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SPECTROPHOTOMETRIC METHODS FOR THE SIMULTANEOUS ESTIMATION OF PARACETAMOL AND ETORICOXIB IN TABLET DOSAGE FORMS

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ABSTRACT

The present work describes two methods for simultaneous estimation of paracetamol (PCT) and etoricoxib (ETX) in solid dosage forms. First method employs the application of simultaneous equation and second, the absorbance ratio (Q-analysis) method. Both methods utilizes methanol as solvent. PCT shows maximum absorbance at a wavelength 249.0 nm and ETX at 271.5 nm. Determination of ratio of absorbance at 249 nm, the maximum absorption of PCT and isabsorptive wavelength 264.5 nm, the linearity ranges for PCT and ETX were 8.3- 41.5 µg/ml and 1-5 µg/ml respectively for both proposed methods. The procedure was successfully applied for the simultaneous determination of both drugs in laboratory prepared mixtures and in commercial tablet preparation. The accuracy of the methods was assessed by recovery studies and was found to be 99.17 ± 1.85 and 100.00 ± 0.95 for the simultaneous equation method, 99.12 ± 1.08 and 100.06 ± 1.57 for the absorbance ratio method for PCT and ETX respectively.

Keywords: Paracetamol, Etoricoxib, Tablets, Spectrophotometry

INTRODUCTION

Paracetamol (PCT), 4- hydroxy acetanilide used as analgesic, antipyretic[1]. Etoricoxib (ETX), 5- chloro- 6- methyl-3[p-sulfonyl phenyl]-2,3- bipyridine used as NSAID[2,3]. Both the drugs are formulated in binary solid dosage form use as analgesic and antipyretic. PCT tablet was determined by spectrophotometrically[4-8] and high performance liquid chromatography[9-13]. ETX was determined spectrophotometrically[14-16], RP-HPLC[17,18] and HPLC-Mass spectroscopy[19,20]. No spectrophotometric method has been reported for the simultaneous estimation of both these components in combined dosage form. The aim of this paper was to develop the simultaneous equation (vierodt's) method and the absorbance ratio (Q – analysis) method for estimating PCT and ETX simultaneously in their mixture form. In the proposed methods no separation is required; the method is fast and convenient.

MATERIALS AND METHODS

Instruments, reagents and chemicals

A dual beam Shimadzu Uv- visible spectrophotometer 1700 was used for experimentation. Methanol was used as solvent. Gift samples of Paracetamol and Etoricoxib were produced from Cadila ltd Mumbai.

Experimental

Standard stock and working stock solution

According to the solubility characteristics of drug, methanol was selected as solvent for analysis.

Standard stock (500µg/ml) and working solution (10µg/ml) of PCT and ETX were prepared in methanol. The aliquot portion (0.2-10 ml) from working solution of PCT and ETX were transferred to 10 ml volumetric flask, the volume was completed with methanol. The absorption spectra between 200- 400 nm of all solutions of PCT and ETX were measured at 249.0 nm (λ max of PCT), 271.5 nm (λ max of ETX), at 264.5 nm (isoabsorptive wavelength), respectively (Fig 1).

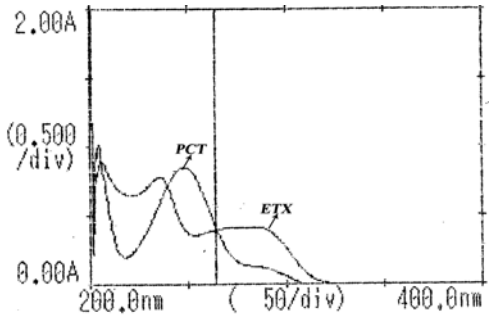

Fig. 1: Overlain spectra of Paracetamol and Etoricoxib

Application of proposed procedures in tablets

The method was first applied to the laboratory mixture which yielded encouraging results and the method was extended to marketed formulation.

The powder equivalent to 500 mg of PCT was transferred to 100 ml volumetric flask and dissolved in methanol by intermittent shaking and volume was made upto 100 ml with the same solvent. The solution was then filtered through a whatmann fiter paper (No. 41). Aliquot portion of the filtrate was diluted with methanol to 50 ml. A 5 ml of the above diluted solution was further diluted to obtain 41.5 µg/ml of PCT and 8.3 µg/ml of ETX (on label claim basis). The final dilution was read at the selected wavelengths against solvent blank.The amount of each was estimated using the following formulae by proposed methods

Simultaneous equation method

The absorptivity values of the drugs were determined at λ_{max} of PCT and ETX. The absorptivity value of the drugs is the ratio of absorbance at selected wavelengths with the concentration of drugs in mg/ml. A set of two simultaneous equations were framed using these absorptivity values.

$A_1 = 928.29\ C_{PCT} + 239.73\ C_{ETX}$ ----------(at λ_{249})

$A_2 = 340.99\ C_{PCT} + 363.79\ C_{ETX}$ ----------(at $\lambda_{271.5}$)

Where, A_1 and A_2 are the absorbance of the tablet sample solution at 249 nm and 271.5 nm respectively.928.29 and 340.99 are absorptivities of PCT at 249 nm and 271.5 nm respectively.239.73 and 363.79 are the absorptivities of ETX at 249 nm and 271.5 nm respectively. C_{PCT} is the concentration of PCT and C_{ETX} is the concentration of ETX in mg/ml.

The graphical absorption ratio method (Q analysis)

In quantitative assay of two components by Q- analysis method, absorbance was measured at the iso-absorptive wavelength and maximum absorption of one of the two components. From overlain spectra of PCT and ETX shown in figure (Fig. 1), absorbances were measured at the selected wavelengths i.e. 264.5 nm (isoabsorptive wavelength) and 271.5 nm (wavelength of maximum absorption of ETX). From the following sets of equations, the concentration of each component in the sample can be calculated.

Concentration of PCT = $(Q_0 - 0.9832)\ A/965.23$

Concentration of ETX = $(2.0231 - Q_0)\ A/360.59$

Where, A = absorbance of sample solution at isoabsorptive wavelength 264.5 nm

Q_0 = ratio of absorbance of sample solution at 249 nm to the absorbance of sample solution at isoabsorptive wavelength 264.5 nm.

The results of estimation of both these drugs by using simultaneous equation and absorbance ratio method are shown in Table 1

Table 1: Result of estimation by the proposed methods

Sample	Simultaneous equation method		Graphical absorbance ratio method	
	PCT	ETX	PCT	ETX
Lab Mixture	101.04	99.60	98.64	98.51
	±0.65	±0.64	±0.67	±1.00
Tablet	100.14	100.03	98.38	98.23
Formulation	±0.43	±1.20	±0.43	±0.50

Mean ±SD of six observations

Table 2: Result of the application of standard addition technique by proposed methods

Claimed amount Taken (µg/ml)		Standard added (µg/ml)		Recovery of added standard (%)[a] ± S.D PCT		ETX	
PCT	ETX	PCT	ETX	SEM[b]	GAM[c]	SEM[b]	GAM[c]
41.6	5	20.80	2.7	100.74	98.31	98.14	99.25
41.6	5	41.6	5.1	99.60	98.10	98.00	100.58
41.6	5	62.2	7.3	98.64	100.86	98.21	102.32
41.6	5	83.0	10.5	101.04	99.23	102.38	98.09
Mean				100.00	99.12	99.17	100.06
± S.D.				±0.95	±1.08	±1.85	±1.57

a: Mean, S.D.: Standard deviation, b: Simultaneous equation method, c:Graphical absorbance ratio method.

The selectivity of the proposed procedures was examined by determining the recovery of the two drugs by standard addition method at four different levels. The samples were prepared in the same manner as for marketed formulation. The results of recovery studies are shown in Table 2

RESULT AND DISSCUSSION

The solubility of Paracetamol (PCT) and Etoricoxib (ETX) was studied and methanol was selected as a choice of solvent.

Paracetamol and Etoricoxib showed well defined λ_{max} at 249.0 nm and 271.5 nm respectively. The two drugs also show an isoabsorptive wavelength at 264.5 nm, where both the drugs have same absorptivity value. The wavelengths 271.5 and 249.0 nm were considered for development of Simultaneous Equation Method whereas 264.5 and 249.0 nm for absorbance ratio method.The two drugs individually and in their mixture were found to follow Beer-Lambert's law over the concentration range of 8.3-41.5 µg/mL and 1-5 µg/mL for PTC and ETX respectively.

Validation

The methods were validated with respect to specificity, accuracy, precision linearity and ruggedness.

Specificity

These studies were carried out to ascertain how accurately and specifically, the analytes of interest are estimated in presence of other components (e.g. impurities, degradation products, etc.) by exposing the samples to different stress conditions such as light, heat, oxidation, acids, alkali and humidity and then analyzing them by proposed methods. However conculsive evidence could not be given but the variation in precent label indicates that drugs are susceptible to stress conditions as shown in Table 3

Table 3: Results of Specificity study

Treated sample	% Undegraded drug			
	Simultaneous equation Method		Absorbance ratio Method	
	PCT	ETX	PCT	ETX
1 N NaOH	20.36	28.07	24.68	31.82
1 N HCl	75.04	102.18	71.18	97.60
3% H_2O	89.88	101.35	85.00	124.96
60^0C	93.98	118.08	90.28	94.19
Humidity (75%)	90.96	99.84	87.30	93.06
UV Exposure	91.19	114.69	86.21	117.60
Photochemical	98.72	102.14	95.04	94.56

Accuracy

Accuracy of the proposed method was ascertained on the basis of recovery studies performed by standard addition method. The recoveries of both the drugs were observed to be very close to 100 % representing the accuracy of the method and also show that excipients have no interference in the estimation

Precision

SD and RSD of series of measurement were found to satisfactory.

Linearity and Range

The Linearity and Range study is indicative of accurate estimation of drug in tablet over range of at least 80 -120 % of label claim.

Ruggedness

In intraday and interday variations, and different analyst results of estimation by proposed methods were found to be satisfactory, indicates ruggedness of the method.

The results of validation parameters are summarized in Table 3.

Table 3. Precision and accuracy of Spectrophotometric method developed for analysis of tablet (n=6)

	Simultaneous equation method	Absorbance ratio method
Paracetamol		
Intraday		
Amount found (Mean %± S.D.)	101.10± 0.25	98.61±1.42
Accuracy, Bias (%)	1.1	-1.39
Precision, RSD(%)	0.25	1.43
Interday		
Amount found (Mean %± S.D.)	100.54± 0.80	98.04± 2.26
Accuracy, Bias (%)	0.54	-1.96
Precision, RSD(%)	0.82	2.25
Etoricoxib		
Intraday		
Amount found (Mean %± S.D.)	101.52± 1.42	97.79± 0.94
Accuracy, Bias (%)	1.52	-2.21
Precision, RSD(%)	1.43	0.95
Interday		
Amount found (Mean %± S.D.)	98.73± 1.90	94.81± 3.65
Accuracy, Bias (%)	-1.27	-5.19
Precision, RSD(%)	1.89	3.68

S. D.: Standard error, % Bias = [100(found – label claim)/ label claim], RSD: Relative standard deviation

CONCLUSION

The proposed methods were found to be simple, accurate, economical, and rapid for routine simultaneous estimation of two drugs. The results obtained for tablet and recovery study are summarized in table 1 and 2 respectively. The results of validation parameters shown in Table 4 are satisfactory level indicates the accuracy of proposed methods for estimation of PCT and ETX. These methods also gave excellent result and can be employed for routine analysis of these two drugs in combined dosage form.

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REFERENCES

1. The Indian Pharmacopoeia Vol. I Ministry of Health and Family Welfare, Controller of publications New Delhi; 1996.
2. Cochrane D J, Jarvis B, and Keating G M. Drug. 2002; 62(18): 2637.
3. Leclercq P and Malasia M G. Etoricoxib. Rev. Med. Liege. 2004; 59: 345.
4. Milch G and Szabo E. Derivative spectrophotometric assay of acetaminophen and spectrofluorimetric determination of its main impurity. J. Pharm Biomed Anal. 1991; 9(10-12): 1107-13.
5. Miceli J N, Aravind M K, and Done AK, A rapid, simple acetaminophen spectrophotometric determination. Pediatrics. 1979; 63(4): 609-11.
6. Morelli B. Spectrophotometric determination of paracetamol in pure form and in tablets. J. Pharm Biomed Anal. 1989; 7(5): 577-84.
7. Elsayed M A, Belal S F, Elwalily A F and Abdine H. Spectrophotometric determination of acetaminophen in tablets, sirups, and suppositories. J. Assoc Off Anal Chem. 1979; 62(3): 549-51.
8. Issopoulus P B. A sensitive spectrophotometric determination of acetaminophen. Acta Pharm Hung. 1992; 62(1-2): 31-8.
9. "The United States Pharmacopoeia" 24/19 National Formulary, The United States Pharmacopoeial Convection, Rockville; 2000: 17- 22.
10. Martin A, Garcia A, and Barbas C. Validation of a HPLC quantification of acetaminophen, phenylephrine and chlorpheniramine in pharmaceutical formulations: capsules and sachets. J. Pharm BioMed Anal. 2002; 29(4): 701-14.
11. Nagaralli B S, Seetharamappa J, Gowda B G, and Merwanki M B, Liquid chromatographic determination of ceterizine hydrochloride and paracetamol in human plasma and pharmaceutical formulations. J. Chromatogr B Analyt. Technol Biomed Life. 2003; 798(1): 49-54.
12. Franeta J T, Agbaba D, Eric S, Pav Kov S, Aleksic M, and Vladimirov S. HPLC assay of acetylsalicylic acid, paracetamol, caffeine and phenobarbital in tablets. Farmaco. 2002; 57(9): 709-13.
13. Aktar M J, Khan S and Hafiz M. High-performance liquid chromatographic assay for the determination of paracetamol, pseudoephedrine hydrochloride and triprolidine hydrochloride**.** J. Pharm Biomed Anal. 1994; 12(3): 379-82.
14. Suhagia B N, Patel H M, Shah S A and Rathod I S. Determination of etoricoxib in pharmaceutical formulations by HPLC method. Ind. J. Pharm. Sci**.,** 2007; 69(5): 703-705.
15. Singh R M, Kumar Y, and Sharma D K, Indian Drugs, 2005; 42(8): 535-36.
16. Vadnerkar G, Jain S K, and Jain D, Determination of Etoricoxib in Bulk Drug, Dosage Form and Human Plasma by UV-Spectrophotometry. Asian J. Chem. 2006; 18(4): 2895-2901.
17. Ansari T A, Jamil S, Singh R M, Mathur S C, Shivraj, and Singh G N, Indian Drugs. 2005; 42(1): 56-58.
18. Shakya A K and. Khalaf N A. High Performance Liquid Chromatographic and Ultra Violet Spectroscopic Determination of Etoricoxib in Pharmaceutical Formulations. Asian J. Chem. 2007; 19(3): 2059-2069.

19. Rose M J, Agrawal N, Woolf E J and Mathiszewski B K. Simultaneous determination of unlabeled and carbon-13-labeled etoricoxib, a new cyclooxygenase-2 inhibitor, in human plasma using HPLC-MS/MS. J. Pharm Sci. 2002; 91: 405.

20. Brautigam L, Nefflen J U and Geisslinger G, Determination of etoricoxib in human plasma by liquid chromatography-tandem mass spectrometry with electrospray ionisation. Journal of Chromatography B, Analytical Technologies in the Biomedical and Life Sciences, 2003; 788(2): 309-15.

21. Skoog D A, West D M, and Holler F J, In; Instrumental analysis - An introduction, 6th edn. Saunder College Publishing, Delhi; 2004: 567.

22. Beckett A H, and Stenlake G H, In; Practical Pharmaceutical Chemistry, 4th edn. CBS Publishers, New Delhi; 2005: 278-300.

23. The United States Pharmacopoeia 24/19 National Formulary, The United States Pharmacopoeial Convection, Rockville; 2000: 2149-52.

24. International conference on Harmonization (ICH), Draft guidelines on validation of analytical procedure- definition and terminology, Federal Register.1995;60: 11260.