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SPECTROPHOTOMETRIC DETERMINATION OF DRUGS BY USING N-BROMOSUCCINAMIDE AND RHODAMINE-B DYE COUPLE

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ABSTRACT

Simple, sensitive and accurate methods are developed for the spectrophotometric determination of five drugs, *viz*., Amoxicillin, Bendamustine, Ceftriaxone Sodium, Diclofenac Sodium and Quetiapine Fumerate based on their reactivity towards N-Bromosuccinamide(NBS) . The method involves addition of a known excess of N-bromosuccinimde to drugs in acidic medium (1*M* HCl) and the residual amount of oxidant (NBS) is estimated with Rhodamine-B dye. The absorbance was measured at 557 nm. These methods have been applied for the determination of above drugs in their pure form as well as in tablet formulations. The method has been validated in terms of guidelines of ICH.

KEYWORDS: Spectrophotometry, NBS, Rhodamine-B, drugs, Quantification and Validation.

1. INTRODUCTION

Amoxicillin (AMO) [(2S,5R,6R)- 6-{[(2R)-2-amino- 2-(4-hydroxyphenyl)- acetyl]amino}-3,3-dimethyl- 7-oxo- 4-thia- 1-azabicyclo[3.2.0]heptane- 24-carboxylic acid] is an antibiotic[1] and used for the treatment of a number of bacterial infections. It is useful to treat many different types of infections caused by bacteria, like tonsillitis, pneumonia, bronchitis, gonorrhea, and infections of the ear, throat, skin, nose, urinary tract. It inhibits the bacterial cell wall.[2] Several analytical methods have been reported for the determination of AMO in pure drug, pharmaceutical dosage forms using Spectrophotometry[3-6], HPLC[7] and LC-MS.[8, 9]

Bendamustine (BEN) chemically [4-[5-[bis (2-chloroethyl) amino]-1-methylbenzimidazole-2-yl] butanoic acid]. It is an alkylating agent. Bendamustine used for the treatment of chronic

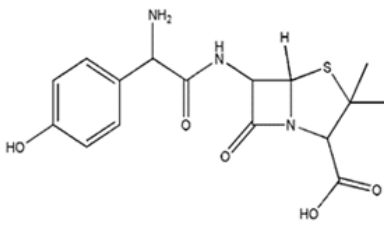
lymphocytic leukemia and lymphomas. It kills the existing cancer cells and stops the growth of new cancer cells.[10, 11] A literature survey has revealed few spectrophotometric[12, 13], LC-MS[14], HPLC[15, 16] and RP-HPLC[17] methods reported for the estimation of BEN.

Ceftriaxone Sodium (CEF) [(6R,7R)-7-[[(2A)-2-(2-amino-1,3.thiazol-4-yl)-2-(methoxyimino) acetyl]amino]-3-{[2-methyl-5,6-tetrahedro-1,2,4-triazin-3-yl)thio]methyl}-8-oxo-5-thia-1-aza bi cyclo[4.2.0]oct-2-ene-2carboxylic acid] is an antibiotic and used to treat different types of bacterial infections like ear, skin, urinary tract, gonorrhea and intra-abdominal infections.[18,19] Several methods were reported for determination of CEF such as Flourimetry[20], UV spectrophotometry[21-24] and NIR.[25, 26]

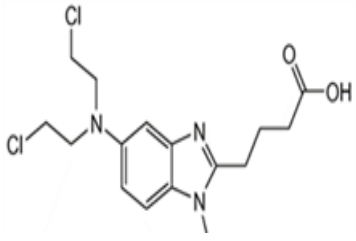
Diclofenac Sodium (DIC) [2-(2, 6-dichloranilino) phenyl acetic acid]] is a non-steroidal anti-inflammatory drug (NSAID). It is used to relieve pain, swelling (inflammation), and joint stiffness caused by arthritis.[27, 28] It stops prostaglandin synthesis by inhibition of cyclooxygenase. A literature survey has revealed some methods have been described for the analysis of DIC by UV-VIS Spectrophotometry.[29-31], FT-Raman spectroscopy[32], FTIR[33] and HPLC.[34]

Quetiapine Fumerate (QUE) chemically [2-(2-(4-dibenzo [b, f] [1, 4] thiazepine11yl-1-piperazinyl) ethoxy) ethanol] and it is marketed as Seroquel. It is an atypical antipsychotic drug used for the treatment of schizophrenia and other psychotic disorders.[35, 36] Various methods cited in literature for determination of QUE include RP-HPLC [37], RP-UPLC[38], UV spectrophotometry[39-41] and LC-MS.[42]

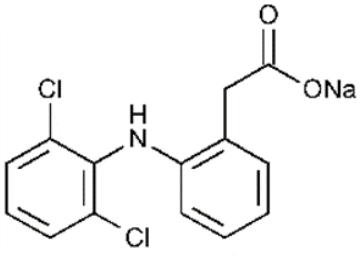
STRUCTURES OF DRUGS



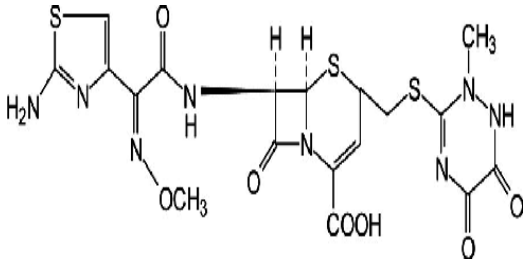
Amoxicillin



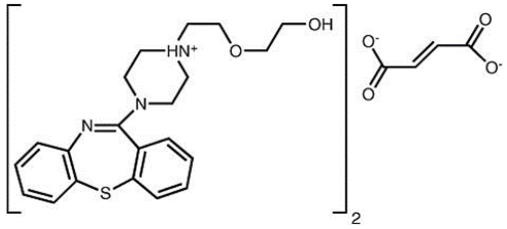
Bendamustine



Diclofenac Sodium



Ceftriaxone sodium



Quetiapine fumerate

Through survey of literature on the above mentioned drugs revealed that quantification based on use of NBS as oxidizing reagent and Rhodamine-B as analytical reagent have not been yet reported. The present work is an attempt to develop accurate, simple, sensitive and cost effective methods for the estimation of above drugs.

2. EXPERIMENTAL

2.1 Instrumentation

All absorption spectra were recorded on Elico SL 210 UV-Visible Double beam spectrophotometer as well as on Thermo Nicolet 100 single beam spectrophotometer using matched pair of Quartz cells of 10mm path length. A high precision analytical balance was used for weighing the reagents.

2.2 Materials and Reagents

All chemicals and reagents used were of analytical or pharmaceutical grade and all solutions are prepared afresh every day. Double distilled water was used throughout the investigation.

An approximately 0.01*M* NBS stock solution was prepared by dissolving N-bromo succinimide (Himedia Laboratories pvt.Ltd, Mumbai) in 100 ml standard flask with double distilled water.[43] The solution was kept in an amber colored bottle and was further diluted with distilled water appropriately to get 70 µg mL^{-1}.

A 500 µg mL^{-1} of Rhodamine-B was prepared by dissolving the dye (s. d. Fine Chem. Ltd., Mumbai) in 100 ml standard flask with double distilled water. The dye solution was further diluted to get 50 µg mL^{-1}. Concentrated Hydrochloric acid (S.D. Fine Chem., Mumbai, India) was diluted appropriately with double distilled water to get 1 *M* HCl. Pharmaceutical grade drugs were kindly supplied by Hetero Drugs Pvt. Lmd. Hyderabad. A stock standard solution of drugs were prepared by dissolving accurately weighed 20 mg of drug transferred in 100ml volumetric flask and made up to mark with distilled water. The solution was diluted stepwise to get required concentrations.

2.3 Method development

Aliquots of pure drug solution (1 to 7 mL) were transferred into a series of 10 mL calibrated flasks. To each flask, 1 mL of HCl was added, followed by 1 mL of NBS solution (70 µg mL^{-1}). The contents were mixed and they were set aside for 10 min under occasional shaking. Finally, 1 mL of Rhodamine- B solution (50 µg mL^{-1}) was added to each flask, diluted to the mark with water and the absorbance of solution was measured at 557 nm against a reagent blank after 10 min.

2.4 Construction of Calibration Curves

The calibration curve was plotted by taking concentration (µg mL^{-1}) of the drugs in X-axis and absorbance in Y-axis. The calibration curves were constructed by taking absorbance data in six replicate experiments. The absorbance to concentration called relative response is calculated. Those points falling between 95% to 105% of the average relative response are only considered for construction of calibration. The linearity graphs are shown in Fig. 1.

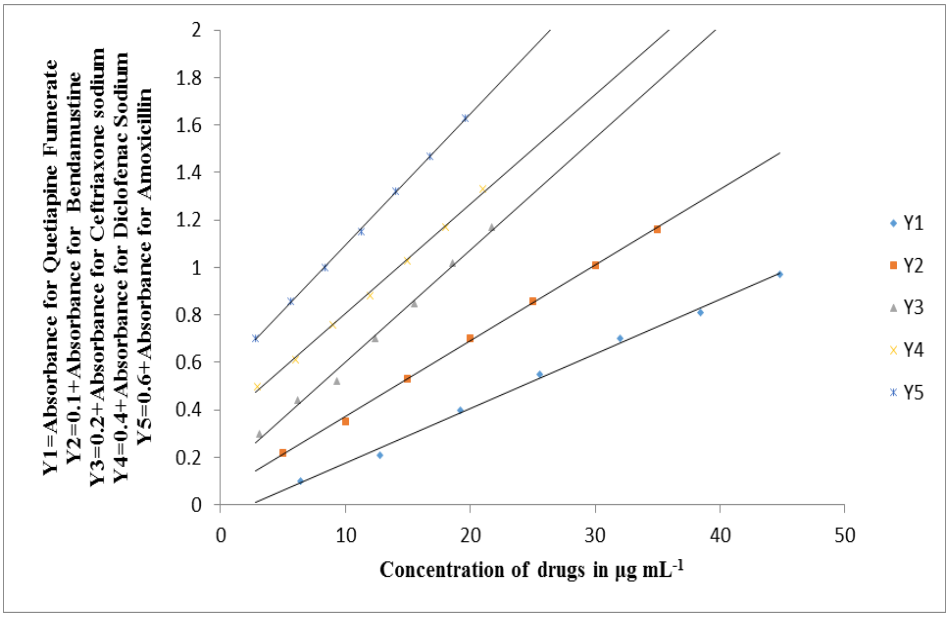


Fig 1 Clibration curves for five drugs

2.5 Accuracy and Precession studies

Accuracy of the methods developed are determined from the recovery studies on pure drug sample. At least four known concentration of solutions of drugs in Beer's law limit were taken and recovery studies were performed. Excellent recovery showed the validity of the calibration curves for each drug.

Precession of the method is demonstrated by repeating experiment (n=6) and %RSD is worked out. %RSD being less than 2 in each case speaks the high precession of the methods.

2.6. Analysis of Pharmaceutical preparations

Three tablets of (NOVAMOX-500mg) were weighed and ground in to fine powder. Weight equivalent to 10mg of Amoxicillin was transferred in 100ml volumetric flask and made up to mark with water. And the solution filtered using a Whatman No. 42 filter paper. The resultant of the solution was further diluted to get a required concentration.

One vial of (BENDIT-100mg) was weighed and ground in to fine powder. The powder equivalent to10mg of Bendamustine was dissolved in10ml of the methanol and diluted to 100ml with distilled water. The solution was filtered through Whatman No.42 filter paper. It was further diluted to get required concentration for the analysis of the drug.

One tablet of (ROCEPHIN-1gr) was weighed and ground in to fine powder. Weight equivalent to 10mg of Ceftriaxone Sodium was transferred in 100ml volumetric flask and made up to mark with water. And the solution filtered using a Whatman No. 42 filter paper. The resultant of the solution was further diluted to get a required concentration.

Three tablets of (VOLTARIN-50mg) were weighed and ground in to fine powder. The powder equivalent to10mg of Diclofenac Sodium was dissolved in 10ml of the methanol. The solution was filtered through Whatman No.42 filter paper. It was further diluted to get required concentration for the analysis of the drug.

Three tablets of (SEROQUEL-50mg) were weighed and ground in to fine powder. Weight equivalent to 10mg of Quetiapine Fumerate was transferred in 100ml volumetric flask and made up to mark with water. And the solution filtered using a Whatman No. 42 filter paper. The resultant of the solution was further diluted to obtain suitable concentration.

The drug solutions obtained from tablet formulations were subjected to oxidation by excess NBS and subsequent determination of NBS and Rhodamine-B was carried out. The concentration of the tablet solutions falling in Beer's law limit were selected for the assay of drug in the tablet. An excellent tally between the concentration of drugs taken and found indicated the applicability of the methods for formulations.

3. RESULTS AND DISCUSSIONS

The proposed spectrophotometric methods are indirect and are based on the determination of the excess of NBS after allowing the oxidation reaction to complete in acidic medium. The excess of NBS was determined by reacting it with a fixed amount of Rhodamine-B dye. The NBS is capable to oxidize drugs and readily bleach the colour of dye. The absorbance λ max (557nm) increased linearly with increasing concentration of a given drug. Acidic medium (Hydrochloric acid) was found to be a convenient medium for this method. For a quantitative reaction between drug and NBS, a contact time of 10 min was found sufficient.

4. ANALYTICAL DATA

Under optimum conditions a linear correlation was found between absorbance at λ max and concentration of all drugs in the ranges given in table 1. Sensitivity parameters such as molar absorptivity, Sandell sensitivity are also presented in Table 1. Regression analysis of Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a), correlation coefficient (r) and is also given in table 1.

The LOD and LOQ were determined based on the standard deviation of the y-intercept and the slope of the calibration curves and presented in table1.

LOD = 3.3 σ /b

LOQ = 10σ/b.

Where σ = standard deviation of the intercept (n = 6)

b = slope of Calibration plot.

Table1 Analytical and regression parameters of spectrophotometric method

Parameter	AMO	BEN	CEF	DIC	QUE
λmax, nm	557	557	557	557	557
Beer's law limits μg mL^{-1}	2.8-19.6	5-35	3.1-21.7	3-21	6.4-44.8
Molar absorptivity, L mol^{-1} cm^{-1}	1.31×10^{5}	9.23×10^{3}	1.96×10^{4}	11.11×10^{3}	0.82×10^{4}
Sandell sensitivity μg cm^{-2}	0.018	0.032	0.021	0.021	0.454
Limit of detection μg mL^{-1}	1.02	2.129	0.035	2.15	4.05
Limit of quantification μg mL^{-1}	3.09	6.45	0.108	6.52	12.27
Intercept, (a)	-0.057	-0.048	-0.06	-0.057	-0.052
Slope, (b)	0.055	0.031	0.046	0.046	0.022
Correlation coefficient, (r)	0.999	0.998	0.991	0.998	0.996
Standard deviation of intercept (σ)	0.017	0.020	0.0005	0.030	0.027
Regression equation, Y	0.055X-0.057	0.031-0.048	0.046X-0.06	0.046X-0.057	0.022X-0.052

X=Concentration of drug

4.1 Linearity and Range

The linearity of the analytical procedure is its ability to obtain the best results which is directly proportional to the concentration of analyte in the sample. The calibration curves of Amoxicillin, Bendamustine, Ceftriaxone sodium, Diclofenac sodium by the proposed method were found to be linear of the ranges of 2.8-19.6 µg mL^{-1}, 5-35 µg mL^{-1}, 3.1-21.7 µg mL^{-1}, 3-21 µg mL^{-1}, 6.4-44.8 µg mL^{-1}.

Table 2 Determination of accuracy and precision of the methods on pure drug samples

Drug	Taken (µg mL^{-1})	Found (µg mL^{-1})	Er (%)	Recovery (%)	RSD (%)	Proposed method Mean ± SD
AMO	3.5 4.5 6.5	3.5 4.55 6.48	0.00 1.11 0.30	100.00 101.11 99.69	0.744	100.26 ± 0.746
BEN	6.0 8.0 12.0	5.98 8.01 12.02	0.33 0.12 0.16	99.66 100.12 100.16	0.277	99.98 ± 0.277
CEF	4.5 6.5 8.5	4.47 6.5 8.51	0.66 0.00 0.11	99.33 100.00 100.11	0.422	99.80 ±0.422
DIC	5.0 7.0 10.0	5.01 6.97 9.98	0.20 0.42 0.20	100.20 99.57 99.80	0.319	99.85 ± 0.318
QUE	7.5 9.5 11.5	7.5 9.46 11.47	0.00 0.42 0.26	100.00 99.57 99.73	0.217	99.76 ± 0.217

Table3: Results of assay of tablets by proposed method and statistical evaluation.

Tablet	Drug in tablet (µg mL^{-1})	Drug Found (µg mL^{-1})	Er (%)	Recovery (%)	RSD (%)	Reference method Mean± SD	Proposed method Mean ± SD	*t-test*	F-test
Novamox (AMO)	10 12 14	9.97 12 14.11	0.30 0.00 0.78	99.7 100.00 100.7	0.512	99.52 ±1.08	100.13 ±0.513	*1.023*	0.225
Bendit (BEN)	15 20 25	15.02 20.05 25	0.13 0.25 0.00	100.13 100.25 100.00	0.124	99.91 ±0.86	100.12 ±0.125	*0.421*	0.059
Rocephin (CEF)	5.5 7.5 9.5	5.45 7.45 9.53	0.90 0.66 0.31	99.09 99.33 100.31	0.649	98.33 ± 0.27	99.57 ±0.646	*3.61*	5.791
Voltarin (DIC)	6.5 8.5 10.5	6.54 8.48 10.5	0.61 0.23 0.00	100.61 99.76 100.00	0.437	102.62 ± 1.38	100.12 ±0.438	*-3.03*	0.100
Seroquel (QUE)	12 14 16	12.03 14.01 15.97	0.25 0.07 0.18	100.25 100.07 99.81	0.221	97.48 ±0.89	100.04 ±0.221	*6.09*	0.060

*Average of four determinations

5. CONCLUSION

The proposed method was found to be very simple, rapid and cost effective than some of the reported methods. The method is suitable for the determination of above drugs in tablet formulation without interference from commonly used excipients. The solvent used for this method are inexpensive and simple to prepare, and could be used in a quality control laboratory for routine drug analysis. Hence this method can be valid for application in laboratories lacking liquid chromatographic instruments.

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REFERENCES

1. Eumkeb G, Siriwong S, Thumanu K. Synergistic activity of luteolin and amoxicillin combination against amoxicillin–resistant Escherichia coli and mode of action. Journal of Photochemistry and Photobiology, 2012; 117: 247-253.
2. Simar preet K, Rekha R, Sanju N. Amoxicillin: A broad spectrum of antibiotic. International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3(3).
3. Rahman BM, Mahmoud KM. Batch and Flow Injection Analysis Spectrophotometric Determination of Amoxicillin using N-bromosuccinimide and Indigo Carmine. American Chemical Science Journal, 2015; 5(3): 214-223.
4. Karpova Svetlana P. Quantitative determination of amoxicillin tri hydrate in medical forms using kinetic method. Journal of Chemical and Pharmaceutical Research, 2014; 6(4): 1120-1125.
5. AL-Uzri WA. Spectrophotometric determination of amoxicillin in pharmaceutical preparations through diazotization and coupling reaction. Iraqi Journal of Science, 2012; 53(4).
6. Prakash K, Narayana raju P, Shanta Kumari K, Lakshmi narasu M. Spectrophotometric Estimation of Amoxicillin Trihydrate in Bulk and Pharmaceutical Dosage Form. E-Journal of Chemistry, 2008; 5(S2): 1114-1116.

7. De Pourcq P, Hoebus J, Roets E, Hoogmartens J, Vanderhaeghe H. Quantitative determination of amoxicillin and its decomposition products by high-performance liquid chromatography. Journal of chromatography, 1985; 321(2): 441-9.
8. De Baere S, De Backer, Patrick. Quantitative determination of amoxicillin in animal feed using liquid chromatography with tandem mass spectrometric detection. Analytica Chimica Acta, 2007; 586(1-2): 319-325.
9. Lugoboni B, Gazzotti T, Zironi E, Barbarossa A, Pagliuca G. Development and validation of a liquid chromatography/tanden mass spectrometry method for quantitative determination of amoxicillin in bovine muscle.Journal of chromatography, 2011; 879(21): 1980-6.
10. Friedberg JW, Cohen P, Chen L, Robinson KS, Forero-Torres A, La Casce AS, Fayad LE, Bessudo A, Camacho ES, Williams ME, van der Jagt RH, Oliver JW, Cheson BD. Bendamustine in patients with rituximab-refractory indolent and transformed non-Hodgkin's lymphoma: results from a phase II multicenter, single-agent study J. Clinical Oncology, 2008; 26(2): 204.
11. Maddocks, Kami J, Lin, Thomas S. Update in the management of chronic lymphocytic leukemia. Journal of Hematology & Oncology, 2009; 2.
12. Mathrusri Annapurna M, Pavani S, Anusha S, Harika M, Venkatesh B. New analytical methods for the determination of Bendamustine hydrochloride: An anti-neoplastic drug. Journal of Chemical and Pharmaceutical Research, 2012; 4(3): 1696-1701.
13. Kiran Kumar K, Venkatanadh R, Nagiji KEV. Determination of bendamustine hydrochloride in pure and dosage forms by ion-associative complex formation. Oriental Journal of Chemistry, 2014; 30(2): 905-910.
14. Dubbelman AC, Tibben M, Rosing H, Gebretensae A, Nan L, Gorman SH, Robertson PJr, Schellens JHM, Beijnen JH. Development and validation of LC-MS/MS assays for the quantification of bendamustine and its metabolites in human plasma and urine. Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences, 2012; 893-894, 92-100.
15. Srinivasulu K, Raja Sekhar Reddy M, Raja Sekhar K, Veerender M, Venkata Suryanarayana M. Stability-indicating LC method for the estimation of bendamustine hydrochloride and its related impurities. Journal of chromatographic science, 2014; 52(7): 573-83.

16. Ivanka P, Anita B, Neli K, Danka O, Kolio T. HPLC study on the stability of bendamustine hydrochloride immobilized onto polyphosphoesters. Journal of pharmaceutical and biomedical analysis, 2008; 48(4): 1143-50.
17. Kiran Kumar K, Venkatanadh R, Nagiji KEV. A validated RP-HPLC method for the determination of Bendamustine hydrochloride in tablet dosage form using Gemcitabine hydrochloride as internal standard. J.Pharm. Sci., 2012; 37(3): 133-139.
18. Liang, Xiao-yan; Zhong, Yu-jie; Liu, Zhong-min. Research progress of mechanisms of ceftriaxone sodium associated gallstones. Yixue Zongshu, 2014; 20(6): 1080-1082.
19. Naimi H M, Rasekh H, Haem Rahimi M, Yousofi H. Assessment of the price-efficacy relationship for multiple brands of ceftriaxone sodium in Kabul: a cross-sectional study. BMC research notes, 2016; 9(1): 86.
20. Zhang, Yuanfu; Wang, Jinzhong; Wang, Chongyan; Li, Yongqiang. Determination of ceftria xone sodium content by fluorometry with complex. Yiyao Daobao, 2007; 26(3): 296-297.
21. Qu, Hai-tao; Sun, Lu; Sun, Yu-qing. Qualitative and quantitative analysis of triazin in ceftriaxone sodium. Shenyang Yaoke Daxue Xuebao, 2007; 24(5): 295-297, 302.
22. Alothman, Zeid A.; Siddiqui, Masoom Raza; Khan, Moonis Ali. Quantitative analysis of ceftriaxone sodium in parenteral dosage form. Asian Journal of Chemistry, 2013; 25(13): 7229-7234.
23. Qian, Yao-jun; Pan, Xue-ping. Determination of ceftriaxone sodium in injection by spectrophotometry. Guangpu Shiyanshi, 2012; 29(5): 3153-3156.
24. Patel, K. R.; Patel, V. D.; Patel, K. P.; Patel, V. G. Development and validation of spectrophotometric method for determination of ceftriaxone sodium in pharmaceutical dosage forms. Pharma Chemica, 2010; 2(5): 255-259.
25. Lu, Ying; Zhao, Yong. Determination of ceftriaxone sodium chromatism by near-infrared analysis. Hecheng Huaxue, 2005; 13(4): 417-418, 421.
26. Hou, Shaorui; Feng, Yanchun; Hu, Changqin. Development of a near-infrared method for rapid determination of ceftriaxone and water content in ceftriaxone sodium for injection. Yaowu Fenxi Zazhi, 2008; 28(6): 936-941.
27. Mahesh SK, Nalik SR, Kohli RK. Anti-inflammatory, antiarthritic and analgesic activity of a herbal formulation (DRF/AY/4012). Indian Jounal of Experimental Biology, 2007; 45: 278-284.
28. Bindu Nair, Regina Taylor-Gjevre. A Review of Topical Diclofenac Use in Musculo skeletal Disease. Pharmaceuticals, 2010; 3: 1892-1908.

29. Botello, Julio C.; Perez-Caballero, Guadalupe. spectrophotometric determination of diclofenac sodium with methylene blue. Talanta, 1995; 42(1): 105-8.
30. Kamath BV, Shivram K. Spectrophotometric determination of diclofenac sodium via oxidation reactions. Analytical Letters, 1993; 26(5): 903-11.
31. Wang, Feng; Huang, Wei; Tang, Bo; Zhao, Qinghua. Spectrophotometric determination of diclofenac sodium based on charge transfer reaction. Yaowu Fenxi Zazhi, 2007; 27(10): 1654-1657.
32. Mazurek, Sylwester; Szostak, Roman. Quantitative determination of diclofenac sodium in solid dosage forms by FT-Raman spectroscopy. Journal of Pharmaceutical and Biomedical Analysis, 2008; 48(3): 814-821.
33. Szostak Roman; Mazurek Sylwester. The influence of sample area on diclofenac sodium quantification by diffuse reflectance IR spectroscopy. Talanta, 2011; 84(2): 583-6.
34. Sivakumar N, Chenthilnathan A, Vairamani A. Development and validation of RP-HPLC method for the Quantitative determination of diclofenac sodium in pharmaceutical dosage form. International Journal of Pharmaceutical Research and Biomedical Analysis, 2014; 3(2): 20-30.
35. Marina Sagud, Alma Mihaljevic-Peles, Drazen Begic, Bjanka Vuksan-Cusa, Milivoj Kramaric , Maja Zivkovic , Miro Jakovljevic. Antipsychotics as antidepressants: what is the mechanism?. Psychiatria Danubina, 2011; 23(3): 302-307.
36. Janicak, Philip G.; Rado, Jeffrey T. Quetiapine monotherapy for bipolar depression. Expert Opinion on Pharmacotherapy, 2011; 12(10): 1643-1651.
37. Raju C, Ashwani S, Deepak K, Augustin Kumar B. Development and validation a RP-HPLC method: application for the quantitative determination of quetiapine fumerate from marketed bulk tablets. Journal of Chemical and Pharmaceutical Research, 2016; 8(1): 142-146.
38. Trivedi Rakshit K, Patel Mukesh C. Development and validation of a stability indicating RP-UPLC method for determination of quetiapine in pharmaceutical dosage form. Scientia pharmaceutica, 2011; 79(1): 97-111.
39. Arulappa, R. Xavier; Sundarapandian, M.; Venkataraman, S, Boopathi, M.; Kauraw, Manish. Spectrophotometric determination of quatiapine fumerate in bulk and dosage form. Research Journal of Pharmacy and Technology, 2009; 2(4): 884-885.
40. Lakshmi, Baby Sudha P, Vardhan SVM, Ramachandram D, Rambabu C. UV Spectro photo metric determination of quetiapine and zonisamide. Asian Journal of Chemistry, 2009; 21(1): 811-813.

41. Vinay KB, Revenasiddappa, HD. Spectrophotometric determination of quetiapine fumerate in pharmaceuticals and human urine by two charge-transfer complexation reactions. Chemical Industry & Chemical Engineering Quarterly, 2012; 18(2): 263-272.
42. Barrett B, Holcapek M, Huclova J, Borek-Dohalsky V, Fejt P, Nemec B, Jelinek I. Validated HPLC-MS/MS method for determination of quetiapine fumerate in human plasma. Journal of pharmaceutical and biomedical analysis, 2007; 44(2): 498-505.
43. Vinay KB, Revanasiddappa HD, Rajendraprasad N, Raghu MS, Ramesh PJ, Cijo MX. Basavaiah. Rapid titrimetric and spectrophotometric assay of tramadol in bulk drug and in formulation using N-bromosuccinimide and methyl orange as reagents. Thai Journal of Pharmaceutical Sciences, 2011; 35(1): 8-17.