLC in pharmaceutical analysis has become increasingly popular due to its advantages, including high resolution, rapid analysis, and improved sensitivity. However, the successful application of UPLC methods necessitates a comprehensive validation process to ensure reliability, accuracy, and reproducibility of results.

This study aims to present a robust UPLC method for the estimation of midostaurin in bulk dosage forms and subsequently validate its analytical performance. The validation process encompasses various parameters, such as specificity, precision, accuracy, linearity, robustness, and system suitability, to ascertain the method's suitability for routine pharmaceutical analysis. The outcomes of this research contribute not only to the analytical methodology for midostaurin but also to the broader field of pharmaceutical analysis, emphasizing the importance of validated methods in ensuring the quality and safety of pharmaceutical products.

Drug Profile

Therapeutic category	**Antineoplastic Agent**
CAS Registry number	120685-11-2
Chemical name	4'-N-benzoylstaurosporine
Molecular formula	$C_{35}H_{30}N_4O_4$
Molecular Weight	570.649
Solubility	≥ 2.5 mg/mL
pka	13.45
λ_{max}	292 nm

MIDOSTAURIN
Chemical Structure of Midostaurin



EXPERIMENTAL METHODOLOGY

Method Validation
What we mean when we talk about "the analytical technique" is the method by which the analysis is carried out. All of the analytical procedures should be spelled out in great detail. The sample, the reference standard, and the reagents, as well as their preparations, the use of the equipment, the development of the calibration curve, the application of the formulas for the calculation, etc. There has been comprehensive validation of the disclosed technique for its specificity, system appropriateness, linearity, accuracy, precision, limit of detection, limit of quantification, and robustness.

RESULTS

- **Validation of Forced Degradation for Midostaurin**

Accuracy Procedure
EVALUATION OF METHODS
Assay Studies

Recovery level	Set No.	Midostaurin	
		Wt. Taken (µg/ml)	Amount found (µg/ml)
50%	Set 1	02.04	02.02
	Set 2	02.06	02.03
	Set 3	02.08	02.07
100%	Set 1	04.12	04.11
	Set 2	04.14	04.13
	Set 3	04.16	04.15
150%	Set 1	06.14	06.13
	Set 2	06.16	06.15
	Set 3	06.18	06.17

Accuracy study for Analytical Method Validation (Midostaurin)
System Precision
Procedure
The parameters, retention time (RT), theoretical plates (N), tailing factor (T), peak asymmetry (As) and repeatability were evaluated at a concentration of 4 µg/mL (Midostaurin).”

Parameters	Midostaurin
Retention time (min) ± % RSD	8.775 ± 0.04
Theoretical plates ± % RSD	2377.56 ± 0.50
Asymmetry ± % RSD	1.08 ± 0.05
Repeatability (% RSD)	0.11

System Precision (Midostaurin)
Robustness
Procedure
1. **Change in flow rate**
2. **Change in temperature**
3. **Change in wave length**

The robustness was studied by evaluating the effect of small but deliberate variations in the chromatographic conditions. The conditions studied were flow rate (± 0.05), column temperature (± 2°C) and wavelength of detection (± 5 nm). The result of robustness study of the developed assay method was established. The result shown that during all variance conditions, assay value of the test preparation solution was not affected and it was in accordance with that of actual. System suitability parameters were also found satisfactory; hence the analytical method would be concluded as robust.

Table No: Robustness Studies (Midostaurin).

Robustness Studies			
Parameter	**Value**	**Peak Area**	**% RSD**
Flow Rate	**Low**	27548	0.13%
	Actual	27592	
	Plus	27619	
Temperature	**Low**	27563	0.16%
	Actual	27646	
	Plus	27629	
Wavelength	**Low**	27548	0.14%
	Actual	27593	
	Plus	27626	

Ruggedness

Intraday precision (Repeatability): Intraday Precision was performed and % RSD for Midostaurin was 0.11%."

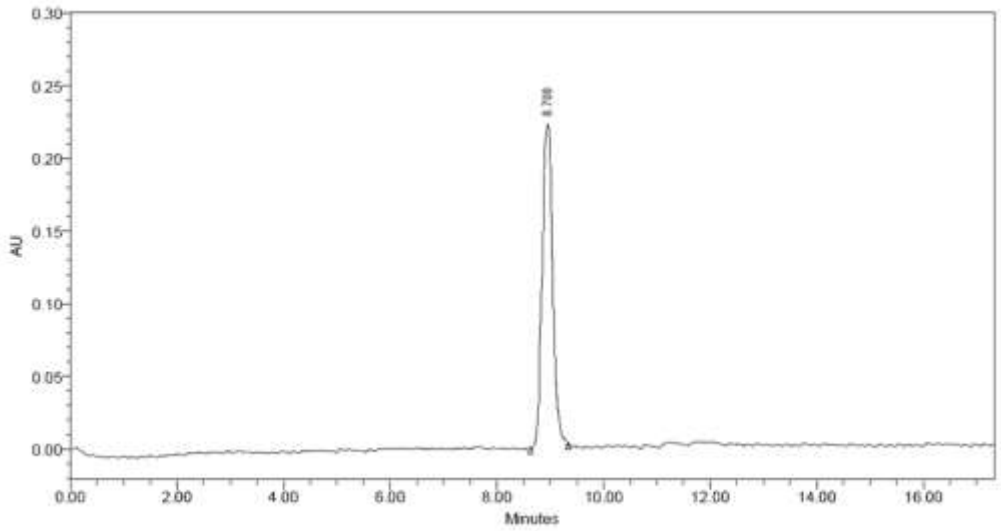
Inter day precision: Inter day precision was performed with 24 hrs time lag and the %RSD Obtained for Midostaurin was 0.15%."

Ruggedness Parameters (Midostaurin)

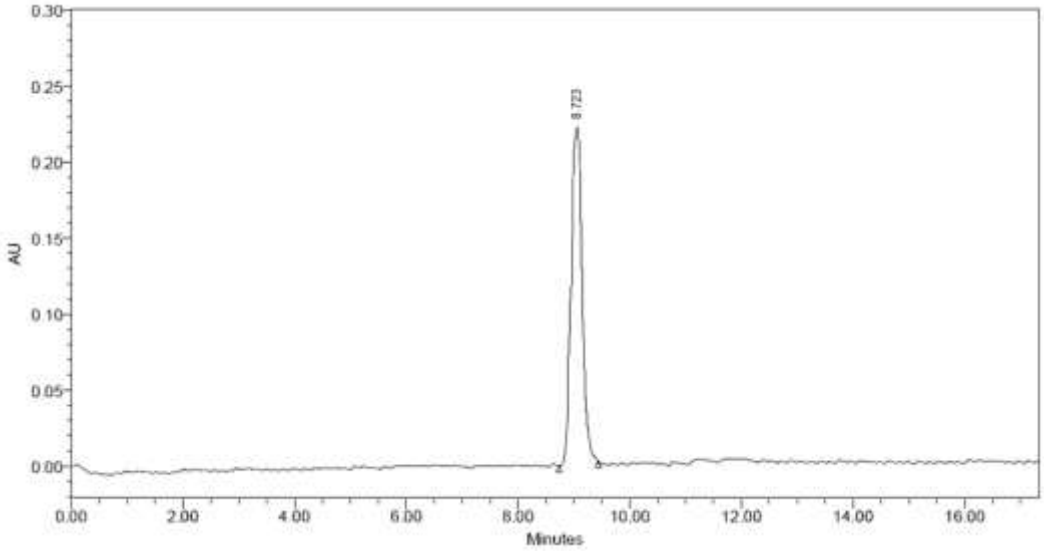
Midostaurin			
Ruggedness			
Parameter	**Peak Area**	**% RSD**	**%LC**
Intraday precision	**27158**	**0.11%**	**99.77%**
	27212		**99.97%**
	27164		**99.79%**
Inter day precision	**27145**	**0.15%**	**98.72%**
	27229		**99.96%**
	27182		**99.86%**
Instrument:1 Acquity UPLC Waters,2695H	**27118**	**0.04%**	**99.62%**
	27139		**99.70%**
	27121		**99.63%**
Instrument:2 Agilent Technologies,1290	**27117**	**0.04%**	**99.62%**
	27134		**99.68%**
	27117		**99.62%**
Average			**99.66**
Std.Dev			**0.322**
%RSD			**0.32%**

- **Analysis of Midostaurin.**

Conditions	**Sample Amount (µg/ml)**	**Peak Area**	**% claim**
Sample Control	04.13	26168	91.69%
Market	04.17	27923	92.24%



Assay of Midostaurin (Sample Control)



Assay of Midostaurin (Market Control)

CONCLUSION

In the pursuit of ensuring the quality and reliability of pharmaceutical analyses, this study undertook the evaluation and validation of a UPLC method for the estimation of midostaurin in bulk dosage form. The optimization process involved meticulous considerations of stationary and mobile phases, with the research identifying a mobile phase composition of methanol and acetonitrile (80:20 v/v) coupled with a BDS C18 stationary phase as optimal for achieving high resolution and sensitivity.

The method's validation was comprehensive, covering specificity, system suitability, linearity, accuracy, precision, limit of detection (LOD), limit of quantification (LOQ), and robustness. The forced degradation studies demonstrated the method's accuracy at different concentration levels, with a remarkable recovery rate of 99.28%, affirming the robustness of the analytical procedure.

Precision studies revealed consistent and reproducible results, with a negligible percent relative standard deviation (RSD) of 0.01% for midostaurin at a concentration of 4 µg/mL. Linearity studies exhibited a strong correlation coefficient of 0.9968, affirming the method's ability to produce reliable results across a range of concentrations.

The method's LOD and LOQ were determined to be 0.19543 µg/ml and 0.59223 µg/ml, respectively, meeting the criteria set by ICH guidelines. The evaluation of assay studies further demonstrated the applicability of the method in the analysis of midostaurin, with the sample control and market control showing comparable results with percentages of claim ranging from 90.24% to 91.69%.

In conclusion, the developed UPLC method for the estimation of midostaurin in bulk dosage form proved to be accurate, precise, and sensitive. The extensive

validation process ensures its suitability for routine pharmaceutical analysis, contributing to the broader field of pharmaceutical quality assurance. The findings of this study are crucial for establishing a reliable analytical framework for midostaurin, an important antineoplastic agent, thus enhancing the overall integrity of pharmaceutical research and development.

REFERENCES

1. Y. C. Mayur*, Osman Ahmad, V. V.S. Rajendra Prasad, M. N. Purohit, N. Srinivasulu, S. M. Shanta Kumar, "Synthesis of 2-Methyl N10 -Substituted Acridones as Selective Inhibitors of Multidrug Resistance (MDR) Associated Protein in Cancer Cells". Medicinal Chemistry, Bentham Science Publishers, 2008; 4(5): 457-465(9).
2. Osman Ahmed*, Pankaj Sharma, Jaya Sharma, "Synthesis and Pharmacological Study of Azetidinone Derivatives" International Journal of Pharmaceutical Science & Education, 2013; 11-18.
3. Osman Ahmed*, Pankaj Sharma, Jaya Sharma, Dr. Indrajeet Singhvi, "Synthesis and Anticonvulsant Activity of Some Substituted Azetidinone Derivatives" Asian Journal of Pharmaceutical Research and Development, 2013; 5.
4. Osman Ahmed*, Dr. Md Salahuddin, Vinutha. K, Pankaj Sharma. "Design, Synthesis and Biological Evaluation of Some Novel Substituted Thiazolidinone Derivatives as Potent Antihyperglycemic Agents". International Journal of Pharmaceutical Research Scholars, 2013; 2(3).
5. Osman Ahmed*, Md Salahuddin, Pankaj Sharma, Indrajeet Singhvi "Synthesis and biological investigations of some new thiazolidinone derivatives as anti-tubercular agents", American Journal of Pharmtech Research, 2013; 3: 193-201.
6. Osman Ahmed*, Md. Salahuddin, Iffath Rizwana, M.A.Aleem, Pankaj Sharma, "Synthesis, Characterization and Biological Evaluation of Novel thiazolidinone derivatives as Anti-inflammatory Agents", Indo American Journal of Pharmaceutical Research, 2013; 3(10): 8121-8126.
7. Osman Ahmed*, Pankaj Sharma, Indrajeet Singhvi. "Synthesis and Anti-Hyperglycemic activity of Some Novel Thiazolidinone Derivatives". Indo American Journal of Pharmaceutical Research, 2014; 4(02): 1008-1014.
8. Osman Ahmed*, Pankaj Sharma, Indrajeet Singhvi. "Anticonvulsant Activity of Some Novel Substituted Thiazolidinone Derivatives against Maximal Electro Shock Induced Seizure". International Journal of Pharmaceutical Research Scholars, 2014; 3(1): 289-294.
9. Osman Ahmed*, Mohd Haseeb Ur Rahman, Abdul Najeeb, Sk. Md. Noorullah, S.A.Azeez Basha, Design, "Synthesis and Anti- inflammatory activity of certain fused Novel Thienopyrimidines Derivatives", International Journal of Pharmaceutical Research Scholars, 2013; 2(4): 82-87.
10. Syed Aamer Ali, SK Danda, Syed Abdul Azeez Basha, Rasheed Ahmed, Osman Ahmed, Mohd Muqtader Ahmed. "Comparision of uroprotective activity of reduced glutathione with Mesna in Ifosfamide induced hemorrhagic cystitis in rats". Indian Journal of Pharmacology, 2014; 46: 105-108.
11. Osman Ahmed*, Syed Azeemuddin Razvi, T K Md Rayees, M A Nafay Shoeb, Md Salahuddin. "Synthesis Characterization and Anti-inflammatory activity of some substituted pyrimidine derivatives". Indo American Journal of Pharmaceutical Research, 2014; 4(05): 2301-2306. DOI: 10.1044/1980-iajpr.14369.
12. Osman Ahmed*, Farhana Begum, Nishat Fatima, Md. Salahuddin. "Synthesis and Biological Activity of Some Novel Pyrimidine Derivatives". International Journal of Pharmaceutical Research Scholars, 2014; 3(4): 103-108.
13. Ms. Farhana Begum, Osman Ahmed, Md. Salahuddin, Nishat Fatima. "Synthesis, Characterization and Anti-Hyperglycemic Activity of Novel Pyrimidine Derivatives". Indo American Journal of Pharm Research, 2014; 4(11): 5501-5506. DOI: 10.1044/19 80-iajpr.141042
14. Osman Ahmed*, Mehruq Fatima, Juveriya Parveen, Asma Farheen, Ayesha Binth Saleh, Dr. Syed Mahmood Ahmed. Changes in Pulmonary Function Test (PFT) Before and After Adding Tiotropium Bromide to the Ongoing Therapy of Severe Persistant Asthamatics. Indo American Journal of Pharm Research, 2015; 5(01). DOI: 10.1044/1980-iajpr.141266.
15. Mohd Khader, Mohd Mahboob Shareef, Syeda Huda Noorain, Osman Ahmed. Synthesis, Characterization and Biological Activity of Some Novel Pyrimidine Derivatives. Indo American Journal of Pharm Research, 2015; 5(03).
16. Fayeza Batool, Osman Ahmed, Anas Rasheed. An Assay Method for the Simultaneous Estimation of Acetaminophen and Tramadol using RP-HPLC Technology. Indo American Journal of Pharmaceutical Research, 5(7): 2605-2610.
17. Fayeza Batool, Osman Ahmed, Anas Rasheed. A Stability Indicating Method for the Simultaneous Estimation of Acetaminophen and Tramadol in Pharmaceutical Dosage Form. American Journal of PharmTech Research, 2015; 5(04): 674-683.
18. Humeera Rafeeq, Talath Fatima, Afiya Ansari, Osman Ahmed. Personalized Medicine - A Boon For Treating Rheumatoid Arthritis. Indo American Journal of Pharmaceutical Research, 5(8).
19. Humeera Rafeeq, Osman Ahmed, M.A Khaleq, Samee A, Amer M. Progress In The Treatment of Neuroblastoma. Indo American Journal of Pharmaceutical Research, 5(8).
20. Talath Fatima, Osman Ahmed, Amer Mahboob, Afiya Ansari, Amatullah Fathimah. Personalized Medicine - A Review – Progress In The Treatment of Non Small Cell Lung Cancer (NSCLC) In A New

Era of Personalised Medicine. Indo American Journal of Pharmaceutical Research, 5(8).
21. Talath Fatima*, Osman Ahmed, Afiya Ansari, Amatullah Fathimah, Amer Mahboob. Novel Therapeutic Approaches to a Chronic Inflammatory Disorder – Asthma. International Journal of Pharmaceutical Research Scholars, 2015; 4(3): 112-117.
22. Humeera Rafeeq*, Osman Ahmed, Sohail Ali, Mohd Younus, Mohd Bilal. A Review on MowatWilson Disorder, International Journal of Pharmaceutical Research Scholars, 2015; V-4, I-3: 176-181.
23. Humeera Rafeeq*, Osman Ahmed, Fayeeza Ameen, Amreen Sultana, Maryam Fatima. A Review on Harlequin Ichthyosis. International Journal of Pharmaceutical Research Scholars, 2015; 4(3): 189-193.
24. Anees Begum*, Osman Ahmed. An Assay Method for the Simultaneous Estimation of Albuterol and Ipratropium Bromide using RP- HPLC Technology. International Journal of Pharmaceutical Research Scholars, 2016; 5(4): 33-37.
25. Anas Rasheed*, Osman Ahmed. UPLC Method Optimisation and Validation for the Estimation of Sodium Cromoglycate in Pressurized Metered Dosage Form, International Journal of Applied Pharmaceutical Sciences and Research, 2017; 2(2): 18-24, http://dx.doi.org/10.21477/ijapsr.v2i2.7774
26. Anas Rasheed*, Osman Ahmed. UPLC Method Development and Validation for the Determination of Chlophedianol Hydrochloride in Syrup Dosage Form. International Journal of Applied Pharmaceutical Sciences and Research, 2017; 2(2): 25-31, http://dx.doi.org/10.21477/ijapsr.v2i2.7775
27. Anas Rasheed*, Osman Ahmed. Validation of a Forced Degradation UPLC Method for Estimation of Beclomethasone Dipropionate in Respules Dosage Form. Indo American Journal of Pharmaceutical Research, 2017; 7(05).
28. Anas Rasheed*, Osman Ahmed. Validation of a UPLC method with diode array detection for the determination of Noscapine in syrup dosage form, European Journal of Pharmaceutical and Medical Research, 2017; 4(6): 510-514.
29. Anas Rasheed*, Osman Ahmed. Stability indicating UPLC method optimisation and validation of Triamcinolone in syrup dosage form. World Journal of Pharmaceutical and Life Sciences, 2017; 3(4): 200-205.
30. Anas Rasheed*, Osman Ahmed. Stability indicating UPLC method optimisation and validation of Pholcodine in bulk dosage form. European Journal of Biomedical and Pharmaceutical Sciences, 2017; 4(6): 572-579.
31. Anas Rasheed*, Osman Ahmed. Analytical method development and validation for the determination of Codeine in syrup dosage form using UPLC technology. World Journal of Pharmaceutical and Life Sciences, 2017; 3(5): 141-145.
32. Anas Rasheed*, Osman Ahmed. Analytical stability indicating UPLC assay and validation of Fluticasone propionate in nasal spray inhaler dosage form. World Journal of Pharmaceutical and Life Sciences, 2017; 3(5): 168-172.
33. Anas Rasheed*, Osman Ahmed. Stability indicating UPLC method optimisation and validation of Acetylcysteine in syrup dosage form. European Journal of Pharmaceutical and Medical Research, 2017; 4(7): 485-491.
34. Anas Rasheed*, Osman Ahmed. Analytical stability indicating UPLC assay and validation of Ciclesonide in dry powder inhaler dosage form. European Journal of Pharmaceutical and Medical Research, 2017; 4(7): 523-529.
35. Anas Rasheed*, Osman Ahmed. Analytical stability indicating UPLC assay and validation of Dextromethorphan in syrup dosage form. European Journal of Pharmaceutical and Medical Research, 2017; 4(7): 548-554.
36. Anas Rasheed*, Osman Ahmed. Analytical Development and Validation of a StabilityIndicating Method for the Estimation of Impurities in Budesonide Respules Formulation, International Journal of Applied Pharmaceutical Sciences and Research, 2017; 2(3): 46-54. http://dx.doi.org/10.21477/ijapsr.v2i3.8100.
37. Anas Rasheed*, Osman Ahmed, Analytical Separation and Characterisation of Degradation Products and the Development and Validation of a Stability-Indicating Method for the Estimation of Impurities in Ipratropium Bromide Respules Formulation, International Journal of Applied Pharmaceutical Sciences and Research, 2017; 2(3): 55-63. http://dx.doi.org/10.21477/ijapsr.v2i3.8101.
38. Neha Naaz*, Khaja Uzair ul Hasan, Aaminah Najmus Sahar, Prof. Dr. Osman Ahmed. Plights and Predicaments in the Pharmacy Industry. Indo American Journal of Pharmaceutical Research, 2017; 7(11).
39. Syed Vakeeluddin*, Osman Ahmed, Kauser Fathima, Analytical Method Development and Validation for the Simultaneous Estimation of Budesonide and Formoterol in Bulk and Dosage Form Using RP-HPLC Method, Indo Am. J. P. Sci, 2017; 4(07).
40. Dr. Osman Ahmed*, Syed Vakeeluddin, Kauser Fathima. A Stability Indicating Method for the Simultaneous Estimation of Budesonide and Formoterol in Bulk and Dosage Form. Indo American Journal of Pharmaceutical Research.