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DEGRADATION UNDER STRESS CONDITIONS: A DETAILED REVIEW FOR SORAFENIB

Alufa Tahreem*[1], Dr. Osman Ahmed[1] and Dr. Anas Rasheed[2]

[1]Department of Pharmaceutical Analysis, Deccan School of Pharmacy, Hyderabad.
[2]CSO, Gaelib Medications Private Limited, Hyderabad.

***Corresponding Author: Alufa Tahreem**
Department of Pharmaceutical Analysis, Deccan School of Pharmacy, Hyderabad.

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ABSTRACT

Background: Sorafenib is a multi-kinase inhibitor used in the treatment of renal cell carcinoma, hepatocellular carcinoma, and thyroid cancer. Despite its efficacy, Sorafenib is prone to degradation under various stress conditions, which can affect its safety, efficacy, and stability. Understanding these degradation pathways is critical for developing robust formulations and ensuring regulatory compliance. **Aim:** This review aims to explore the degradation behavior of Sorafenib under different stress conditions, including acidic, basic, oxidative, thermal, and photolytic environments, and to analyze the implications for its stability and quality control. **Research Methodology:** A comprehensive literature review was conducted, focusing on forced degradation studies and their impact on Sorafenib. The research evaluated the degradation mechanisms, analytical techniques for identifying degradation products, and the stability profile of Sorafenib under various stress conditions. **Conclusion:** Sorafenib undergoes significant degradation under acidic, basic, oxidative, thermal, and photolytic conditions, leading to the formation of degradation products that can compromise its therapeutic efficacy. Stress testing, including chromatography and mass spectrometry, is essential for assessing and controlling these degradation pathways, ensuring the drug's safety and effectiveness in clinical use.

KEYWORDS: Sorafenib, degradation, stability.

INTRODUCTION

Sorafenib is a potent oral multi-kinase inhibitor commonly used in the treatment of advanced renal cell carcinoma (RCC), hepatocellular carcinoma (HCC), and thyroid cancer. By inhibiting various kinases involved in tumor cell proliferation and angiogenesis, Sorafenib plays a crucial role in managing these malignancies. However, the chemical complexity of Sorafenib and its susceptibility to degradation under stress conditions necessitate a thorough understanding of its stability profile. Degradation can lead to the formation of impurities, which can compromise the drug's efficacy, safety, and quality. Therefore, stress testing is essential for developing robust analytical methods and ensuring the stability of Sorafenib during formulation and storage.

This review discusses the degradation of Sorafenib under various stress conditions, including acidic, basic, oxidative, thermal, and photolytic conditions. These stress conditions are essential for understanding how Sorafenib behaves under environmental and physiological stresses, and the review focuses on the mechanisms behind its degradation, the formation of degradation products, and the methods used to study its stability.

Chemical Structure and Stability of Sorafenib: Sorafenib (chemical name: N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoyl pyridin-4-yloxy) phenyl) urea) has a molecular weight of 464.82 g/mol. It is slightly soluble in water and more soluble in organic solvents such as methanol and acetonitrile. This physicochemical profile influences the choice of analytical techniques for its stability testing.

The structural complexity of Sorafenib contributes to its instability under various environmental conditions. It is prone to degradation due to hydrolysis, oxidation, and photolysis. The stability of Sorafenib in pharmaceutical formulations is, therefore, an important consideration for maintaining its therapeutic efficacy and ensuring patient safety. Stress testing Sorafenib under various conditions helps in identifying potential degradation products, which may affect the drug's quality.

Stress Testing: Overview and Regulatory Framework: The International Council for Harmonisation (ICH) guidelines (specifically ICH Q1A and Q1B) recommend the use of forced degradation studies as part of the stability testing for pharmaceutical substances. These studies aim to accelerate the degradation process and identify potential degradation products, which can then be evaluated for their potential impact on the drug's safety and efficacy.

Stress testing typically involves exposing the drug substance to extreme conditions, such as elevated temperatures, high humidity, acidic or basic conditions, or exposure to light. By understanding the degradation pathways, regulatory authorities can assess the stability of the drug and determine appropriate storage conditions.

Degradation under Acidic Conditions: Acidic hydrolysis is a common degradation pathway for many pharmaceutical compounds. Sorafenib, when exposed to acidic conditions, undergoes hydrolysis that can lead to the breaking of chemical bonds, particularly in the urea moiety of its structure. This type of degradation is typically studied by exposing the drug to strong acid solutions such as hydrochloric acid (HCl) at elevated temperatures, mimicking accelerated storage conditions.

For example, Sorafenib undergoes hydrolysis under acidic conditions, which affects its functional groups. Degradation under these conditions can lead to the formation of acidic degradation products, which can be identified using chromatographic techniques like high-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC).

Mechanism of Acidic Degradation: The hydrolysis of the urea bond in Sorafenib may break down the molecule into smaller components, potentially generating inactive or toxic byproducts. Forced degradation studies have shown that the formation of these degradation products can reduce the potency of the drug and may result in adverse effects when these impurities are present in the final formulation.

Degradation under Basic Conditions: Basic hydrolysis is another critical stress condition for Sorafenib. The degradation under basic conditions is typically studied by exposing Sorafenib to strong alkaline solutions, such as sodium hydroxide (NaOH), at elevated temperatures. In this condition, the molecule may undergo cleavage at susceptible sites, such as the urea or aromatic moieties.

Mechanism of Basic Degradation: Under basic conditions, Sorafenib may experience nucleophilic attack from hydroxide ions, leading to the cleavage of bonds in the drug's structure. The formation of degradation products under basic stress conditions is crucial to assess, as these products may alter the drug's pharmacological activity. Studies suggest that base-catalyzed degradation of Sorafenib leads to the formation of carboxylated byproducts, which could compromise the drug's therapeutic value.

Analysis of Basic Degradation: Chromatographic techniques such as UPLC are used to identify and quantify degradation products formed under basic conditions. The retention times of Sorafenib and its degradation products can be monitored to evaluate the extent of degradation. Additionally, these methods help confirm the stability of Sorafenib in formulations under alkaline conditions, ensuring that the degradation products do not exceed acceptable levels.

Oxidative Degradation: Oxidative degradation is another critical pathway for Sorafenib, particularly because oxidation can occur during the drug's storage, leading to the formation of reactive oxygen species (ROS) that affect the drug's stability. Oxidative degradation typically involves exposing the drug to agents such as hydrogen peroxide (H2O2) or oxygen, which promotes the breakdown of chemical bonds in Sorafenib.

Mechanism of Oxidative Degradation: In the case of Sorafenib, oxidative stress can lead to the oxidation of sensitive functional groups, particularly those in the aromatic rings or the urea moiety. Oxidative degradation can result in the formation of oxidized byproducts, which may reduce the drug's efficacy or lead to toxic effects.

Oxidative degradation of Sorafenib is of particular concern for the pharmaceutical industry, as exposure to oxygen or oxidizing agents can occur during manufacturing, packaging, or storage. Understanding the degradation products formed during oxidative degradation is essential to developing appropriate storage conditions and packaging materials.

Analysis of Oxidative Degradation: Degradation products of Sorafenib under oxidative conditions are typically analyzed using HPLC, UPLC, or mass spectrometry (MS). These techniques enable the detection of even trace levels of oxidation products, ensuring that the drug remains within acceptable limits for therapeutic use.

Thermal and Photolytic Degradation: Thermal degradation refers to the breakdown of Sorafenib when exposed to elevated temperatures. Sorafenib may degrade at high temperatures due to bond cleavage or structural rearrangement. This is typically studied by exposing the drug to heat at temperatures higher than those encountered during typical storage or processing.

Mechanism of Thermal Degradation: Under high temperature conditions, the rate of molecular motion increases, which can promote bond dissociation and the formation of degradation products. Sorafenib's stability at higher temperatures is assessed by simulating

accelerated degradation conditions, helping to define appropriate storage temperatures.

Photolytic degradation, on the other hand, involves the breakdown of Sorafenib due to exposure to light. Sorafenib's chemical structure contains chromophores that can absorb ultraviolet (UV) or visible light, potentially leading to chemical reactions and the formation of degradation products.

Analysis of Thermal and Photolytic Degradation: Thermal degradation studies are typically conducted by storing Sorafenib samples at high temperatures for extended periods and analyzing them for the presence of degradation products. Photolytic degradation can be studied by exposing Sorafenib to UV light and assessing the stability of the drug. Both thermal and photolytic degradation studies are essential to determine the stability of Sorafenib in different environmental conditions, such as varying storage temperatures or light exposure during transport.

Impurity Profiling and Identification: One of the most critical aspects of degradation studies is the identification and quantification of degradation products or impurities. These impurities are formed as a result of the degradation of Sorafenib under stress conditions, and their presence can significantly affect the drug's efficacy and safety.

Chromatographic Techniques for Impurity Profiling: Chromatographic methods such as HPLC, UPLC, and gas chromatography (GC) are commonly employed for impurity profiling in Sorafenib. These techniques allow for the separation of Sorafenib from its degradation products, facilitating the identification of impurities based on their retention times and spectral characteristics.

Mass Spectrometry for Structural Elucidation: Mass spectrometry (MS), often coupled with chromatography (LC-MS or GC-MS), is used to determine the molecular weights of the degradation products and confirm their structures. This helps in understanding the chemical nature of the degradation products and assessing whether they pose any risks to drug safety.

CONCLUSION

Degradation under stress conditions is a crucial aspect of evaluating the stability of Sorafenib and ensuring its quality throughout its lifecycle, from manufacturing to storage and use. Sorafenib undergoes degradation under a variety of stress conditions, including acidic, basic, oxidative, thermal, and photolytic conditions, which can result in the formation of impurities that may affect the drug's efficacy and safety. Forced degradation studies play a vital role in understanding these degradation pathways and in identifying potential impurities that can compromise the drug's therapeutic potential.

Through the use of various analytical techniques, including HPLC, UPLC, and MS, the pharmaceutical industry can monitor the degradation of Sorafenib and ensure that it remains within acceptable limits for clinical use. Understanding the degradation behavior of Sorafenib under stress conditions is essential for developing stability-indicating methods and ensuring regulatory compliance, thereby supporting the safe and effective use of this important anti-cancer drug.

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 Pharm Tech 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 Stability Indicating 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.
41. Kauser Fathima*, Dr. Osman Ahmed, Syed Vakeeluddin, Analytical Method Development and Validation for the Simultaneous Estimation of Ofloxacin and Metronidazole in Bulk and Dosage Form Using RP-HPLC, Indo Am. J. P. Sci., 2017; 4(07).
42. Dr. Osman Ahmed*, Kauser Fathima, Syed Vakeeluddin. A Stability Indicating Method for the Simultaneous Estimation of Ofloxacin and Metronidazole in Bulk and Dosage Form. Indo American Journal of Pharmaceutical Research, 2018; 8(01).
43. Mohd Shafi, Osman Ahmed, Anas Rasheed, Validation Of A UPLC Method With Diode Array Detection Using C18 Column For The Determination Of Fluorometholone In Parenteral Dosage Form, Indo Am. J. P. Sci; 2018; 05(07).
44. Validation Of A Forced Degradation Uplc Method For Estimation Of Glibenclamide In Oral Dosage Form, Dr. Osman Ahmed, Mohd Kareem Ahmed and Dr. Anas Rasheed. World Journal of Pharm. and Life Sci., 2019; 5(10): 74-82.
45. Evaluation and Validation of A UPLC Method for Simultaneous Estimation Of Glimepiride, Metformin And Voglibose In Oral Dosage Form, Mohd Kareem Ahmed, Dr. Osman Ahmed and Dr. Anas Rasheed. European Journal of Biomedical and Pharmaceutical Sciences, 2019; 6(13): 329-337.
46. Stability Indicating Method Evaluation And Validation For Simultaneous Estimation Of Glimepiride, Metformin And Voglibose In Oral Dosage Form Using LCMS, Mohd. Kareem Ahmed, Dr. Osman Ahmed and Dr. Anas Rasheed European Journal of Biomedical and Pharmaceutical Sciences, 2019; 6(13): 338-349.
47. Stability Indicating Method Evaluation And Validation For Simultaneous Estimation Of Metformin And Sitagliptin In Oral Dosage Form Dr. Osman Ahmed, Mohd Kareem Ahmed and Dr. Anas Rasheed, European Journal Of Pharmaceutical And Medical Research, 2019; 6(12): 494-502.
48. Evaluation And Validation Of A UPLC Method For Simultaneous Estimation Of Metformin And Sitagliptin In Oral Dosage Form Dear Dr. Osman Ahmed, Mohd Kareem Ahmed and Dr. Anas Rasheed European Journal Of Pharmaceutical And Medical Research, 2019; 6(12): 494-502.
49. Evaluation and Validation of A UPLC Method For Estimation Of Amoxyclav In Oral Dosage Form. Dr. Osman Ahmed*, Sumaiya Fatima and Dr. Anas Rasheed, World Journal of Pharm. and Life Sci., 2020; 6(9): 107-113.
50. RESPULES *Sumaiya Fatima, Dr. Osman Ahmed and Dr. Anas Rasheed, World Journal of Pharm. and Life Sci., 2020; 6(9): 68-77.
51. POLYMORPHISM Sumaiya Fatima*, Dr. Osman Ahmed and Dr. Anas Rasheed World Journal of Pharm. and Life Sci., 2020; 6(9): 78-93.
52. Chemical force degradation assay method evaluation for simultaneous estimation of amoxicillin and potassium clavulanate in oral dosage form Sumaiya Fatima*, Dr. Osman Ahmed and Dr. Anas Rasheed, European Journal of Pharmaceutical and Medical Research, 2020; 7(9): 320-325.
53. Characterization of force degradation assay method evaluation for simultaneous estimation of amoxicillin and potassium clavulanate in oral dosage form using UPLC-MS/MSN Sumaiya Fatima*, Dr.

Osman Ahmed and Dr. Anas Rasheed ejbps; 2020; 7(9): 285-294.
54. Evaluation and validation of a uplc method for simultaneous estimation of amoxicillin and potassium clavulanate in oral dosage form. Sumaiya Fatima*, Dr. Osman Ahmed and Dr. Anas Rasheed. European Journal of Pharmaceutical And Medical Research, 2020; 7(9): 326-335.
55. Spiked force degradation assay method evaluation for estimation of amoxyclav in oral dosage form. Dr. Osman Ahmed*, Sumaiya Fatima and Dr. Anas Rasheed. World Journal of Pharm. and Life Sci., 2020; 6(9): 185-191.
56. Anas Rasheed Et.Al; Validation Of A Uplc Method With Diode Array Detection Using C18 Column For The Determination Of Fluorometholone In Parenteral Dosage Form, Indo American Journal Of Pharmaceutical Sciences, Iajps; 2016; 5(7): 6209-6215.
57. Anas Rasheed Et.Al; Analytical Method Development And Validation For The Determination Of Fluorometholone Using C8 Column In Parenteral Dosage Form By Uplc Technology, World Journal Of Pharmaceutical And Life Sciences, Wjpls; 2018; 4(8): 106-109.
58. Anas Rasheed ET. Al; Analytical Stability Indicating Uplc Assay And Validation Using C18 Column For Fluorometholone In Parenteral Dosage Form, World Journal Of Pharmaceutical And Life Sciences, Wjpls; 2018; 4(8): 110-114.
59. Anas Rasheed Et.Al; Validation Of A Forced Degradation Uplc Method Using C8 Column For Fluorometholone In Parenteral Dosage Form, European Journal Of Pharmaceutical And Medical Research, Ejpmr; 2018; 5(8): 311-318.
60. Anas Rasheed Et.Al; Analytical Separation And Characterisation Of Degradation Products Method For The Estimation Of Impurities In Fluorometholone In Parenteral Dosage Form, European Journal Of Pharmaceutical And Medical Research, Ejpmr; 2018; 5(8): 319-324.
61. Anas Rasheed Et.Al; Validation Of A Forced Degradation Uplc Method For Estimation Of Glibenclamide In Oral Dosage Form, World Journal Of Pharmaceutical And Life Sciences, Wjpls; 2019; 5(10): 74-82.
62. Anas Rasheed Et.Al; Evaluation And Validation Of A Uplc Method For Simultaneous Estimation Of Glimepiride, Metformin And Voglibose In Oral Dosage Form, European Journal Of Biomedical And Pharmaceutical Sciences, Ejbps; 2019; 13(6): 329-337.
63. Anas Rasheed Et.Al; Stability Indicating Method Evaluation And Validation For Simultaneous Estimation Of Glimepiride, Metformin And Voglibose In Oral Dosage Form Using Lcms, European Journal Of Biomedical And Pharmaceutical Sciences, Ejbps; 2019; 6(13): 338-349.
64. Anas Rasheed Et.Al; Evaluation And Validation Of A Uplc Method For Simultaneous Estimation Of Metformin And Sitagliptin In Oral Dosage Form, European Journal Of Pharmaceutical And Medical Research, Ejpmr; 2019; 6(12): 365-371.
65. Anas Rasheed Et.Al; Stability Indicating Method Evaluation And Validation For Simultaneous Estimation Of Metformin And Sitagliptin In Oral Dosage Form, European Journal Of Pharmaceutical And Medical Research, Ejpmr; 2019; 6(12): 494-502.
66. Anas Rasheed Et.Al; 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.
67. Anas Rasheed Et.Al; 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.
68. Anas Rasheed Et.Al; Analytical Method Development And Validation For The Determination Of Codeine In Syrup Dosage Form Using Uplc Technology, World Journal Of Pharmaceutical And Life Sciences, Wjpls; 2017; 3(5): 141-145.
69. Anas Rasheed Et.Al; 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, Ejpmr; 2017; 4(6): 510-514.
70. Anas Rasheed Et.Al; Validation Of A Forced Degradation Uplc Method For Estimation Of Beclomethasone Dipropionate In Respules Dosage Form Indoamerican Journal Of Pharmaceutical Research, 2017; 7(05): 8608-8616.