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Original Article

METHOD DEVELOPMENT AND VALIDATION OF TIVOZANIB BY USING RP-HPLC IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Objective: The current investigation was pointed at developing and progressively validating novel, simple, responsive and stable RP-HPLC method for the measurement of active pharmaceutical ingredient of Tivozanib.

Methods: A simple, selective, validated and well-defined stability that shows isocratic RP-HPLC methodology for the quantitative determination of Tivozanib. The chromatographic strategy utilized X-bridge phenyl column of dimensions 150x4.6 mm, 3.5 micron, using isocratic elution with a mobile phase of acetonitrile and 0.1 percent formic acid (50:50). A flow rate of 1 ml/min and a detector wavelength of 216 nm utilizing the PDA detector were given in the instrumental settings. Validation of the proposed method was carried out according to an international conference on harmonization (ICH) guidelines.

Results: LOD and LOQ for the two active ingredients were established with respect to test concentration. The calibration charts plotted were linear with a regression coefficient of R^2>0.999, means the linearity was within the limit. Recovery, specificity, linearity, accuracy, robustness, ruggedness were determined as a part of method validation and the results were found to be within the acceptable range.

Conclusion: The proposed method to be fast, simple, feasible and affordable in assay condition. During stability tests, it can be used for routine analysis of the selected drugs.

Keywords: Tivozanib, RP-HPLC, Development, Validation, ICH guidelines

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INTRODUCTION

Tivozanib, sold under the brand name Fotivda, is a medication used for the treatment of relapsed [1, 2] or refractory advanced renal cell carcinoma (RCC) [3-5]. It is an oral VEGF receptor tyrosine kinase inhibitor [6]. The most common side effects include fatigue [7], hypertension [8, 9], diarrhea, decreased appetite [10], nausea, dysphonia [11], hypothyroidism [12, 13], cough [14], and stomatitis [15]. Tivozanib must not be combined with St. John's Wort, an inducer of the liver enzyme [16, 17] CYP3A4. It should not be taken during pregnancy as it is teratogenic [18, 19], embryotoxic and fetotoxic in rats. Administration of a single dose of tivozanib with rifampicin, a strong inducer of the enzyme CYP3A4 [20, 21], cuts the biological half-life and total exposure (AUC) of tivozanib in half, but has no relevant influence on highest concentrations in the blood. Combination with ketoconazole, a strong CYP3A4 inhibitor, has no relevant effects. The clinical significance of these findings is not known. A quinoline urea derivative, tivozanib suppresses angiogenesis [22, 23] by being selectively inhibitory against vascular endothelial growth factor (VEGF) [24, 25]. It is designed to inhibit all three VEGF receptors [26, 27]. After tivozanib is taken by mouth, highest blood serum levels are reached after 2 to 24 h. The total AUC is independent of food intake. When in the bloodstream, over 99% of the substance are bound to plasma proteins, predominantly albumin. Although the enzymes CYP3A4 and CYP1A1 [28] and several UGTs are capable of metabolising the drug, over 90% circulate in unchanged form. The metabolites are demethylation, hydroxylation and N-oxidation products and glucuronides [29]. The biological half-life is 4.5 to 5.1 d; 79% being excreted via the faeces, mostly unchanged, and 12% via the urine, completely unchanged. Tivozanib is used in form of the hydrochloride monohydrate. The aim of the study is to estimate the pharma ingredient Tivozanib by using RP-HPLC.

MATERIALS AND METHODS

Chemicals

Acetonitrile, HPLC-grade formic acid, water were purchased from Merck India Ltd, Mumbai, India. API of Tivozanib standard was procured from Glenmark, Mumbai.

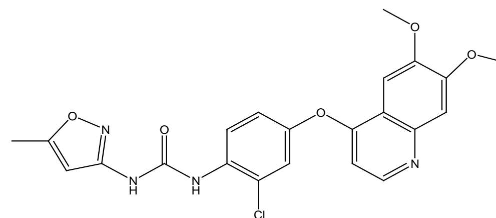


Fig. 1: Structure of tivozanib

The instrumentation

Waters alliance liquid chromatography (model 2695) monitored with empower 2.0 data handling system and a detector of photo diode array (model 2998) was used for this study [30].

Method optimization

To optimize the chromatographic conditions, different ratios of phosphate buffer and the acetonitrile in the mobile phase with isocratic mode was tested. However the mobile phase composition was modified at each trial to enhance the plate count and also to achieve acceptable retention times. Finally 0.1% formic acid buffer and acetonitrile with isocractic elution was selected because it results in a greater response of active pharmacy ingredient. During the optimization of the method various stationary phases such as C_8, C_{18} and amino, phenyl columns were tested. From these trials the peak shapes were relatively good with X-bridge phenyl column of 150 x 4.6 mm, 3.5 µ with a PDA detector. The mobile phase flow rate has been done at 216 nm in order to obtain enough sensitivity. By using above conditions we get retention time of Tivozanib was about 4.07 min with a tailing factor of 1.21. The number of theoretical plates for Tivozanib was 4257 which indicate the column's successful output the % RSD for six replicate injections was around 1.35%, the proposed approach suggests that it is extremely precise. According to ICH guidelines, the method established was validated.

Till today there are no HPLC methods were reported in the literature. Hence we developed a method for the quantification of Tivozanib. The developed HPLC method was utilized for the estimation of the drug by *in vitro* method. Different extractions were tried using acetonitrile, methanol, and dimethylformamide.

Validation procedure

The analytical parameters such as system suitability, precision, specificity, accuracy, linearity, robustness, LOD, LOQ, forced degradation and stability were validated according to ICH Q2 (R1) guidelines [31-34].

Preparation of buffer

1 ml of formic acid is dissolved in 1 lt of HPLC grade water and filter through 0.45 µ filter paper.

Chromatographic conditions

The HPLC analysis was performed on reverse phase HPLC system with isocratic elution mode using a mobile phase of acetonitrile and 0.1% formic acid (50:50 v/v) and X-bridge phenyl (150x4.6 mm, 3.5 µ) column with a flow rate of 1 ml/min.

Diluent

Mobile phase was used as diluent.

Preparation of the standard solution

For standard stock solution preparation, add 70 ml of diluents to 13.4 mg of Tivozanib taken in a 100 ml volumetric flask and sonicate for 10 min to fully dissolve the contents and then make up to the mark with diluent. 5 ml of solution is drawn from the above normal stock solution into a 50 ml volumetric flask and diluted up to the level.

Preparation of the sample solution

For sample solution preparation, add 70 ml of diluents to 52.8 mg of Tivozanib sample (each tablet contains 1.34 mg of Tivozanib) taken in a 10 ml volumetric flask and sonicate it for 20 min to fully dissolve the contents and then make up to the mark with diluent. 1 ml of solution is drawn from the above sample stock solution into a 10 ml volumetric flask and diluted up to the level.

RESULTS AND DISCUSSION

The main analytical challenge during development of a new method was to separate active Pharma ingredients. In order to provide a good performance the chromatographic conditions were optimized.

System suitability

In System suitability injecting standard solution and reported USP tailing and plate count values are tabulated in table 1 [35].

Table 1: Results of system suitability

System suitability parameter	Acceptance criteria	Tivozanib
USP Plate Count	NLT 2000	4257
USP Tailing	NMT 2.0	1.21
USP Resolution	NLT 2.0	-
% RSD	NMT 2.0	1.35

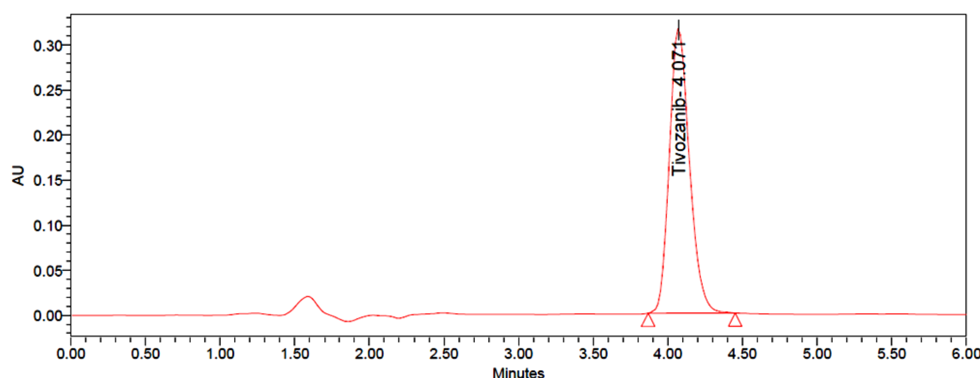


Fig. 2: Chromatogram of standard

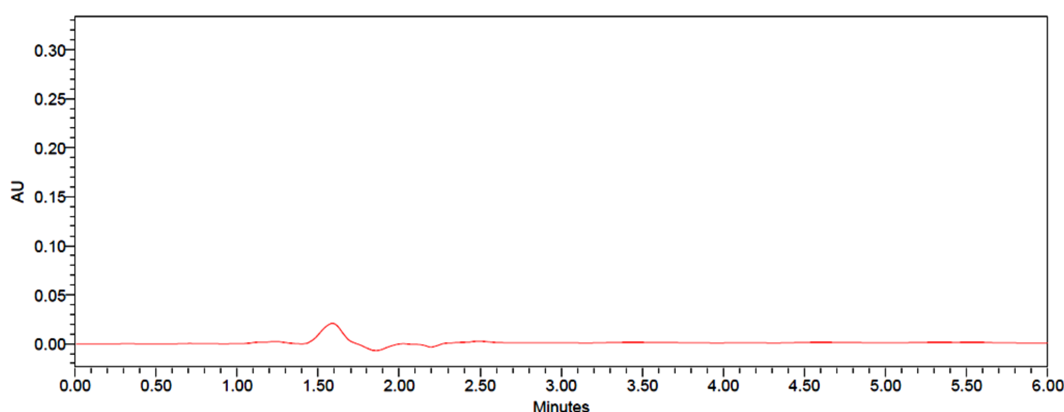


Fig. 3: Chromatogram of blank

Specificity

In this test method placebo, standard and sample solutions were analyzed individually to examine the interference. The below fig. shows that the active ingredient was well separated from blank and their excipients and there was no interference of placebo with the principal peak. Hence the method is specific.

Linearity

The area of the linearity peak versus different concentrations has been evaluated for Tivozanib, as 10, 25, 50, 75, 100, 125, 150 percent respectively. Linearity was performed in the range of 1.34-20.1µg/ml of Tivozanib. The correlation coefficient achieved was greater than 0.9991.

Table 2: Linearity of tivozanib

S. No.	Conc µg/ml	Tivozanib area count
1	1.34	371255
2	3.35	826268
3	6.70	1703314
4	10.05	2350807
5	13.40	3059642
6	16.75	4068593
Correl coef		0.99910
Slope		236568.29
intercept		28236.13

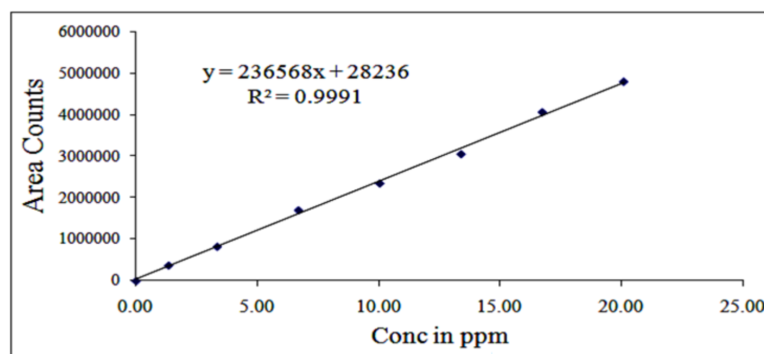


Fig. 4: Calibration plot of tivozanib

Accuracy

In this method, Accuracy was conducted in triplicate by analyzing active pharma ingredient sample solution at three kinds of concentration levels of 50, 100 and 150% of each at a specified limit. The percentage recovery was measured and found to be within the limit. The accuracy and reliability of the developed method was established. The percentage recovery values were found to be in the range of 99.65-100.93% for Tivozanib. The results are given in table 3.

Table 3: Results of accuracy

S. No.	% Level	Tivozanib % recovery
1	50	99.65
2	100	100.12
3	150	100.93
mean		100.23
SD		0.648

mean+SD (n=3)

Table 4: Intraday precision results of tivozanib

Tivozanib			
S. No.	**Conc.(µg/ml)**	**Area counts**	**% assay as is**
1	13.4	2948264	99.2
2		2949491	99.3
3		2937437	98.9
4		2944641	99.1
5		2931517	98.7
6		2946124	99.2
% RSD	0.238		
mean	99.07		
SD	0.22509		

mean+SD (n=6)

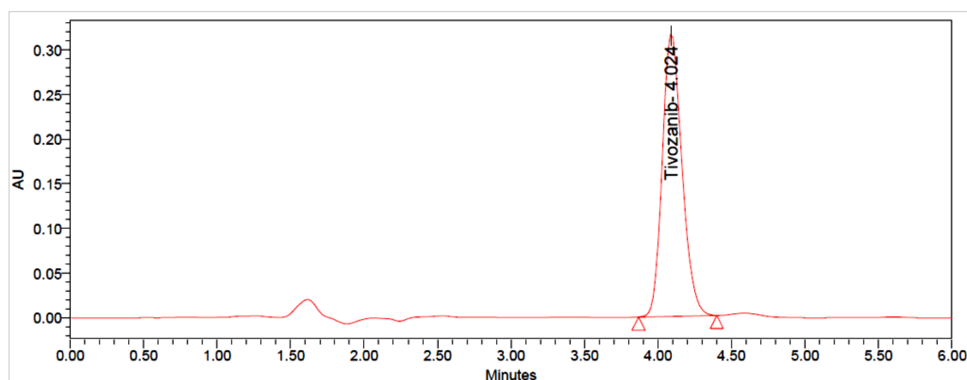


Fig. 5: Chromatogram of method precision

Precision

In method precision study prepare six different standard solutions in the concentration of Tivozanib (13.4 µg/ml) are injected into HPLC system. Tivozanib %assay found to be in the range of 99.74-100.63.

Intraday precision

Six replicates of a sample solution containing Tivozanib (13.4 µg/ml) were analysed on the same day. Peak areas were calculated, which were used to calculate mean, SD and %RSD values. These results are given below table 4.

Intermediate precision

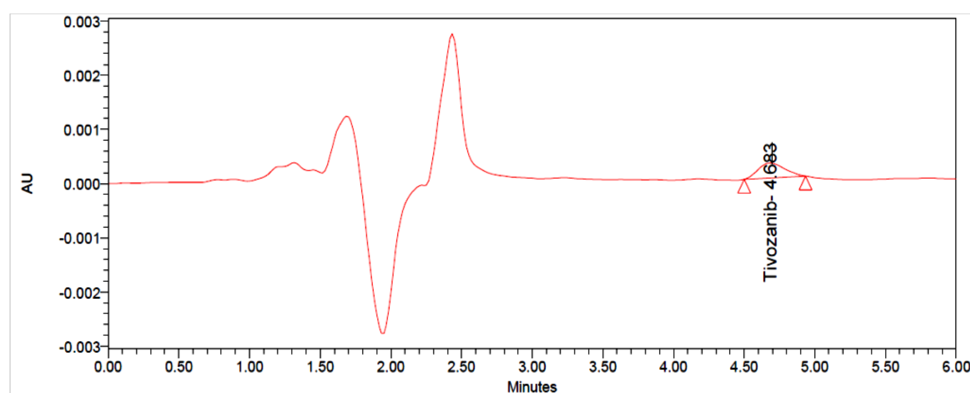
Six replicates of the sample solutions were studied by various researchers, and on separate days different instruments were tested. The peak regions used to determine mean percent RSD values have been calculated. The results are given in the following table.

Inter-day precision

Six replicates of a sample solution containing Tivozanib (13.4 µg/ml) were analysed on a different day. Peak areas were calculated which were used to calculate mean, SD and %RSD values. The present method was found to be precise as the RSD values were less than 2% and also the percentage assay values were close to be 100%. The results are given in table 5 [36].

LOD and LOQ

The LOD concentration for Tivozanib was 0.017 µg/ml and s/n values is 6. The LOQ concentration for Tivozanib was 0.055 µg/ml and the s/n value was 27. The method is validated as per the ICH guidelines [37]. Results of LOD and LOQ were shown in table 6.



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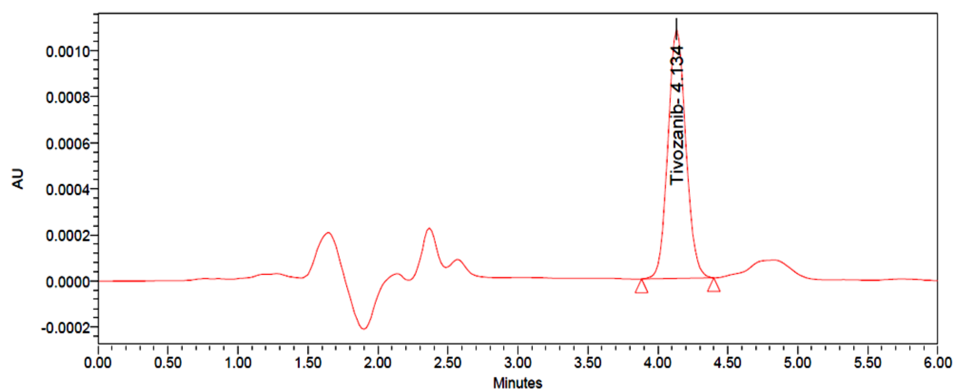

B

Fig. 6: Chromatogram of (A) LOD and (B) LOQ

Table 5: Inter-day outcomes of tivozanib

Tivozanib			
S. No.	**Conc.(µg/ml)**	**Area counts**	**% assay as is**
1		2938262	98.9
2	13.4	2936513	98.8
3		2947542	99.2
4		2954684	99.5
5		2931509	98.7
6		2976118	100.2
%RSD	0.554		
Mean	99.22		
SD	0.56362		

mean+SD (n=6)

Table 6: LOD and LOQ for tivozanib

Tivozanib			
LOD		**LOQ**	
Concentration	s/n	Concentration	s/n
0.017µg/ml	6	0.055µg/ml	27

Robustness

The conditions of the experiment were designed to test the robustness of established system intentionally altered, such as flow rate, mobile phase in organic percentage in all these varied conditions. Robustness results for Tivozanib found to be within the limit and results are tabulated in table 7 [38].

Table 7: Robustness data of tivozanib

Parameter name	% RSD of tivozanib
Flow minus (0.8 ml/min	0.17
Flow plus (1.2 ml/min)	0.06
Organic minus (-10%)	1.20
Organic plus (+10%)	0.49

Stability

The sample solution was kept at room temperature and at 2-8 °C up to 24 h. Then these solutions were pumped into the device and calculate the % of deviation from initial to 24 h [39]. There was no significant deviation observed and confirmed that the solutions were stable up to 24 h percentage of the assay was not quite 2%. There is no effect in storage conditions for Tivozanib drug. The results are given below table 8.

Table 8: Stability results of tivozanib

Stability	Tivozanib	
	Purity	**% of deviation**
Initial	98.9	0.00
6 h	98.5	-0.40
12 h	98.5	-0.40
18 h	95.5	-3.44
24 h	92.2	-6.77

Degradation studies

The Tivozanib sample was subjected into various forced degradation conditions to effect partial degradation of the drug. Studies of forced degradation have carried out to find out that the method is suitable for products of degradation [40]. In addition, the studies provide details about the conditions during which the drug is unstable, in order that the measures are often taken during formulation to avoid potential instabilities [41].

Acid degradation

Acid degradation was done by using 1N HCl and 15.2% of Tivozanib degradation was observed.

Alkali degradation

Alkali degradation was done at 1N NaOH and 16.5% of Tivozanib degradation was observed.

Peroxide degradation

Peroxide degradation was performed with 30% hydrogen peroxide and 14.8% Tivozanib degradation was observed.

Reduction degradation

Reduction degradation was performed with 30% sodium bi sulphate solution, 13.9% Tivozanib degradation was observed.

Thermal degradation

In thermal degradation the sample was degraded to 12.7% of Tivozanib.

Photo degradation

In photo degradation the sample was degraded to 11.9% of Tivozanib.

All degradation results are tabulated in table 9.

Table 9: Forced degradation results of tivozanib

Degradation condition	Tivozanib	
	% assay	**%Deg**
Control degradation	99.8	0.2
Acid degradation	84.6	15.2
Alkali degradation	83.3	16.5
Peroxide degradation	85	14.8
Reduction degradation	85.9	13.9
Thermal degradation	87.1	12.7
Photo degradation	87.9	11.9

CONCLUSION

We present in this article simple, selective, validated and well-defined stability that shows isocratic RP-HPLC methodology for the quantitative determination of Tivozanib. All the products of degradation formed during the stress conditions and the active pharma ingredient were well separated and peaks were well resolved from each other and separate with an appropriate retention time indicating that the proposed method to be fast, simple, feasible and affordable in assay condition. Therefore the developed method during stability tests, it can be used for routine analysis of production standards and to verify the quality of drug standards during stability studies.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Van den Oever MC, Spijker S, Smit AB, De Vries TJ. Prefrontal cortex plasticity mechanisms in drug seeking and relapse. Neurosci Biobehav Rev. 2010;35(2):276-84. doi: 10.1016/j.neubiorev.2009.11.016, PMID 19932711.
2. Hudson A, Stamp JA. Ovarian hormones and propensity to drug relapse: a review. Neurosci Biobehav Rev. 2011;35(3):427-36. doi: 10.1016/j.neubiorev.2010.05.001, PMID 20488201.
3. Rini BI, Rathmell WK, Godley P. Renal cell carcinoma. Curr Opin Oncol. 2008;20(3):300-6. doi: 10.1097/ CCO.0b013e3282f9782b, PMID 18391630.
4. Quinn DI, Lara PN. Renal-cell cancer--targeting an immune checkpoint or multiple kinases. N Engl J Med. 2015;373(19):1872-4. doi: 10.1056/NEJMe1511252, PMID 26406149.
5. Ljungberg B, Campbell SC, Choi HY, Jacqmin D, Lee JE, Weikert S, Kiemeney LA. The epidemiology of renal cell carcinoma. Eur Urol. 2011;60(4):615-21. doi: 10.1016/j.eururo.2011.06.049, PMID 21741761.
6. Levitzki A, Mishani E. Tyrphostins and other tyrosine kinase inhibitors. Annu Rev Biochem. 2006;75:93-109. doi: 10.1146/annurev.biochem.75.103004.142657, PMID 16756486.
7. Mills RJ, Young CA, Pallant JF, Tennant A. Development of a patient reported outcome scale for fatigue in multiple sclerosis: the neurological fatigue index (NFI-MS). Health Qual Life Outcomes. 2010;8:22. doi: 10.1186/1477-7525-8-22, PMID 20152031.
8. Lackland DT, Weber MA. Global burden of cardiovascular disease and stroke: hypertension at the core. Can J Cardiol. 2015;31(5):569-71. doi: 10.1016/j.cjca.2015.01.009, PMID 25795106.
9. Musini VM, Gueyffier F, Puil L, Salzwedel DM, Wright JM. Pharmacotherapy for hypertension in adults aged 18 to 59 y. Cochrane Database Syst Rev. 2017;2017(8):CD008276. doi: 10.1002/14651858.CD008276.pub2.
10. Kaplan RJ, Greenwood CE. Influence of dietary carbohydrates and glycaemic response on subjective appetite and food intake in healthy elderly persons. Int J Food Sci Nutr. 2002;53(4):305-16. doi: 10.1080/09637480220138160, PMID 12090026.
11. Van Houtte E, Van Lierde K, Claeys S. Pathophysiology and treatment of muscle tension dysphonia: a review of the current knowledge. J Voice. 2011;25(2):202-7. doi: 10.1016/j.jvoice.2009.10.009.
12. Pantalone KM, Hatipoglu BA. Hyponatremia and the thyroid: causality or association? J Clin Med. 2014;4(1):32-6. doi: 10.3390/jcm4010032, PMID 26237016.
13. Wiersinga WM, Duntas L, Fadeyev V, Nygaard B, Vanderpump MP. 2012 ETA Guidelines: The use of L-T4+L-T3 in the treatment of hypothyroidism. Eur Thyroid J. 2012;1(2):55-71. doi: 10.1159/000339444, PMID 24782999.
14. Goldsobel AB, Chipps BE. Cough in the pediatric population. J Pediatr. 2010;156(3):352-8. doi: 10.1016/j.jpeds.2009.12.004, PMID 20176183.
15. Fourie J, van Heerden WF, McEachen SC, van Zyl A. Chronic ulcerative stomatitis: a distinct clinical entity? SADJ. 2011;66(3):119-21. PMID 21874892.
16. Johnston DE. Special considerations in interpreting liver function tests. Am Fam Physician. 1999;59(8):2223-30. PMID 10221307.
17. Gowda S, Desai PB, Hull VV, Math AA, Vernekar SN, Kulkarni SS. A review on laboratory liver function tests. Pan Afr Med J. 2009;3:17. PMID 21532726.
18. Cerrizuela S, Vega Lopez GA, Aybar MJ. The role of teratogens in neural crest development. Birth Defects Res. 2020;112(8):584-632. doi: 10.1002/bdr2.1644, PMID 31926062.
19. Bellinger DC. Teratogen update: lead and pregnancy. Birth Defects Res A Clin Mol Teratol. 2005;73(6):409-20. doi: 10.1002/bdra.20127, PMID 15880700.
20. Qiu H, Mathäs M, Nestler S, Bengel C, Nem D, Gödtel Armbrust U, Lang T, Taudien S, Burk O, Wojnowski L. The unique complexity of the CYP3A4 upstream region suggests a nongenetic explanation of its expression variability. Pharmacogenet Genomics. 2010;20(3):167-78. doi: 10.1097/FPC.0b013e328336bbeb, PMID 20147837.
21. Bishop Bailey D, Thomson S, Askari A, Faulkner A, Wheeler Jones C. Lipid-metabolizing CYPs in the regulation and dysregulation of metabolism. Annu Rev Nutr. 2014;34:261-79. doi: 10.1146/annurev-nutr-071813-105747, PMID 24819323.
22. Birbrair A, Zhang T, Wang ZM, Messi ML, Olson JD, Mintz A, Delbono O. Type-2 pericytes participate in normal and tumoral angiogenesis. Am J Physiol Cell Physiol. 2014;307(1):C25-38. doi: 10.1152/ajpcell.00084.2014, PMID 24788248.
23. McDougall SR, Anderson AR, Chaplain MA. Mathematical modelling of dynamic adaptive tumour-induced angiogenesis: clinical implications and therapeutic targeting strategies. J Theor Biol. 2006;241(3):564-89. doi: 10.1016/j.jtbi.2005.12.022, PMID 16487543.
24. Campas C, Bolos J, Castaner R. Tivozanib. Drugs Fut. 2009;34(10):793-6. doi: 10.1358/dof.2009.034.10.1417872.
25. Karkkainen MJ, Petrova TV. Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis. Oncogene. 2000;19(49):5598-605. doi: 10.1038/sj.onc.1203855, PMID 11114740.
26. Stuttfeld E, Ballmer Hofer K. Structure and function of VEGF receptors. IUBMB Life. 2009;61(9):915-22. doi: 10.1002/iub.234, PMID 19658168.
27. Zygmunt T, Gay CM, Blondelle J, Singh MK, Flaherty KM, Means PC, Herwig L, Krudewig A, Belting HG, Affolter M, Epstein JA, Torres Vazquez J. Semaphorin-PlexinD1 signaling limits angiogenic potential via the VEGF decoy receptor sFlt1. Dev Cell. 2011;21(2):301-14. doi: 10.1016/j.devcel.2011.06.033, PMID 21802375.
28. Badal S, Delgoda R. Role of the modulation of CYP1A1 expression and activity in chemoprevention. J Appl Toxicol. 2014;34(7):743-53. doi: 10.1002/jat.2968, PMID 24532440.
29. Yang G, Ge S, Singh R, Basu S, Shatzer K, Zen M, Liu J, Tu Y, Zhang C, Wei J, Shi J, Zhu L, Liu Z, Wang Y, Gao S, Hu M. Glucuronidation: driving factors and their impact on glucuronide disposition. Drug Metab Rev. 2017;49(2):105-38. doi: 10.1080/03602532.2017.1293682, PMID 28266877.
30. Cijo M. Xavier, Kanakapura Basavaiah. RP-UPLC Development and validation of metformin hydrochloride in pure drug and pharmaceutical formulations. World J Pharm Pharm Sci. 2015;4:1649-68.
31. Sri Girija K, Bikshal Babu K, Venkateswara Rao A. A new high - performance liquid chromatography method for the separation and simultaneous quantification of Eeptifibatide and its impurities in pharmaceutical injection formulation. Int J Appl Pharm. 2021;13:165-72.
32. VLN Balaji Gupta, VLN T Venkateswara Rao B, Kishore Bbabu B. RP-HPLC (stability indicating) based assay method for the simultaneous estimation of Doravirine, tenofovir disoproxil fumarate and lamivudine. Int J Appl Pharm. 2021;13:153-9.
33. Murali Krishnam Raju P, Venkata Narayana B, Shyamala P, Srinivasu K, HSN Raju HSN D. A validated RP-HPLC method for impurity profiling of Sodium nitroprusside in injection dosage form. Int J Appl Pharm. 2021;13:160-9.
34. Sanathoiba Singha L, Srinivasa Rao T. Development and validation of an RP-HPLC method for the determination of Uulipristal acetate in pharmaceutical dosage form. Asian J Pharm Clin Res. 2021;14:83-9.
35. Asha Eluru A, Surendra Babu K. A study of method development, validation and forced degradation for simultaneous quantification of povidone iodine and ornidazole in bulk and pharmaceutical dosage form by using RP-HPLC. Int J Res Pharm Sci. 2021;12:1217-22.
36. Malathi S, Devakumar D. Development and validation of rp-hplc method for the estimation of escitalopram oxalate and

flupentixol dihydrochloride in combined dosage form and plasma. Int J Pharm Pharm Sci. 2021;13:61-6.

37. Syed Rafi, Kantipudi Rambabu. Stability indicating validated HPLC method for the determination of aceclofenac and misoprostol in bulk and pharmaceutical formulation. IJRPS 2020;11(4):7848-53. doi: 10.26452/ijrps.v11i4.4669.
38. Gunturu Raviteja, Kantipudi Rambabu. A study of development and validation of a method for simultaneous estimation of cidofovir and famciclovir using RP-HPLC. IJRPS 2020;11(4): 7878-84. doi: 10.26452/ijrps.v11i4.4673.
39. Vijayakumari M, Balasekhar Reddy Ch B. Stability indicating validated hplc method for the determination of zanubrutinib in bulk and pharmaceutical dosage form. Asian J Pharm Clin Res. 2020;13:159-62.
40. Charu Pandya P, Sadhana Rajput J. Development and validation of stability indicating method RP-HPLC method of Aacotiamide. Int J Pharm Pharm Sci. 2018;10:1-8.
41. Athavia BA, Dedania ZR, Dedania RR, Swamy SMV, Prajapati CB. Stability indicating HPLC method for determination of vilazodone hydrochloride. Int J Curr Pharm Sci 2017;9(4):123-9. doi: 10.22159/ijcpr.2017v9i4.20975.