

LC–MS/MS PROFILING OF STRESS-INDUCED DEGRADATION PRODUCTS OF AVAPRITINIB AND DEVELOPMENT OF A STABILITY-INDICATING HPLC METHOD FOR ITS QUANTIFICATION AND IMPURITY ANALYSIS

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References:

1. Wu C. P., Lusvarghi S., Wang J. C., Hsiao S. H., Huang Y. H., Hung T. H., Ambudkar S. V. Avapritinib: A Selective Inhibitor of KIT and PDGFR α that Reverses ABCB1 and ABCG2-Mediated Multidrug Resistance in Cancer Cell Lines. *Mol Pharm.* **2019**, 16 (7), 3040-3052. <https://doi.org/10.1021/acs.molpharmaceut.9b00274>
2. Mazzocca A., Napolitano A., Silletta M., Spalato Ceruso M., Santini D., Tonini G., Vincenzi B. New frontiers in the medical management of gastrointestinal stromal tumours. *Ther. Adv. Med. Oncol.* **2019**, 11, 1758835919841946 <https://doi.org/10.1177/1758835919841946>
3. Li J., Zhang X., Deng Y., Wu X., *et al.*, Efficacy and Safety of Avapritinib in Treating Unresectable or Metastatic Gastrointestinal Stromal Tumors: A Phase I/II, Open-Label, Multicenter Study. *Oncologist.* **2023**, 28 (2), 187-e114 <https://doi.org/10.1093/oncolo/oyac242>
4. Amgoth K. M., Tummala S. R. LC-MS/MS approach for the quantification of five genotoxic nitrosoimpurities in varenicline. *J. Pharm. Res.* **2022**, 26 (6), 1685-1693. <https://doi.org/10.29228/jrp.259>
5. Rajesh Varma Bhupatiraju., Srinivasa Kumar B., Pavani Peddi., Venkata Swamy Tangeti. An effective HPLC method for evaluation of process related impurities of Letermovir and LC-MS/MS characterization of forced degradation compounds. *J. Chem. Metrol.* **2023**, 2 (2), 181-198. <https://doi.org/10.25135/jcm.98.2311.2975>
6. Tummala S. R., Gorrepati N., Tatapudi H. K. Head Space GC-MS/MS Method for Quantification of Five Nitrosoamine-Genotoxic Impurities in Metformin HCl. *Curr. Pharm. Anal.* **2024**, 20 (8), 944 –952. <https://doi.org/10.2174/0115734129332940240919113159>
7. Rajesh Varma Bhupatiraju., Bikshal Babu Kasimala., Lavanya Nagamalla., Fathima Sayed. Structural evaluation of degradation products of Loteprednol using LC-MS/MS: Development of an HPLC method for analyzing process-related impurities of Loteprednol. *Anal. Sci. Technol.* **2024**, 37 (2), 98-113. <https://doi.org/10.5806/AST.2024.37.2.98>
8. Tummala S. R., Amgoth K. P. Development of GC-MS/MS Method for Simultaneous Estimation of Four Nitrosoamine Genotoxic Impurities in Valsartan. *Turk. J. Pharm. Sci.* **2022**, 19 (4), 455-461. <https://doi.org/10.4274/tjps.galenos.2021.17702>
9. Ravinder Bairam., Hemant Kumar Tatapudi., Vijay Srinivas Pothula., Likhitha Akaram., Sambasiva Rao Tummala., Naveena Gorrepati. Analytical quality by design approach in RP-HPLC method development for the quantification of mirabegron and solifenacin succinate in pharmaceutical formulation. *Letf. Appl. Nano. BioScience.* **2024**, 14 (1), 1-12. <https://doi.org/10.33263/LIANBS141.048>
10. Rajesh Varma Bhupatiraju., Pavani Peddi., Subhashini Edla., Kandula Rekha., Bikshal Babu Kasimala. Green Analytical Approach for HPLC Method Development for Quantification of Sorafenib and Its Pharmacopeia Impurities: LC–MS/MS Characterization and Toxicity Prediction of Stress Degradation Products. *Sep. sci. plus.* **2024**, 7 (9), e202400106. <https://doi.org/10.1002/sscp.202400106>
11. Suvasish Mishra., Koushik Sarker., Avijit Ghosh., Abhijit Saha., Subrata Sen. A Validated Stability Indicating RP-HPLC method for estimation of Avapritinib in bulk and tablet dosage form. *Int. J. App. Pharm.* **2022**, 14 (2), 95-101. <https://dx.doi.org/10.22159/ijap.2022v14i2.43432>
12. Sruthi Uppari., Gade Sammaiah. Stability Indicating RP-HPLC method development and validation for the quantitative estimation of avapritinib in API form and marketed pharmaceutical dosage form. *Int. j. pharm. res. Health. sci.* **2023**, 11 (3): 3636-3643.
13. Thakur Gajender Singh., Jagadeesh Babu Vadlakonda., Rama Mohan Gupta V. Analytical method development and validation of avapritinib by RP-HPLC method. *WJPPS.* **2020**, 9 (10), 1834-1840. <https://dx.doi.org/10.20959/wjpps202010-17283>
14. Rasagna P., Kalyani G. Development and validation of analytical RP-HPLC method for the quantitative determination of avapritinib in pure substances and marketed pharmaceutical tablet forms. *IJMGE.* **2024**, 05 (01), 100-107.
15. Sridhar Babu R., Syed Hafeez Ahmed., Shaik Mohd Khasim., Syeda Nusrath Fatima., Qayam Ali Khan., Lubna Hashmi., Hajira Samreen., Muneeza Fatima. RP-HPLC method development and validation for the estimation of avapritinib in bulk form and marketed pharmaceutical dosage form. *IJMGE.* **2024**, 05 (01), 161-167.

16. Xuegu Xu., Shunbin Luo., Qiang Yang., Yingjie Wang., Wenlong Li., Guanyang Lin., Ren-ai Xu. Development and validation of the quantitative determination of avapritinib in rat plasma by a bioanalytical method of UPLC-MS/MS. *Arab. J. Chem.* **2021**, 14 (6), 103152. <https://doi.org/10.1016/j.arabjc.2021.103152>
17. Gowri Kusuma Kumari., Kantipudi Rambabu. Bio-analytical Method Development and Validation for avapritinib in Rat Plasma by LC-MS/MS. *J. Pharm. Sci. & Res.* **2021**, 13 (3), 134-137.
18. Baher Salman I., Roshdy Saraya E., Yasser Hassan F., Ahmed Hassan I., Hany Batakoushy A., Mohamed Abdel-Aal A. A., Ahmed Al-Harrasi., Adel Ehab Ibrahim. A green bioanalytical spectrofluorimetric approach for estimation of avapritinib anti-tumor drug; application to quality control and clinical studies. *Bioanal.* **2025**, 17 (1), 31-40. <https://doi.org/10.1080/17576180.2025.2451518>
19. Teuber A., Schulz T., Fletcher B. S., Gontla R., Mühlenberg T., Zischinsky M.L., Niggenaber J., Weisner J., Kleinbölting S. B., Lategahn J., Sievers S., Müller M. P., Bauer S., Rauh D. Avapritinib-based SAR studies unveil a binding pocket in KIT and PDGFRA. *Nat. Commun.* **2024**, 15, 63-71. <https://doi.org/10.1038/s41467-023-44376-8>
20. I.C.H. Validation of Analytical Procedures: Text and Methodology, Q2 (R1), International Conference on Harmonization IFPMA, Geneva, 2005.
21. Rajesh Varma Bhupatiraju., Srinivasa Kumar B., Venkata Swamy Tangeti., Kandula Rekha., Fathima Sayed. LC and LC-MS/MS studies for identification and characterization of related substances and degradation products of abrocitinib. *Toxicol. Int.* **2024**, 31 (2), 321-334. <https://doi.org/10.18311/ti/2024/v31i2/36370>
22. Rajesh Varma B., Pavani P., Venkata Swamy T., Rekha K., Sreenivasa Rao B. Characterization of Pimavanserin stress degradation products by LCMS/MS and optimization of green analytical HPLC method for quantification of pimavanserin and its impurities. *Asian J. Chem.* **2024**, 36, 2452-2460. <https://doi.org/10.14233/ajchem.2024.32475>