Contents lists available at UGC-CARE

International Journal of Pharmaceutical Sciences and Drug Research

[ISSN: 0975-248X; CODEN (USA): IJPSPP]

Available online at www.ijpsdronline.com

Research Article

An LC-MS/MS Method Development and Validation for the Quantification of Infigratinib in K2EDTA Human Plasma

P. Jogeswara Rao, D.V.R.N. Bhikshapathi*

Bir Tikandrajit University, Canchipur, Imphal West, Manipur, India.

ARTICLE INFO

Article history:

Received: 10 November, 2023

Revised: 11 December, 2023

Accepted: 12 December, 2023

Published: 30 January, 2024

Keywords:

Infigratinib, Giant-cell tumor, LC-MS/MS, Healthy rabbits, Bioavailabilitystudies.

DOI:

10.25004/IJPSDR.2024.160112

ABSTRACT

A validated liquid chromatography with tandem mass spectrometry (LC-MS-MS) technology was developed for the quantification of infigratinib, using a simple and specific approach. This method utilizes a liquid-liquid extraction (LLE) strategy to achieve high sensitivity. The analytical approach that was developed underwent validation in terms of many characteristics including specificity, sensitivity, carry-over, recovery, precision, matrix effect, accuracy, and stability. The elution of the drug and IS occurred in a time frame of 6.5 minutes using a PhenomenexSB-C18 column (250 × 4.6 mm x 5 µm). The mobile phase consisted of a mixture of acetonitrile and 0.1% v/v formic acid in water, with a ratio of 80:20. The infusion flow rate was set at 0.9 mL/min. The retention times (RT) of infigratinib and IS were determined to be 5.12 and 3.31 minutes, respectively. The elution time required for complete separation of infigratinib was 6.5 minutes. The equation of the linear regression line was determined to be y = 0.994x + 2.662, and the coefficient of determination (r2) was calculated to be 0.999. The coefficient of variation (%CV) obtained for the calibration graph of infigratinib was determined to be less than or equal to 3.73. The matrix effect was assessed by calculating the coefficient of variation (%CV) for the High and low quality control (QC) samples, yielding values of 1.64 and 0.70% respectively.

Introduction

Infigratinib is a pharmaceutical compound that functions as a broad-spectrum inhibitor of fibroblast growth factor receptor (FGFR) kinases. The suppression of tumor development is achieved by infigratinib by the inhibition of the FGFR pathway, which is often dysregulated in several malignancies, including cholangio carcinoma. Cholangio carcinoma is the prevailing primary malignancy that often affects the biliary system, and it ranks as the second most prevalent primary hepatic malignancy. Infitratinib is classified as a pan-FGFR inhibitor due to its ability to competitively block the adenosine triphosphate (ATP) binding of all four subtypes of FGFR receptors.

The Food and Drug Administration (FDA) granted accelerated approval to a drug called infigratinib, which will be marketed as Truseltiq. This approval was given on May 28, 2021, and it is specifically intended for the treatment of adults who have previously received treatment for cholangiocarcinoma, a type of cancer that is locally advanced or has spread to other parts of the body and cannot be surgically removed. The patients eligible for this treatment must have a specific genetic alteration known as a FGFR2 fusion or another rearrangement, which can be detected using a test approved by the FDA. The approval of this drug is in line with the prior approval of pemigatinib, another FGFR inhibitor, by the FDA for the same therapeutic indication.Infigratinib with a molecular weight and formula of 560.48 and $C_{26}H_{31}Cl_2N_7O_3$(Fig. 1).[1-3] FGFRs are tyrosine kinase receptors that regulate cell proliferation, differentiation, migration, survival, and angiogenesis. After attaching to external signals, such as fibroblast growth factors, FGFR dimerizes to phosphorylate downstream molecules and activate the Ras-MAPK pathway. FGFR signalling pathway disruptions cause uncontrolled cell proliferation and expansion, including malignant cells, in several malignancies. FGFR

***Corresponding Author:** Dr. D. V. R. N. Bhikshapathi

Address: Bir Tikandrajit University, Canchipur, Imphal West, Manipur, India.

Email ✉**:** dbpathi71@gmail.com

Tel.: +91-9848514228

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

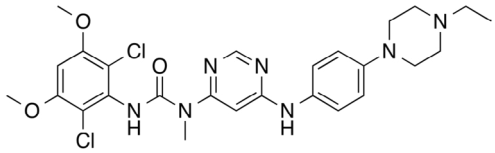

Fig. 1: Structure of infigratinib

receptor mutations, amplifications, and fusions are linked to prostate, urothelial, ovarian, breast, and liver cancers. Recent investigations suggest that up to 45% of intrahepatic cholangio carcinoma patients have gene rearrangements that produced FGFR2 fusion proteins. Tumors with FGFR mutations may encourage malignant cell growth and survival via constitutive signaling. In cancer cell lines with activating FGFR amplification, mutations, or fusions, infigratinib blocks FGFR signaling and suppresses cell proliferation. It is a reversible, non-competitive inhibitor of all four FGFR subtypes. Infigratinib binds best to FGFR1, FGFR2, and FGFR3 among the four subtypes. The allosteric location between the two FGFR kinase lobes, or ATP-binding cleft, is where infigratinib binds. Binding to this gap hinders receptor autophosphorylation and downstream signaling cascades that activate MAPK.[3,4]

The available literature on infigratinib indicates that a single analytical approach has been published using liquid chromatography with tandem mass spectrometry (LC-MS-MS).[5] The use of high throughput techniques, such as LC-MS/MS, is of utmost importance in order to accurately quantify infigratinibin biological matrices.

MATERIALS AND METHODS

Chemical Reagents

From MSN Labs in Hyderabad, India, ledipasvir (IS) was obtained. Acquired infigratinib from Sreeni Labs Pvt. Ltd., located in Hyderabad. The laboratory water used in this study was obtained from water purification systems (Milli Q, USA) that were installed. The formic acid used was of analytical grade and was supplied by J. T. Baker, Hyderabad.

Equipment and Software

An LC-MS/MS instrument of Quattros X.E premier combined with LC2695 separation module was employed for the present work. The software version of Mass Lynx V 4.1 was utilized for the processing of chromatograms and data generation during the research work.

Calibration Controls

A newly generated stock solution of infigratinib was created by dissolving 10 mg of the medication in 10 mL of 70% methanol, resulting in a concentration of 1-mg/mL. The calibration standards consisted of eight distinct concentration levels. These levels were achieved by adding infigratinib standard solution to blank plasma, resulting in concentrations of 72.45, 150, 325, 650, 1020, 1420, 1780, and 2173.50 ng/mL.

Standard Quality Controls

The solutions were created at three distinct levels of quality control, namely lowest quality control (LQC), median quality control (MQC), and highest quality control (HQC) standards. The quality control (QC) samples were generated in accordance with calibration standards in order to determine the concentrations of 150, 1449, and 2173.5 ng/mL for the low quality control (LQC), medium quality control (MQC), and high quality control (HQC) samples, respectively. The prepared solutions were stored at a temperature of -200°C until the time of analysis.

Chromatographic Parameters

The separation of the sample using isocratic liquid chromatography (LC) was conducted on a Phenomene x SB-C18 column with dimensions of 4.6 x 250 mm x 5 µm. The mobile phase consisted of a mixture of acetonitrile and water containing 0.1% v/v formic acid, with a ratio of 80:20. The LC equipment was used at a flow rate of 0.90 mL/min, and the entire duration of a single run was 6.5 minutes. The temperatures of the column and auto-sampler were kept constant at 40.0 and 5.0°C, respectively.

Mass Equipment Parameters

The mass spectrometer was used in the positive ionizationmode. The optimized mass instrument settings for the particular compounds infigratinib and IS were as follows: the curtain gas (CG) was set to 25 pounds per square inch (psi), ion source gas 1was set to 50 psi, ion source gas 2 was set to 50 psi, the ion spray voltage was set to 4500 volts, and the turbo spray temperature was set to 550°C. The quantitative study included the use of multiple reactions monitoring (MRM) to examine the transition pairings of m/z 560.19→189.13 for infigratinib and 889.4→130.0 for ledipasvir. Each transition was allotted a dwell duration of 100 ms. Infigratinib and IS precursor ions were generated by the application of a declustering potential (DP) of 150 and 155 V, respectively. Subsequently, the precursor ions of infigratiniband IS underwent fragmentation at collision energies of 20 eV, using nitroge gas at a pressure of 5 arbitrary units.

Sample Preparation

A representative sample was generated by transferring 250 µL of plasma and 50µL of ledipasvir (1-µg/mL) into a polypropylene tube, followed by vortexing for a duration of 2 minutes. The extraction of infigratiniband IS was conducted using 4 mL of ethyl acetate as the solvent. The resulting solution was then subjected to centrifugation at a speed of 5000 rpm for duration of 25 minutes at a temperature of 5.0°C. Following the centrifugation process, the organic phase was isolated and then subjected to drying using a lyophilizer. The resultant product was

solubilized in 250 µL of the mobile phase and thereafter placed into vials that had been pre-labeled.[6-8] The vials were stored inside an automated sample handling device and then introduced into a LC-MS/MS system.

Validation

The developed method was validated for the parameters: specificity, selectivity, linearity, stability, matrix effect, carry-over effect, recovery, precision and accuracy.[9,10]

Specificity and selectivity

The identification of analyte interference with endogenous matrix components was accomplished by meticulous examination of six separate batches of blank human plasma samples obtained from various sources. Samples with blank and lower limit of quantification (LLoQ-72.45 ng/mL) were produced for each batch and thereafter introduced into the LC-MS/MS system for analysis of the obtained data. In order to assess the interference between the internal standard (IS) and the analyte, blank samples were deliberately contaminated with the analyte and IS individually. The obtained outcomes were thereafter analyzed and interpreted. The size of the interference peak should not exceed 20% of the area of the LLoQ peak, and it should also be less than 5% of the average peak area of the internal standard. The deviation of the LLoQ from the nominal concentration should not exceed 20%.[11,12]

Linearity

In this study, a set of calibration standards (non-zero) consisting of eight distinct concentrations were generated and quantified in three independent runs. The concentrations used for the calibration standards were 72.45, 150.0, 325.0, 650.0, 1020.0, 1420.0, 1780.0, and 2173.5 ng/mL. These calibration standards were newly prepared before to each run to ensure accuracy and reliability of the quantification process. Calibration curves were generated using the least squares linear regression method, where the peak area ratio of analyte and internal standard (IS) peaks was plotted against the nominal concentration. To account for the variability in concentration measurements, a weighting factor was applied by using the reciprocal of the squared concentration ($1/x^2$). The acceptable range for deviation in the LLoQ should be between ± 20%, while for the remaining concentrations, it should be within +15%.[13,14]

Recovery studies

The assessment of infigratinib recovery included a comparison of the average peak area response between extracted samples and unextracted samples at different concentration levels, namely the LQC, MQC, and HQC standards. The mean percentage recovery was determined by calculating the average of the percentage recovery values obtained at each concentration level.[10,12]

$$\% \text{ Recovery of analyte} = \frac{\text{Mean analyte peak response in extracted samples}}{\text{Mean analyte peak response in unextracted sample}} \times 100$$

Precision and accuracy

Both intraday and interday assessments of these metrics were made. By randomly introducing QC standards (150, 1449, and 2173.5 ng/mL) and LLOQ (72.45 ng/mL) into five repetitions each day, intra-day precision and accuracy were examined. The analysis of each QC standard (150, 1449, and 2173.5 ng/mL) and the LLoQ QC standard (72.45 ng/mL) thrice a day for five distinct days was used to assess the inter-day precision and accuracy. With the exception of LLoQ QC, for which the within- and between-batch percentages should not exceed 20%, the percentages for low, medium, and high concentrations should all be under 15%.

Matrix effect

After extraction, prepare one LQC sample and one HQC sample for each of the six blank matrix lots (post extraction spiked samples). Prepare six duplicates of the same aqueous or neat quality control samples at the same time, and then examine them. Apply the following formula to get each lot's matrix factor for the analyte and IS:

$$\text{Matrix Factor} = \frac{\text{Peak response in presence of matrix ions}}{\text{Average peak response in aqueous samples}}$$

Carry-over test

Two blank plasma samples and a sample at the upper limit of quantification (ULQC) of 2898 ng/mL were infused immediately after the ULQC infusion in order to assess the carry-over test. At the retention time of infigratinib, the peak reaction of the first blank sample should be less than 20% of the peak response of an LLoQ sample.

Stability studies

Three samples were processed without residue from blank plasma by directly spiking the analyte into the reconstitution solution. We conducted a stability analysis on 3 aliquots of low and high QC samples held at 10°C for 24 hours in an auto sampler. The obtained concentrations were compared to the actual values. Three samples of low and high QCs were kept at -70°C for 36 days in a deep freezer. The concentrations of the samples were compared to QC standard samples to evaluate analyte stability over time. To determine the short-term stability of the analyte, three aliquots of low and high QC (unprocessed) samples were stored at 25°C (ambient) for 19 hours. Three freeze-thaw cycles at low and high QC samples evaluated analyte freeze-thaw stability. Samples were stored at -70°C for 24 hours during the freeze cycle and at room temperature for the thaw cycle. Standard sample concentration was measured after 3 freeze-thaw cycles. Standard working solutions with infigratinib and IS were stored at 25°C and 2 to 8°C for 20 hours and 17 days individually. The

Table 1: Linearity of infigratinib

Actual conc. (ng/mL)	*72.45*	*150*	*325*	*650*	*1020*	*1420*	*1780*	*2173.5*	*Slope*	*Intercept*
1	68.54	137.25	322.12	642.83	1023.06	1416.51	1836.37	2124.596	0.995	2.635
2	70.13	144.98	328.25	649.56	1025.45	1407.38	1871.97	2132.747	1.002	2.351
3	72.02	147.52	330.78	640.04	1007.41	1397.90	1821.53	2108.295	0.986	3
Mean	70.23	143.25	327.05	644.14	1018.64	1407.26	1843.29	2121.879	0.994	2.662
±SD	1.74	5.35	4.46	4.89	9.79	9.30	25.92	12.45029	0.0080	0.325
%CV	2.48	3.73	1.36	0.76	0.96	0.66	1.41	0.586757		
% Accuracy	96.93	95.5	100.63	99.09	99.87	99.10	103.56	97.62		

SD- standard deviation; CV- coefficient of variance

two medications' peak responses were computed and compared to newly produced solutions.[9-12]

Results and Discussion

Figs 2 to 5 show the chromatograms of the blank, high, median, and low quality control (QC) samples. The study approach that was created underwent validation for many criteria including linearity, specificity, sensitivity, carry-over, accuracy, precision, and stability investigations. The validation settings yielded the following results.

Specificity

No interference peaks originating from matrix components were seen during the retention durations of the drug sample and internal standard, as shown in Figs 2 and 3. The retention times of infigratinib and IS were determined to be 5.12 and 3.31 minutes, respectively. The elution time required for complete separation of infigratinib was determined to be 6.5 minutes.

Linearity

The calibration graphs were constructed using eight calibration standards within the concentration range

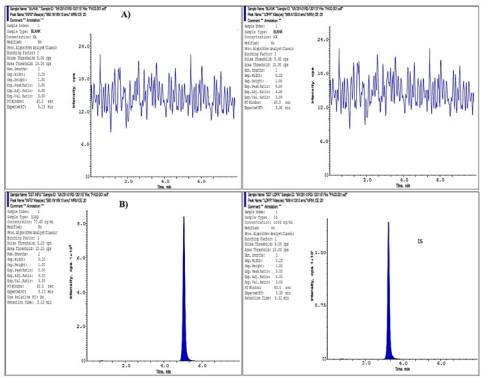

Fig. 2: Chromatograms of blank plasma (A) and LLoQ (B) samples

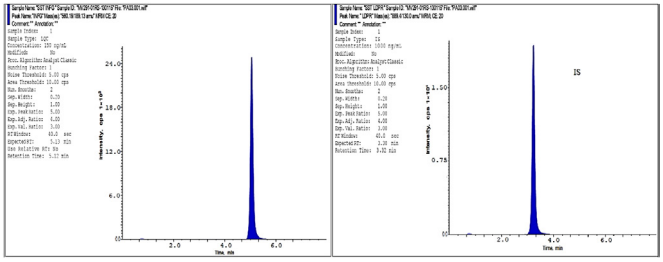

Fig. 3: Chromatograms of infigratinib at LQC level

Table 2: %Mean recovery of infigratinib

	LQC			*MQC*			*HQC*		
ID	*Un-extracted**	*Extracted**	*% Recovery*	*Un-extracted**	*Extracted**	*% Recovery**	*Un-extracted**	*Extracted**	*% Recovery*
1	0.144	0.131	90.972	0.749	0.614	81.982	1.177	1.038	88.191
2	0.137	0.126	91.971	0.763	0.628	82.312	1.217	1.024	84.142
3	0.143	0.126	88.112	0.770	0.635	82.470	1.214	0.994	81.883
4	0.143	0.133	93.007	0.715	0.640	89.511	1.248	1.046	83.810
5	0.142	0.131	92.254	0.72	0.655	90.970	1.189	1.051	88.391
6	0.149	0.131	87.919	0.725	0.665	91.721	1.173	1.041	88.752
Mean	0.143	0.130	90.706	0.740	0.640	86.493	1.203	1.032	85.861
±SD	0.004	0.003	2.184	0.023	0.018	4.705	0.029	0.021	2.939
%CV	2.693	2.274	2.413	3.171	2.883	5.441	2.381	2.023	3.421

*peak area ratio; SD- standard deviation; CV- coefficient of variance

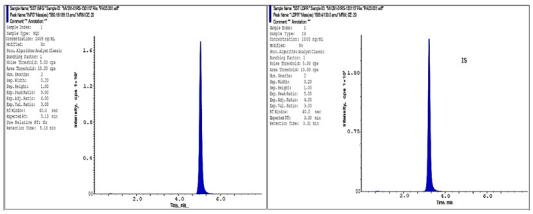

Fig. 4: Chromatograms of infigratinib at MQC level

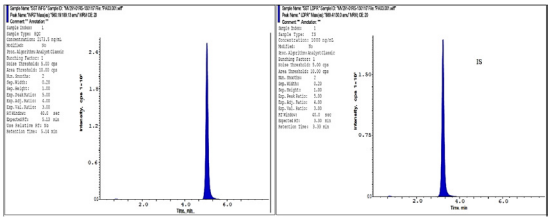

Fig. 5: Chromatograms of infigratinib at HQC level

of 72.45 to 2173.5 ng/mL, for the purpose of linear regression analysis. The equation of the linear regression line was determined to be y = 0.994x + 2.662, and the coefficient of determination (r2) was calculated to be 0.999. The coefficient of variation (%CV) determined for the calibration graph of infigratinib was observed to be less than or equal to 3.73. The results were recorded and organized in Table 1.

Recoveryand Matrix Effect

The average percentage recovery of infigratinib in low, middle, and high quality control samples (Figs 3 to 5) was determined to be 90.70, 86.49, and 85.86% correspondingly. These findings have been organized and presented in Table 2. The metric in question was computed by assessing the coefficient of variation (%CV) for the High and Low quality control samples. The %CV values obtained were 1.64 and 0.70% for the high and low QC samples, respectively. The results were presented in Table 3.

Table 3: Matrix effect results for infigratinib

S. No.	*LQC*	*HQC*
	150 ng/mL	*2173.5 ng/mL*
1	148.36	2182.60
2	141.63	2169.78
3	147.62	2149.82
4	150.56	2010.27
5	149.29	1993.36
6	149.86	2186.80
Mean	147.89	2115.44
± SD	3.24	89.11
% CV	2.19	4.21
% Accuracy	98.59	97.33

SD- standard deviation; CV- coefficient of variance

Precision and Accuracy

The assessment of precision and accuracy included the calculation of the mean intra-day and inter-day precision of the analytical method using the quality controlsamples. All of the measured values fell within the acceptable range of accuracy, namely 15%. The results pertaining to precision and accuracy were provided in Table 4.

Table 4: Intra-day and inter-day QC samples for infigratinib

Intra batch	*LLoQ (72.45 ng/mL)*	*LQC (150 ng/mL)*	*MQC (1449 ng/mL)*	*HQC (2173.5 ng/mL)*
Average	70.89	146.21	1409.38	1956.12
SD	1.81	0.67	11.24	17.47
%CV	2.35	3.33	2.30	0.95
Average	71.02	147.26	1416.18	1987.87
SD	1.76	2.56	10.79	43.88
%CV	3.14	3.31	2.14	2.32
Average	69.18	145.8	1429.85	1941.65
SD	2.14	1.60	9.84	38.09
%CV	1.94	3.08	1.98	2.07
Inter-batch (ng/mL)	LLoQ (72.45)	LQC (150)	MQC (1449)	HQC (2173.5)
Average	69.14	147.84	1416.45	2012.98
SD	2.05	8.15	5.68	6.61
%CV	1.90	2.78	1.12	1.42

SD- standard deviation; CV- coefficient of variance

Table 5: Stability of infigratinib in human plasma

Post preparative (24 hours at 10°C)	150	2.78	-5.65
	2173.5	1.05	-4.45
Short-term (19 hours at 25°C)	150	0.91	-6.98
	2173.5	0.66	-4.05
Long-term (36 day at -70°C)	150	1.22	-0.54
	2173.5	0.75	-2.16
Three freeze/thaw (3 cycles)	150	5.67	0.48
	2173.5	0.56	1.26
Stock solution (20 hours at 25°C)	150	3.55	2.45
	2173.5	8.76	-1.78
Stock solution (17 day at 2 ~ 8°C)	150	4.49	-1.57
	2173.5	1.50	-0.53

CV- coefficient of variance

Stability Studies

Based on the findings of stability tests, it was observed that there was no notable degradation of the analyte throughout the various stages of the chromatographic method, extraction process, and storage of infigratinib plasma samples under different storage settings. The stability statistics were given in Table 5.

Conclusion

A validated LC-MS/MS technology was developed for the quantification of infigratinib, using a simple and specific approach. This method utilizes a liquid-liquid extraction strategy to achieve high sensitivity. The analytical approach that was developed underwent validation in terms of many characteristics including specificity, sensitivity, carry-over, recovery, precision, matrix effect, accuracy, and stability. The elution of the drug and IS occurred in a time frame of 6.5 minutes using a PhenomenexSB-C18 column (250 × 4.6 mm x 5 µm). The mobile phase consisted of a mixture of acetonitrile and 0.1% v/v formic acid in water, with a ratio of 80:20. The infusion flow rate was set at 0.9 mL/minute. The RT of infigratiniband IS were determined to be 5.12 and 3.31 minutes, respectively. The elution time required for complete separation of infigratinib was 6.5 minutes. The equation of the linear regression line was determined to be y = 0.994x + 2.662, and the coefficient of determination (r^2) was calculated to be 0.999. The coefficient of variation (%CV) obtained for the calibration graph of infigratinib was determined to be less than or equal to 3.73. The matrix effect was assessed by calculating the coefficient of variation (%CV) for the high and low QC samples, yielding values of 1.64 and 0.70%, respectively.

References

1. Botrus G, Raman P, Oliver T, Bekaii-Saab T. Infigratinib (BGJ398): an investigational agent for the treatment of FGFR-altered intrahepatic cholangiocarcinoma. Expert OpinInvestig Drugs. 2021;30(4):309-316. Available formdoi: 10.1080/13543784.2021.1864320.
2. Blechacz B. Cholangiocarcinoma: Current Knowledge and New Developments. Gut Liver. 2017;11(1):13-26. Available formdoi: 10.5009/gnl15568.
3. Lima NC, Atkinson E, Bunney TD, Katan M, Huang PH. Targeting the Src Pathway Enhances the Efficacy of Selective FGFR Inhibitors in Urothelial Cancers with FGFR3 Alterations. Int J Mol Sci. 2020;21(9):21093214. Available formdoi: 10.3390/ijms21093214.
4. FDA Approved Drug Products: TRUSELTIQ (infigratinib) capsules, for oral use.https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214622s000lbl.pdf
5. Mostafa GAE, Kadi AA, AlMasoud N, Attwa MW, Al-Shakliah NS, AlRabiah H. LC-MS/MS method for the quantification of the anti-cancer agent infigratinib: Application for estimation of metabolic stability in human liver microsomes. J Chromatogr B AnalytTechnol Biomed Life Sci. 2021;1179:122806. Available form DOI: 10.1016/j.jchromb.2021.122806
6. Nirav P Patel, Mallika Sanyal, Naveen Sharma, Dinesh S Patel, Pranav S Shrivastav, Bhavin N Patel. Highly sensitive LC–MS/MS method to estimate doxepin and its metabolite nordoxepin in human plasma for a bioequivalence study Highly sensitive LC–MS/MS method to estimate doxepin and its metabolite nordoxepin in human plasma for a bioequivalence study. J Pharm Anal. 2017; 6:145-50. Available form https://doi.org/10.1016/j.jpha.2017.06.004
7. Yen-An Chen, Kuang-Yang Hsu. Development of a LC-MS/MS-based method for determining metolazone concentrations in human plasma: Application to a pharmacokinetic study. J food drug anal. 2013; 21:154-9.Available form https://doi.org/10.1016/j.jfda.2013.05.004
8. Jaivik V, ShahaPriyanka A, ShahaPriya V, ShahbMallika, SanyalcPranav S, Shrivastav. Fast and sensitive LC–MS/MS method for the simultaneous determination of lisinopril and hydrochlorothiazide in human plasma.J Pharm Anal. 2017;7:163–169. Available formdoi: 10.1016/j.jpha.2016.11.004
9. ICH guidelines for validation of analytical procedures: text and methodology. Q2(R1) ICH, Geneva; 2005. p. 1-14.Available form
10. US FDA, Guidance for Industry Bioanalytical Method Validation, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Rockville, Maryland, USA, 2001.
11. Rana S, Uralets VP, Ross W. A new method for simultaneous determination of cyclic antidepressants and their metabolites in urine using enzymatic hydrolysis and fast GC-MS, J Anal Toxicol. 2008;32:355–363.Available form DOI: 10.1093/jat/32.5.355
12. Titier K, Castaing N, Le-Deodic M. Quantification of tricyclic antidepressants and monoamine oxidase inhibitors by high-performance liquid chromatography-tandem mass spectrometry in whole blood. J Anal Toxicol. 1997;21:200–207.Available form DOI: 10.1093/jat/31.4.200
13. Patel DS, Sharma N, Patel MC. Development and validation of a selective and sensitive LC–MS/MS method for determination of cycloserine in human plasma: application to bioequivalence study. J. Chromatogr B. 2011;879: 2265–2273.Available formdoi: 10.1016/j.jchromb.2011.06.011.
14. Shashidhar Reddy D, PrakashRao and Devaraj VC. A Highly Sensitive LC-Ms/Ms Method for Determination of Desvenlafaxine in Rabbit Plasma and its Application to Rabbit Pharmacokinetic Study. J Anal Bio Tech. 2011; 2(5): 2-6. Available formDOI:10.4172/2155-9872.1000125

HOW TO CITE THIS ARTICLE: Rao PJ, Bhikshapathi DVRN. An LC-MS/MS Method Development and Validation for the Quantification of Infigratinib in K2EDTA Human Plasma. Int. J. Pharm. Sci. Drug Res. 2024;16(1):86-91. **DOI:** 10.25004/IJPSDR.2024.160112