P. Ravi Sankar et al /J. Pharm. Sci. & Res. Vol. 13(6), 2021, 313-318

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

# Analytical Methods For Determination Of Different Members Of FDA approved Tyrosine Kinase Inhibitors Like Dasatinib, Lapatinib, Imatinib, Sorafenib, Nintedanib, Sunitinib And Pazopanib: A Review

**P. Ravi Sankar*, A. Bhavani Sailu, M. M. Eswarudu, M. Nithya Satya, P. Sreeja, P. Roja, Sk. Rijwana**

*Department of Pharmaceutical Analysis,*
*Vignan Pharmacy College, Vadlamudi- 522213,*
*Chebrolu (M), Guntur (Dist), Andhra Pradesh, India.*

**Abstract**

Tyrosine kinase inhibitors (TKIs) are effective in the targeted treatment of various malignancies. KIs including small molecue KIs and monoclonal antibodies directed against kinases, have emerged over the past decade as an important class of anticancer agents. Imatinib was the first to be introduced into clinical oncology, and it was followed by drugs such as gefitinib, erlotinib, sorafenib, sunitinib, and dasatinib. TKIs are also called tyrphostins, the short name for "tyrosine phosphorylation inhibitor", originally coined in a 1988 publication, which was the first description of compounds inhibiting the catalytic activity of the epidermal growth factor receptor (EGFR). Nibs are either in dosage form, blood serum, or biological fluids. This paper reviewes the reported analytical methods for the determination of Dasatinib, Lapatinib, Sorafenib, Imatinib, Nintedanib, Sunitinib, Pazopanib individually or in combination with other drugs are represented in tables 2-8. Table 9 is concerned with the reported methods for the combination of different members of Nibs.

**Keywords:**-Dasatinib, Imatinib, Lapatinib, Nintedanib, Sorafenib, Sunitinib, RP-HPLC method.

## INTRODUCTION

Tyrosine kinase inhibitors are most promising and rapidly expanding class of molecular targeted therapies for the treatment of various types of cancer and other diseases. Among the tyrosine kinase inhibitors that are commercially available as yet, the agents that target EGFR, erlotinib, and gefitinib, display the broadest spectrum of adverse effects on skin and hair, including folliculitis, paronychia, facial hair growth, facial erythema, and varying forms of frontal alopecia. Imatinib was the first fruitful small molecule tyrosine kinase inhibitor approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in 2001. Since that time, over 30 small molecule kinase inhibitors have been approved for clinical use in cancer therapy and other disease. Thus, pharmacological inhibition of tyrosine kinases has been established as a clinically useful approach for the treatment of numerous types of cancer, and other diseases.

**Dasatinib:** Dasatinib (anhydrous) is an aminopyrimidine that is 2-methyl pyrimidine which is substituted at position 4 by the primary amino group of 2-amino-1,3-thiazole-5-carboxylic acid and position 6 by a 4-(2-hydroxyethyl)piperazine-1-yl group, and in which the carboxylic acid group has been formally condensed with 2-chloro-6-methyl aniline to afford the corresponding amide. A multi-targeted kinase inhibitor, it is used, particularly as the monohydrate, for the treatment of chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukemia is represented in Table 2.

**Lapatinib:** Lapatinib is a synthetic, orally active quinazoline with potential antineoplastic properties. Lapatinib is a small-molecule inhibitor of several tyrosine kinase receptors involved in tumor cell growth that is used in the therapy of advanced breast cancer and other solid tumors. Lapatinib therapy is associated with transient elevations in serum aminotransferase levels and rare instances of clinically apparent acute liver injury.represented in table 3.

**Table.1. Different brand names of tyrosine kinase inhibitors**

| Tyrosine kinase inhibitors | Marketed brand names |
|---|---|
| Dasatinib | Sprycel, Invista 50, Dasa-50, Invista 70, In vista 100, Dasa-50, Dasatrue-50, Dasatrue-70, Daslemia 100, Dasanat 50, Lucidas 70. |
| Lapatinib | Tykerb, Hertab, Herdu, Combinib, Herlapsa, Abnib |
| Sorafinib | Sorafenat, Soranib, Fluoranib. |
| Imatinib | Imat, Veenat, Imatib, Imatero, Chemotinib, Imatirel, Levin 400, Glivec 400. |
| Nintedanib | Nindanib, Cyendiv, Ofev, Nintena. |
| Sunitinib | Suninat, Sunitix, Lucisun. |

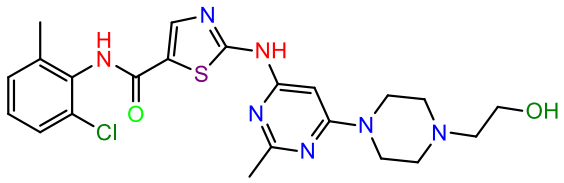

**Figure 1: Chemical structure of Dasatinib**

**Table 2: HPLC method for the determination of Dasatinib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Dosage form | $C_{18}$ column | Methanol and acetonitrile mixed in the ratio of 50:50 v/v | UV, 323 nm | 1 |
| Dosage form | $C_{18}$ column | Sodium phosphate buffer pH 6.5 ± 0.1 and Methanol in a ratio of 70:30 v/v | UV, 323 nm | 2 |
| Dosage form | $C_{18}$ column | (Methanol, Acetonitrile) in (50:50 v/v) | UV, 315 nm | 3 |
| Dosage form | $C_{18}$ column | Methanol | UV, 248 nm | 4 |
| Dosage form | $C_{18}$ column | Phosphate buffer and acetonitrile in (85:15 v/v) | UV, 300 nm | 5 |
| Dosage form | $C_{18}$ column | Methanol and Acetonitrile 50:50 v/v | UV, 315 nm | 6 |

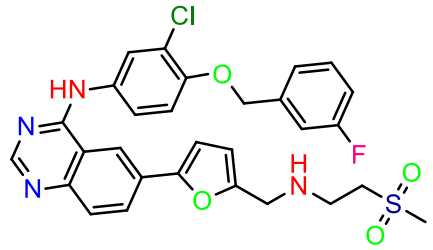

**Figure 2: Chemical structure of Lapatinib**

**Table.3: HPLC method for the determination of Lapatinib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Human Plasma | ODS $C_{18}$ RP column | Acetonitrile/20 Mm ammonium acetate in a proportation (53:47 v/v) | UV, 260 nm | 7 |
| Tablet dosage form | ODS $C_{18}$ RP column | Acetonitrile and water (50:50 v/v) | UV, 232 nm. | 8 |
| Formulations | Zorbax Eclipse $C_{18}$ (3.5 µm, 100 × 4.6 mm) | Ammonium formate buffer and acetonitrile | UV, 261 nm. | 9 |
| Degraded products | $C_{18}$ MZ-Analytical Column | Acetonitrile and water (70/30; V/V) | UV, 227 nm | 10 |

**Imatinib:** Imatinib is an antineoplastic agent that inhibits the Bcr-Abl fusion protein tyrosine kinase, an abnormal enzyme produced by chronic myeloid leukemia cells that contain the Philadelphia chromosome. Imatinib also inhibits the receptor tyrosine kinases for a platelet-derived growth factor (PDGF) and stem cell factor (SCF)/c-kit; the SCF/c-kit receptor tyrosine kinase is activated in gastrointestinal stromal tumor (GIST). This agent inhibits proliferation and induces apoptosis in cells. that overexpress these oncoproteins.

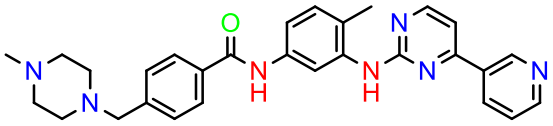

**Figure 3: Chemical structure of Imatinib**

**Table.4: HPLC methods for the determination of Imatinib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Rat Serum | End-capped $C_{18}$ column | Methanol and aqueous triethyl amine (pH 10.5; 1%, v/v) (60:40, v/v) | UV, 227 nm | 11 |
| Human plasma | Capcell pak $C_{18}$ column | Acetonitrile-methanol (55:25:20 v/v/v) | UV, 265 nm | 12 |
| Human plasma | Nucleosil 100-5 micron C18 AB column | Methanoland water containing both 0.05% ammonium acetate | UV at 261 nm | 13 |
| Pharmaceutical dosage form | Phenomenex column (4.6 mm X 150 mm i.d) 5µ | Orthophosphoric buffer (pH 2.5): Methanol (50:50). | UV, 263 nm | 14 |
| Pharmaceutical dosage form | $C_{18}$ column | o-phosphoric acid:Acetonitrile (70:30 v/v) | UV, 266 nm | 15 |

**Sorafenib:** Sorafenib is a synthetic compound targeting growth signaling and angiogenesis. Sorafenib blocks the enzyme RAF kinase, a critical component of the RAF/MEK/ERK signaling pathway that controls cell division and proliferation; in addition, sorafenib inhibits the VEGFR-2/PDGFR-beta signaling cascade, thereby blocking tumor angiogenesis.

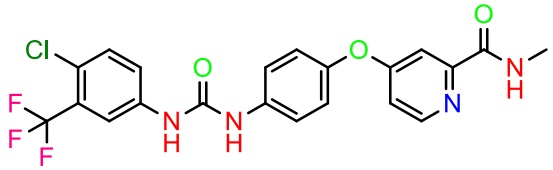

**Figure 4: Chemical structure of Sorafenib**

**Table.5. Application of HPLC to the determination of Sorafenib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Plasma | Discovery HS $C_{18}$ column | Acetonitrile and TFA (65:35V/V) | UV, 245 nm | 16 |
| Tablet formulation | Phenomenex $C_{18}$ column | Acetonitrile and water in the ratio of 82.5 : 17.5, v/v. | UV, 265 nm | 17 |
| Tablet formulation | C18 column | Acetonitrile and disodium phosphate buffer (55:45v/v) | UV, 248 nm | 18 |

**Nintedanib:** Nintedanib is an orally bioavailable, indolinone-derived inhibitor of multiple receptor tyrosine kinases (RTKs) and non-receptor tyrosine kinases (nRTKs), with potential antiangiogenic, antifibrotic, and antineoplastic activities. Upon administration, nintedanib selectively binds to and inhibits vascular endothelial growth factor receptor (VEGFR), fibroblast growth factor receptor (FGFR), platelet-derived growth factor receptor (PDGFR), and colony-stimulating factor 1 receptor (CSF1R) tyrosine kinases, which may result in the induction of endothelial cell apoptosis, the reduction in tumor vasculature, the inhibition of tumor cell proliferation and migration, and antifibrotic activity in pulmonary fibrosis. is represented in Table 6.

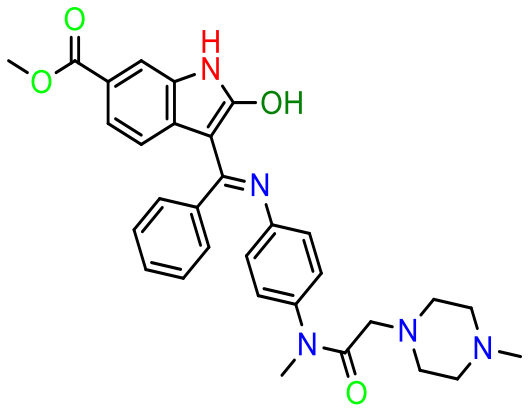


**Figure 5: Chemical structure of Nintedanib**

**Table.6. Application of HPLC to the determination of Nintedanib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Degradation products | YMC Pack ODS-AQ ($C_{18}$) column | Water: Acetonitrile | UV, 210 nm | 19 |
| Formulation | $C_{18}$ column | 0.1 % (v/v) Trifluoroacetic acid in water and Acetonitrile in the ratio of 60: 40 (v/v) | UV, 265 nm | 20 |
| Degradation product | ACQUITY UPLC CSH $C_{18}$ | acetonitrile:methanol (90:10) | Flour.282 ,450 nm | 21 |
| Rat plasma | Mightysil RP-18 GP II ODS column | phosphate buffer (pH 3.0) and acetonitrile (7:3, v/v) | UV, 390 nm | 22 |
| Formulation | $C_{18}$ column | methanol:water (80:20 v/v) | UV, 287 nm | 23 |
| Drug | Silica gel 60 F254 | Chloroform: Methanol in the ratio 7:3 v/v. | UV, 386 nm | 24 |
| Human plasma | +Pentafluorophenyl (PFP) reversed phase column (50 × 2 mm, 3µm) | Acetonitrile:water(60:40 v/v) | QqQ MS detector | 25 |

**Sunitinib:** Sunitinib is an indolinone derivative and tyrosine kinase inhibitor with potential antineoplastic activity. Sunitinib blocks the tyrosine kinase activities of vascular endothelial growth factor receptor 2 (VEGFR2), platelet-derived growth factor receptor b (PDGFRb), and c-kit, thereby inhibiting angiogenesis and cell proliferation. This agent also inhibits the phosphorylation of Fms-related tyrosine kinase 3 (FLT3), another receptor tyrosine kinase expressed by some leukemic cells.

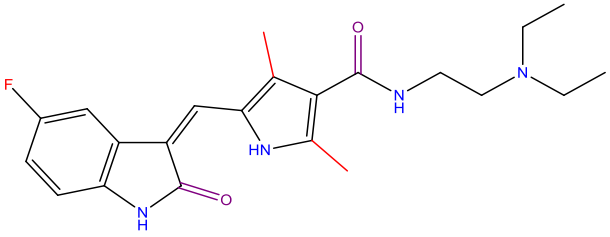


**Fig.6. Chemical Structure of Sunitinib**

**Table.7. Applications of HPLC to the determination of Sunitinib**

| Materials | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Human plasma | Cyanopropyl column | Ammonium acetate buffer: acetonitrile (55:45, v/v) | UV, 431 nm | **26** |

**Pazopanib:** Pazopanib is a small molecule inhibitor of multiple protein tyrosine kinases with potential antineoplastic activity. Pazopanib selectively inhibits vascular endothelial growth factor receptors (VEGFR)-1, -2 and -3, c-kit, and platelet-derived growth factor receptor (PDGF-R), which may result in inhibition of angiogenesis in tumors in which these receptors are up regulated.

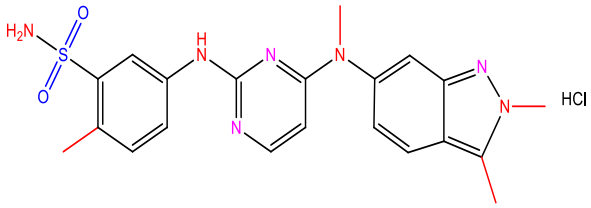


**Figure.7. Chemical structure of Pazopanib**

**Table.8. Application of HPLC to the determination of Pazopanib**

| Material | Column | Mobile phase | Detection | Ref |
|---|---|---|---|---|
| Pharmaceutical dosage form | Inertsil $C_{18}$ (250 mm × 4.6 mm, 5µ) column | 0.1 % ortho phosphoric acid and acetonitrile in the ratio 55:45 (%v/v) | UV, 269 nm | 27 |
| Characterization of forced degradation products of pazopanib | UPLC HSS T3 ( 100 x 2.1 mm, 1.7µm) column in gradient mode | Ammonium acetare buffer (10mM, pH 5.0) and acetonitrile | LC/atomspheric pressure chemical ionization –quadruple-timeof flight Mass spectrometry | 28 |
| Bulk and Pharmaceutical dosage form | Phenomenex Enable $C_{18}$ column | ACN and Phosphate buffer (60:40 % v/v) | UV, 290 nm | 29 |
| Pharmaceutical dosage form | Eclipse plus $C_{18}$ column | 0.1% Orthophosphoric acid: Acetonitrile (55:45% v\v) | UV, 271.4 nm | 30 |
| Human plasma | Ultra base $C_{18}$ column | vol/vol proportion of 47:53 of ammonium acetate, acetonitrile/methanol (70:30, vol/vol) | UV, 260 nm | 31 |

**Table.9. Methods for the simultaneous determination of different drugs**

| Drugs | Material | Column | Method/Mobile Phase | linearity | Ref |
|---|---|---|---|---|---|
| Erlo+Gefi+Ima+Lapa +Nilo+Sora +Dasa+Suni | Human plasma | Gemini $C_{18}$ column (50 × 2.0 mm i.d., 5.0 µm particle size | HPLC-MS/MS eluted with a gradient | linear range from 20.0 to 10,000 ng/mL | 32 |
| Ima+Dasa+Nilo | Human plasma | Xtimate Phenyl column | UPLC-MS/MS 0.15 % formic acid and 0.05 % ammonium acetate: ACN ( 40:60v/v) | 2.6-5250.0 ng/mL for imatinib, 2.0-490.0 ng/mL for dasatinib and 2.4-4700.0 ng/mL for nilotinib. | 33 |
| Das+Lenva | Pharmaceutical dosage form | Inertsil ODS $C_{18}$ column | methanol: phosphate buffer mixed in the ratio of 70:30 % v/v | 100-500 ng/ml for dasatinib, 1-5 ng/mL for lenvatinib | 34 |
| Pcm+Dfz+Chz | Pharmaceutical dosage form | Welchrom $C_{18}$ column | Phosphate buffer ( pH 6.65): acetonitrile (60:40 v/v) | PCM, DFS, CHZ were found to be in the range of 10-50 µg/mL, 1-5 µg/mL, and 5-25 µg/mL respectively. | 35 |
| Ruxolitinib+Vismodegib+Olaprarib+ Pazopanib | Human plasma | UPLCsystem coupled with mass tandem spectrometry in a positive ionization mode | 10 mmol/L formate ammonium buffer containg 0.1% v/v formic acid in phase A and acetonitrile with 0.1%v/v formic acid phase B. | 10 to 2500 ng/mL for ruxolitinib and from 100 to 100,000 ng/mL for olaparib, vismodegib, and Pazopanib. | 36 |

**Abbreviations: erlo:erlotinib, grfi:gefitinib, ima:imatinib, lap:lapatinib, nilo:nilotinib, sora: Sorafenib, dasa:dasatinib, suni:sunitinib.**

## CONCLUSION:

This paper describes the individual and simultaneous estimation of a different important class of Tyrosine kinase inhibitors. Several analytical methods have been reported for analyzing TKIs in biological fluids and pharmaceutical formulations for the determination of tyrosine kinase individually or in combination. Presentation of various methods for the determination of tyrosine kinase in the formulation and in body fluids. All of the above mentioned methods were validated as per ICH guidelines[37-42]. The researchers who are interested to study this class of anti-cancers further. The information compiled in this article reduces valuable time and money spent on the analytical method development in the analysis of tyrosine kinase inhibitors from the first step onwards. A researcher can use this information and go appoint forward.

## REFERENCES:


1. Panchumarthy Ravi Sankar, Saranu Anusha, Development and validation of RP-HPLC method for the determination of dasatinib in the tablet dosage form, International journal of pharmaceutical sciences and research,2019; 10(10): 4531-37.
2. Bandi Ramachandra, N.V.S.Naidu, Validation of RP-HPLC method for estimation of dasatinib in bulk and its pharmaceutical dosage forms, Research Article Biological Sciences,2014; 4(1):61-68.
3. M. Madhuri1, L. Sangeetha Kumari, P. Susmitha, Y. Lakshmi Gayatri, S. K. Sahoo, Method development and validation of stability indicating rp-hplc method for the estimation of dasatinib in tablet dosage form, Journal of pharmacy research, 2017;11(5):419--423.
4. Saili Madur, Vinod Matole, Mallinath Kalshetti, UV visible spectrophotometric method development and validation of dasatinib in bulk and solid dosage form, International Journal of Current Pharmaceutical Research,2020;12(4):90-93.
5. Panchumarthy Ravi Sankar, Saranu Anusha, Development and validation of novel HPLC method for the estimation of dasatinib in bulk and pharmaceutical dosage forms, International journal of pharmaceutical sciences and research,2013; 3(3):2231-2781.
6. K. S. Nataraj, P. Sivalingachari, S. Sai Naveen, K. Alekhya, Method development and validation for the estimation of Dasatinib Monohydrate tablets by RP-HPLC. Asian Journal of Research in Chemistry, 2013;6(9):859-862.
7. Vanesa Escydero-Ortiz, Juan Jose Perez-Ruixo, Belen Valenzuela, Development and validation of a high-performance liquid chromatography ultraviolet method for lapatinib quantification in human plasma, Ther Drug Monit,2013;35(6):796-802.
8. K. K. Kumar, K. E.V. Nagoji, R. V. Nadh, A Validated RP-HPLC Method for the Estimation of Lapatinib in Tablet Dosage forms using Gemcitabine Hydrochloride as an Internal Standard, Indian Journal of Pharmaceutical Sciences,2012;74(6):580-583.
9. Ramu Ivaturi, Manikya T. Sastry, S. Satyaveni, Development and validation of stability indicating HPLC method for the determination of lapatinib impurities in bulk and finished formulations, International Journal of Pharmaceutical Sciences and Research,2071;8(7):3081-91.
10. Ebrahim Saadat, Pooya Dehghan Kelishady, Fatemeh Ravar, Farzad Kobarfard, Farid A.Dorkoosh, Development and Validation of Rapid Stability-Indicating RP-HPLC-DAD Method for the Quantification of Lapatinib and Mass Spectrometry Analysis of Degraded Products, Journal of Chromatographic Science,2015;53(6):932-939.
11. Girish Bende, Sivacharan Kollipara, Snehalatha Movva, Ganesh Moorthy, Ranendra Saha, Validation of an HPLC method for determination of imatinib mesylate in rat serum and its application in a pharmacokinetic study, Journal of Chromatographic Sciences,2010;48(5):334-41.
12. Masatomo Miura, Naoto Takahashi, Ken-ichi Sawada.Quantitative, Determination of Imatinib in Human Plasma with High-Performance Liquid Chromatography and Ultraviolet Detection Journal of Chromatographic Sciences,2011;49(5):412-415.
13. N.Widmer, ABeguin, B. Rochat, T. Buclin, T. Kovacsovics, M.A. Duchosal, S. Leyvraz, A. Rosselet, J. Biollaz, L.A. Decosterd, Determination of Imatinib (Gleevec) in human plasma by solid-phase extraction-liquiod chromatography –ultraviolet absorbance detection,2004;803(2):285-92.
14. P. Sandhya, P.Vishnu Priya, Shyamala, N. Anjali Devi, JVC. Sharma, Method development and validation of imatinib mesylate in pharmaceutical dosage form by RP-HPLC, world journal of pharmacy and pharmaceutical sciences,2013; 3(1);682-688.
15. Naga Sindhu, Y Srinivasa Rao, T. Hemant Kumar and K. Vara Prasada Rao, Method development and validation of RP-HPLC method for estimation of imatinib mesylate in pure and pharmaceutical dosage form.Scholars Research Library,2015;7 (3):33-38.
16. Ismail Khan, Zafar Iqbal, Abad Khan, Muhammad Hassan, Fazle Nasir, Abida Raza, Lateef Ahmad, Amjad Khan, Muhammad Akhlaq Mughal, A simple, rapid and sensitive RP-HPLC-UV method for the simultaneous determination of sorafenib & paclitaxel in plasma and pharmaceutical dosage forms, Application to pharmacokinetic study, J Chromatogr B Analyt Technol Biomed Life Sci,2016;33(1):261-270.
17. R. Kalaichelvi, E. Jayachandran, Quantitative Estimation of Sorafenib Tosylate Its Pure Form and in Its Tablet Formulation by RP-HPLC Method, Hindawi Journal of Chemistry, Volume 2013,2013; https://doi.org/10.1155/2013/539264.
18. S.VenkataRao, G.Ramu1 , A.Biksham Babu1, T.Neeharika, C.Rambabu, Determination of sorafenib in bulk and tablet formulation by a new validated reverse phase high-performance liquid chromatography, Rasayan Journal of Chemistry,2011;4(2): 477-480.
19. Dasari Purnachand, Arava Veerareddy , Bhoomireddy Ramadevi, Ch. V. S. L. Kameswarrao , Gogireddy Surendra Reddy, Bethi Madhusudhanreddy, Development and validation of simple and sensitive stability-indicating RP-HPLC assay method for determination of Nintedanib and stress degradation studies, Journal of Chemical and Pharmaceutical Research,2015,7(8):774-782.
20. Rohit Kumar, Vijaya Kumar Munipalli, Raman Mohan Singh, Sayali Warde, Validated RP-HPLC Method for Determination and Quantification of Nintedanib in Pharmaceutical Formulation, Journal of Advancement in pharmacology, 2020;1(1):38-47.
21. Vivek Dhiman, Ankit Balhara, Saranjit Singh, Shristy Tiwari, Samanthula Gananadhamu, M. V. N. Kumar Talluri, Characterization of stress degradation products of Nintedanib by UPLC, UHPLC-Q-TOF/MS/MS and NMR: Evidence of a degradation product with a structure alert for mutagenicity, Journal of Pharmaceutical and Biomedical Analysis,Volume 199, 30 May 2021. https://doi.org/10.1016/j.jpba.2021.114037.
22. Kohei Togami, Kenta Fukuda, Kotaro Yamaguchi, Sumio Chono, Hitoshi Tada, Facile and sensitive HPLC-UV method for determination of nintedanib in rat plasma, International Journal of Pharmacy and Pharmaceutical sciences,2018;10(6):133-137.
23. Rohan S. Patil, Moreshwar P. Mahajan, Development and Validation of RP-HPLC Method for the Estimation of Nintedanib Esylate in Bulk and Its Formulation, A Journal of Pharmaceutical Science,2015;7(8):774-782.
24. Debanchal Dutta , Soumyajit Das, Manik Ghosh, Validated HPTLC Method for the Determination of Nintedanib in Bulk Drug, MDPI,2019;9(1):22.
25. Hany W. Darwish, Mohamed W. Attwa, Adnan A. Kadi, Rapid validated liquid chromatographic method coupled with Tandem mass spectrometry for quantification of Nintedanib in human plasma, Journal of Pharmaceutical Research,2016; 15 (11): 2467-2473.
26. Benoit Blanchet, Carole Saboureau, Anne Sophie Benichou, Bertrand Billemont, Fabrice Taieb, Stanislas Ropert, Alain Dauphin, François Goldwasser, Michel Tod, Development and validation of an HPLC-UV-visible method for sunitinib quantification in human plasma,Clin Clim Acta,2009 Jun 27;404(2):134-9.
27. Gorja ashok, Sumanta Mondal, S. Ganapaty, Jahnavi Bandla, Development and validation of stability indicating method for the estimation of pazopanib hydrochloride in pharmaceutical dosage forms by RP-HPLC, Scholars Reserach Library,2015; 7 (12):234-

241.
28. Prinesh N Patel, Pradipbhai D Kalariya, et al. Characterization of Forced Degradation Products of Pazopanib Hydrochloride by UHPLC-Q-TOF/MS and in Silico Toxicity Prediction. Journal of Mass Spectrometry. 2015; 50(7):918-28.
29. Kiran Kumar Buralla, Varadarajan Parthasarathy, Quality by Design based Developed and Validation of RP-HPLC Method for Simultaneous Estimation of Pazopanib in Bulk and Pharmaceutical Dosage Forms, International Journal of Pharmaceutical Investigation,2019;9(3):135-140.
30. P. Ravi Sankar, K. Saisneha Latha, A.Bhavani Sailu, SK.Taheera, B. Madhuri, Development and Validation of RP-HPLC Method for the Determination of Pazopanib Hydrochloride (A Tyrosine Kinase Inhibitor) in Pharmaceutical Dosage Form, Research Journal of Pharmacy and Technology,2021;14(3):1549-1554.
31. Vanesa Escudero-Ortiz, Juan J Perez-Ruixo, Belen Valenzuela, Development and validation of an HPLC-UV method for Pazopanib quantification in human plasma and application to patients with cancer in routine clinical practice, Ther Drug Monit,2015 Apr;37(2):172-9.
32. N. A. G. Lankheet, M. J. X. Hillerbrand, H. Rosing, J. H. M. Schellens. J. H. Beijnen, A. D. R. Huitema, Method development and validation for the quantification of dasatinib, erlotinib, gefitinib, imatinib, lapatinib, nilotinib, sorafenib and sunitinib in human plasma by liquid chromatography coupled with tandem mass spectrometry, Biomedical Research,2013;27(4):466-76.
33. Jing Zeng, Hua Lin Cai, Zhi ping Jiang, Qing Wang, Yan Zhu, Ping Xu, Xie LanZhao, A validated UPLC–MS/MS method for simultaneous determination of imatinib, dasatinib and nilotinib in human plasma, Journal of Pharmaceutical Analysis,2017;9(17):30097-7.
34. Sunil Junapudi, Ramreddy Godela, Meddi srinivas, Sadhana Namadi, Method Development and Validation for Simultaneous Estimation of Dasatinib and Lenvatinib by Using RP-HPLC in Pharmaceutical Dosage Form, Research Gate,2017;(4):231-238
35. Ravisankar Panchumarthy, Devala Rao Garikapati, Abhinay Akula, Srinivasa Babu Puttagunta, A validated RP-HPLC method for simultaneous estimation of Paracetamol, Diclofenac sodium and Chlorzoxazone in combination tablet dosage form, 2013;6(3):181-188.
36. Claire Pressiat, Huu-Hien Huynh, Alain Ple, et al. Development and Validation of a Simultaneous Quantification Method of Ruxolitinib, Vismodegib, Olaparib, and Pazopanib in Human Plasma Using Liquid Chromatography Coupled With Tandem Mass Spectrometry. The Drug Monit. Journal. 2018; 40(3):337-343.
37. Ravisankar P, Naga Navya Ch, Pravallika D, Navya Sri D, A review on step-by-step analytical method validation, IOSR Journal of Pharmacy.2015;5:7-19.
38. Ravisankar P, Gowthami S, Devala Rao G, A review on analytical method development, Indian journal of research in pharmacy and Biotechnology, 2014; 2:1183-1195.
39. Panchumarthy Ravisankar, Anusha S, Supriya K, Ajith Kumar U, Fundamental chromatographic parameters, Int. J. Pharm. Sci. Rev.Res.2019; 55(2):46-50.
40. Ravi Sankar P, Sai Snehalatha K, Tabassum Firdose Shaik, Srinivasa Babu P, Applications of HPLC in Pharmaceutical Analysis. Int.J.Pharm.Sci.Rev.Res.2019; 59(1): 117-124.
41. Lavanya G, Sunil M, Eswarudu MM, Eswaraiah MC, Harisudha K and Spandana BN: Analytical Method Validation: An Updated Review. Int J Pharm Sci Res 2013, 4(4), 1280-1286.
42. ICH Q2 (R1), Validation of analytical procedures, Text, and methodology, International Conference on Harmonization, Geneva, 2005;1-17.