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Spectrophotometric Quantitative Estimation of Lornoxicam and Paracetamol in Bulk Drugs and Dosage Form

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ABSTRACT

Two accurate, precise, sensitive and economical spectrophotometric methods were developed and validated for simultaneous estimation of Lornoxicam and Paracetamol in tablet dosage form. These methods were developed based on the simultaneous estimation of drugs in a binary mixture without previous separation. The methods employed were Absorbance Ratio Method (Q-Analysis) (I) and Simultaneous Equation Method (Vierodt's Method) (II). The first method employs 271.5 nm as λ_1 (Isobestic point) and 286 nm as λ_2 (λ_{max} of Lornoxicam) for formation of equations. The second method employs estimation of a drug concentration by selecting λ_{max} where the absorbances of these drugs were maximum. So λ_{max} for Lornoxicam and Paracetamol is 286 nm and 257 nm respectively. Lornoxicam and Paracetamol obey Beer's law in the concentration range 8-40 μgmL^{-1} (r^2=0.9998) and 10-50 μgmL^{-1} (r^2=0.9999) in 0.1 N NaOH. The mean recovery for Lornoxicam and Paracetamol were found to be 98.38±1.28% and100±0.50% from method I and 100.33±0.56% and100± 0.40% from method II. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values. Thus the proposed methods were successfully applied for simultaneous determination of lornoxicam and paracetamol in routine industrial work.

Keywords: Lornoxicam, Paracetamol, Absorbance Ratio Method, Simultaneous Equation Method, Spectrophotometric

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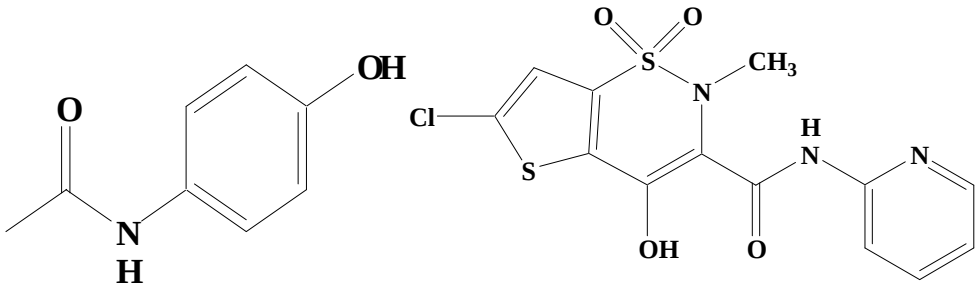
INTRODUCTION

Paracetamol, (PCM) chemically, (N-(4-hydroxyphenyl) acetamide) (Fig.1A) has analgesic and antipyretic activity and is used for the treatment of pain such as headache, toothache, rheumatism and neuralgia [1]. The mechanism of action of paracetamol is due to its inhibition of the

cyclooxygenase enzyme and the prostaglandin synthesis in the central nervous system [2] and its direct activity on the centre for the body temperature regulation in the hypothalamus [3]. Lornoxicam, (LOX) chemically, (6-chloro-4-hydroxy-2-methyl- N-2-pyridyl-2H-thieno[2, 3-*e*]-1, 2-thiazine-3-carbox- amide-1,1-dioxide) (Fig.1B) is a novel non-steroidal anti-inflammatory drug (NSAID) with marked analgesic properties [4]. Lornoxicam is a yellow crystalline substance with a pKa of 4.7 and a partition coefficient of 1.8 determined in octanol–phosphate pH 7.4. Paracetamol alone or in combination with other drugs is reported to be estimated by spectrophotometric method [5-6] HPLC [7], TLC [8], HPTLC [9], LC-MS [10], FT-IR [11], amperometric determination [12], Fluorimetry [13] and Micellar electrokinetic chromatographic method [14]. Few analytical methods for determination of Lornoxicam using a voltammetric [15], polarograhic [16], UV spectrophotmetric [17], LC/MS/MS [18-19] and high performance liquid chromatographic [20-23] in plasma and pharmaceutical formulation have been reported.

Extensive literature survey reveals that no UV method is reported for simultaneous determination of LOX and PCM in tablet dosage form by Absorbance Ratio Method and Simultaneous Equation Method. Fixed dose combination containing paracetamol (500 mg) and Lornoxicam (8 mg) is available in tablet form in the market. Therefore, an attempt was made to develop a new, rapid and sensitive UV method for the simultaneous determination of PCM and LOX in tablet dosage form.



(A) (B)

Fig-1 Chemical structures of (A) Paracetamol (B) Lornoxicam

MATERIALS AND METHODS

Experimental

Instrumentation

The proposed work was carried out on a shimadzu UV-visible spectrophotometer (model UV-1700 series), which possesses a double beam double detector configuration with a 1 cm quartz matched cell. All weighing was done on electronic balance (Citizen).

Reagents and chemicals

Analytically pure sample of LOX and PCM was kindly supplied by Lupin Laboratories Mumbai, India. The pharmaceutical dosage form used in this study was a Neucam-P (Lupin (mexter) Laboratories Mumbai) tablets containing 500 mg Paracetamol and 8 mg Lornoxicam were obtained from the local drug market

Theory

Absorbance Ratio Method (Method I)

In this method, the isoabsorptive points for both the drugs were determined from the spectra of standard drug solutions, The wavelengths selected were 271.5 nm as λ_1 (Isoabsorptive point) and 286 nm (λ_{max} for LOX) as λ_2 for formation of equations as shown in Equ 1, 2. The concentration of individual components calculated by mathematical treatment of the simultaneous equations

where Qm = A_2/ A_1, A_1 is absorbance of sample at isoabsorptive point, A_2 is absorbance of sample at λ_{max} of LOX, Qx (1.184) = ax_2/ax_1, Qy (0.618) = ay_2 /ay_1, ax_1 and ax_2 represent absorptivities of LOX at λ_1 (271.5 nm, isoabsorptive point) and λ_2 (286 nm, λ_{max} of LOX) and ay_1 and ay_2 denote absorptivities of PCM at λ_1 (271.5 nm, isoabsorptive point) and λ_2 (286 nm, λ_{max} of LOX) respectively; C_{LOX} and C_{PCM} be the concentration of LOX [should lie outside the range of (0.1-0.2)] and PCM, component by the mechanism of the absorbance respectively.

Vierordt's Simultaneous Equation Method (Method II)

This method of analysis is based on the absorption of drugs (X and Y) at the wavelength maximum of the other. The quantification analyses of LOX and PCM in a binary mixture were performed with the following equations:

$$C_{PCM} = (A_2\, ay_1 - A_1 ay_2)/ax_2 ay_1 - ax_1 ay_2 \qquad \text{(Eqn. 3)}$$

$$C_{LOX} = (A_1\, ax_2 - A_2 ax_1)/ax_2 ay_1 - ax_1\, ay_2 \qquad \text{(Eqn. 4)}$$

where C_{PCM} and C_{LOX} are the concentrations of PCM and LOX respectively in the diluted sample, ax_1 and ax_2 are absorptivities of PCM at λ_1 (257 nm, λ_{max} of PCM) and λ_2 (286 nm, λ_{max} of LOX) , ay_1 and ay_2 are absorptivities of LOX at λ_1 (257 nm, λ_{max} of PCM) and λ_2 (286 nm, λ_{max} of LOX). The absorbance of the diluted samples at 257nm and 286 nm are A_1 ($A_1 = ax_1 bcx + ay_1 bcy$) and A_2 ($A_2 = ax_2\, bcx + ay_2 bcy$), respectively.

Preparation of Standard Stock Solutions

Standard stock solutions were prepared by dissolving separately 100 mg of each drug in 100 mL of 0.1 N NaOH to get concentration of 1000 µg mL^{-1}. The standard solution (1000 µg mL^{-1}) was further diluted with 0.1 N NaOH to obtain concentration range 8, 16, 24, 32 and 40 µg mL^{-1} for LOX and 10, 20, 30, 40, and 50 µg mL^{-1} for PCM. Working standard solution of concentration 16 µg mL^{-1} of LOX and 20 µg mL^{-1} of PCM were scanned in the wavelength range of 200-400 nm against 0.1 N NaOH as blank the overlain spectra of the two were recorded (Fig 3).The overlain spectra exhibit major absorbance maxima at 257 nm and 286 nm for PCM and LOX, respectively, and at 271.5nm as isoabsorptive point which revealed that the peaks are well satisfying the criteria for obtaining maximum precision based on LOX and PCM, respectively.

Preparation of Analysis of Tablet sample

Twenty tablets (Neucam-P, Lupin (mexter) Laboratories Mumbai) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 0.8 mg of LOX and 50 mg PCM were transferred to 100 ml of volumetric flask containing 0.1 N NaOH solution. The flask was sonicated for about 10 min to solubilize the drug and the volume was made up to mark. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with 0.1 N NaOH and was analyzed on UV spectrophotometer. The absorbance at 242 (λ_{max} of LOX), 273 (λ_{max} of PCM) and 261 (Isobestic point) as in Fig-2 were recorded. Drug content of tablet formulation was calculated by using the equations mentioned above in method I and method II and value are reported in Table-1.

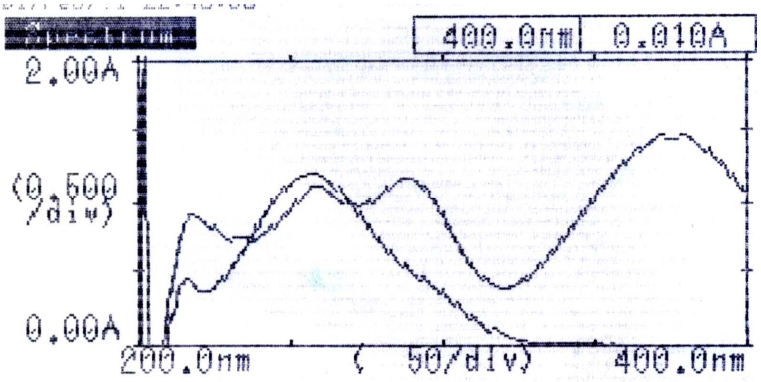


Fig-2 overlay spectra of LOX and PCM

Table 1. Results of commercial tablet analysis

Method	Amount of drug claimed (mg/TAB)		% Label Claim estimated* (Mean ± S.D)		% R. S. D.		Standard error of standard deviation (SEσ)	
			LOX	PCM	LOX	PCM	LOX	PCM
I	LOX- 8	PCM-500	100.69± 1.84	99.53±0.55	1.183	0.556	0.754	0.226
II	LOX- 8	PCM-500	98.97±1.150	99.38±0.458	1.162	0.461	0.470	0.187

** Mean of six determinations, R.S.D. is relative standard deviation*

Recovery studies

To evaluate the recovery studies, to pre-analyzed tablet solution, a definite amount of drug was added and then its recovery was studied. These studies were performed, in pre-analyzed tablet solution ranging from 8-24 µg mL^{-1} of LOX and 10-30 µg mL^{-1} of PCM, bulk drug samples 8 and 10 µg mL^{-1} of LOX and PCM respectively was added as spiked concentrations. This was repeated three times with three concentrations to emphasize validation and drug contents were determined by the proposed analytical methods. Result of recovery studies are reported in Table-2.

Table 2. Result of recovery studies of tablet formulation with statically evaluation

Method	Theoretical conc. (µg mL^{-1})		Amount added (µg mL^{-1})		Percentage recovery Mean ± S.D. (n=6)		% coefficient of variation		* Standard error of standard deviation (SEσ)	
	LOX	PCM	LOX	PCM	LOX	PCM	LOX	PCM	LOX	PCM
I	8	10	8	10	97.87±0.81	100.2±0.38	0.83	0.38	0.19	0.09
	16	20	8	10	99.75±0.72	100.6±0.41	0.72	0.41	0.17	0.10
	24	30	8	10	97.5±0.64	99.6±0.49	0.66	0.49	0.15	0.12
II	8	10	8	10	100.75±0.42	100.1±0.21	0.42	0.21	0.10	0.05
	16	20	8	10	99.75±0.28	99.7±0.29	0.28	0.29	0.07	0.07
	24	30	8	10	100.37±0.27	99.3±0.39	0.21	0.39	0.06	0.09

** Mean of nine determinations (3 replicates at 3 concentration level)*

Precision studies

To evaluate precision at different parameter like repeatability, intermediate precision, five dilutions in three replicates were analyzed in same day, in two different days and by two analysts for day to day and analyst to analyst variation and results were shown in Table-3.

Table 3. Result of Precision

Method	Validation Parameter	Percentage Mean ± S.D*		Percentage RSD*	
		LOX	PCM	LOX	PCM
I	Repeatability	99.02±0.14	99.77±0.007	0.72	0.022
	Intermediate precision				
	Day to Day	99.13±0.03	99.66±0.04	0.023	0.19
	Analyst to Analyst	98.93±0.01	99.72±0.13	0.09	0.59
II	Repeatability	99.35 ±0.04	100.30±0.05	0.18	0.16
	Intermediate precision				
	Day to Day	109.92±0.01	100.61±0.02	0.11	0.09
	Analyst to Analyst	99.85±0.05	100.65±0.01	0.39	0.04

* Mean of fifteen determinations (3 replicates at 5 concentration level)

RESULTS AND DISCUSSION

In the present work, two methods, namely graphical absorbance ratio method (Q – Analysis) and simultaneous equation (Vierordt's method), were developed for the simultaneous spectroscopic estimation of LOX and PCM in commercially available tablet dosage form using 0.1 N NaOH. From the overlain spectra of the two drugs the wavelengths used for graphical absorbance ratio method is 271.5 nm (isoabsorptive point) and 286 nm (λ_{max} of LOX) and for simultaneous equation method, 257 nm (λ_{max} of PCM) and 286 nm (λ_{max} of LOX) were selected to give optimum accuracy, precision, time, economy, and sensitivity. The mean percent label claims in tablet were found by the proposed methods 100.69± 1.84%, 99.53±0.55% (Method I) and 98.97±1.150%, 99.38±0.458% (Method II) for LOX and PCM respectively Tables-1. In order to demonstrate the validity and applicability recovery studies were performed by spiking of bulk drugs in pre analyzed tablets and the percentage recoveries for LOX and PCM were found to be ranging from 97.5-100.57%, 99.3-100.6% by methods I and Method II respectively, and the results presented in Tables-2. The values of percent relative standard deviation for the validation parameters of LOX and PCM were found to be less than 2 in method Table-3, indicating good accuracy, precision and repeatability of the proposed methods.

CONCLUSION

The validated spectrophotometric methods employed here proved to be simple, economical, rapid, precise and accurate. Thus these can be used for routine simultaneous determination of LOX and PCM in bulk drug and tablet dosage form instead of processing and analyzing each drug separately.

REFERENCES

[1]. S. Budavari, The Merck Index, Edn.12, Merck Research Lab., Division of Merck and Co., Inc., Whitehouse Station, N.J, **1996**, 9.
[2]. P. Amadio , *Am. J. Med*., **1984**, 77, 17.
[3]. C. Dollery, Therapeutic Drugs, Churchill Livingstone, Edinburgh, **1999**, A19.
[4]. J.A. Balfour, A. Fitton, L.B. Barradell, *Drugs.* **1996**, 51, 639–657.
[5]. M. Nogowska, I. Muszalska, M. Zajac, Chem. *Anal*., **1999**, 44, 1041-1048.
[6]. E. Dinc, C. Yucesoy, F. Onur, *J. Pharm. Biomed Anal.*, **2002**, 28, 1091-1100.
[7]. S.S. Zarapkar, U.P. Hulkar UP, N.P. Bhandari, *Indian Drugs.* **1999**, 36, 710-713.

[8]. Y.R. Liang, J. Hu, H.L. Wu, L.Y. Le, W.J. Wang, *Yaowu Fenxi Zazhi (Chinese).*, **2006**, 26,411-414.
[9]. A.P. Argekar, J.G. Sawant, *J. Planar Chromatography-Mod.TLC.*, **1999**, 12, 361-364.
[10]. M. Godejohann, L.H. Tseng, U. Braumann, J. Fuchser, M. Spraul, *J. Chromatogr. A.*, **2004**, 1058.191- 196.
[11]. S. Ekgasit, N. Pattayakkorn, D. Tongsakul, C. Thammancharoen, T. Kongyou, Anal. *Sci.*, **2007**, 23,863-868.
[12]. S.J.R. Prabakar, S.S. Narayanan, *Talanta., 2007*, 72:1818-1827.
[13]. E.J Llorent Marinez, D. Satinsky, P. Solich, P. Orega Barrales, A. Molina Diaz, *J. Pharm. Biomed. Anal.*, **2007**, 45, 318-321.
[14]. D. Emre, N. Ozaltin, J. *Chromatogr., B.*, **2007**, 847:126-132.
[15]. M.M. Ghoneim, A.M. Beltagi, A. Radi, *Anal. Sci.*, 2002, 18, 183-186.
[16]. C. Ibrahim, K. Nisa, A. Sule, *C.B.U. J. Sci*., **2009**, 5, 11-18.
[17]. E. Nemutlu, S. Demircan, S. Kir, *Pharmazie.*, **2005**, 60, 421-425.
[18]. H.K. Young, Y.J. Hye, S.P. Eun, et al., *Arch Pharmacal Res*., **2007**, 30, 905-910.
[19]. Y.L. Zeng, X. Y. Chen, Y.F. Zhang, et al., *Yao Xue Xue Bao*., **2004**, 39, 132-5.
[20]. S. Radhofer-Welte, P. Dittrich, *J. Chromatogr. B.*, **1998**, 707, 151-159.
[21]. N. Akiko, M.N. Nakashima, W. Mitsuhiro, et al., *Bunseki Kagaku.*, **2005**, 54, 755.
[22]. E.A. Taha, N.N. Salama, S. Abdel Fattah, J *AOAC Int.*, **2004**, 87, 366-73.
[23]. R.P. Kiran, S.B. Devanand, V.P. Rane, J.N. Sangshetti, *Chromatographia.*, **2009**, 69, 1001-1005.