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Simultaneous Estimation of Lornoxicam and Paracetmaol by Vierodt's Method in API and in Synthetic mixture

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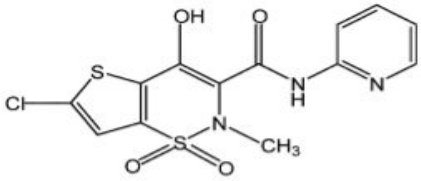
Abstract : The simple, accurate, precise, sensitive, rapid and economical Vierodt's spectrophotometric method have been developed and validated for the simultaneous determination of Lornoxicam (LOR) and paracetamol (PCM) in API and synthetic mixture containing common tablet additives. The method developed employs formation and solving simultaneous equations using 289.4nm (λ max of Lornoxicam) and 257 nm (λ max of Paracetamol) as two wavelengths for formation of equations. Lornoxicam and Paracetamol obey Beer's law in the concentration range 2-12 µgmL-1 (r2=0.9996) and 2-30 µgmL-1 (r2=0.9997) in 0.05 N NaOH. The mean recovery for Lornoxicam and Paracetamol were found to be 100.75±0.74% and100.27 ±0.70%.
Keywords: Vierodt's method, Lornoxicam, Paracetamol.

INTRODUCTION

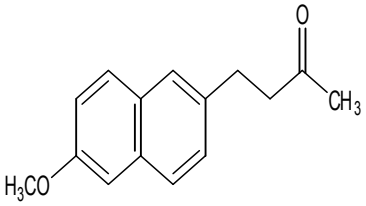
Lornoxicam, 6-chloro-4-hydroxy-2-methyl-N-2-pyridyl-2H-thieno-[2,3-e]-1,2-thiazine-3-carboxamide-1,1-dioxide is a nonsteroidal anti-inflammatory drug (NSAID) of oxicam class. Lornoxicam is used to treat acute mild to moderate pain, and to treat pain and inflammation of the joints caused by certain types of rheumatic diseases. Lornoxicam inhibits both isoforms in the same concentration range i.e., COX1/COX2 = 1. Thus, a perfectly balanced inhibition of COX-1 and COX-2 is achieved.[1]. Paracetamol is chemically N-(4-hydroxyphenyl) acetamide. It is used mainly as analgesic and antipyretic [2,3]. The combination offers faster as well as prolonged relief from pain and inflammation. Literature survey reveals that many UV Spectrophotometric[5], RP-HPLC[6-7] and Polarographic methods [8], have been reported for the determination of Lornoxicam in human plasma and in tablet dosage form. Paracetamol [9-16] individually and in combination with other drugs like Valdecoxib, Aceclofenac, Chlorpheniramine maleate, Dipyrone, caffeine and Cetrizine in human plasma and pharmaceuticals were reported to be estimated by UV Spectroscopy and RP-HPLC. But no method is

available for simultaneous estimation of Lornoxicam and Paracetamol in bulk and in synthetic mixture.
This paper describes simple, rapid, accurate, reproducible and economical method for the simultaneous determination of Lornoxicam and Paracetamol in bulk and in synthetic mixture. Method is validated also according to ICH guideline [17].



Lornoxicam

Lornoxicam



Paracetamol

Figure 1: Structure of Lornoxicam and Paracetamol [1, 4]

EXPERIMENTAL

Materials And Method

A SHIMAZDU UV-Visible double beam spectrophotometer with matched quartz cells (1cm), Model: 1700 was used. The reference standard of Lornoxicam and Paracetamol were obtained as gift samples from Shree Pramukh Laboratories. Sodium hydroxide having analytical grade of Ranchem Laboratory was used.

Preparation of Standard Stock Solutions

Lornoxicam (10 mg) and Paracetamol (10 mg) were accurately weighed and dissolved in 0.05 M NaOH to give stock solution having concentration of 100 µg/ml. From these stock solutions, working standard solutions of drugs (2:12.5 µg/ml) was prepared by appropriate dilutions.

Preparation of calibration curve

Working standard solutions were scanned in the entire UV range to determine the λ-max. [Figure 1] represents the overlain spectra of both the drugs. The λ-max of Lornoxicam and Paracetamol were found to be 289.4nm and 257.0 nm respectively. Standard solutions were prepared having concentrations 2, 4, 6, 8, 10, 12 µg/ml for Lornoxicam and 2, 5, 10, 15, 20, 25 and 30 µg/ml for Paracetamol using the working standard solution. For simultaneous study according to Vierodt's method, the absorbance values were recorded at the both wavelength 289.4nm and at 257.0 nm.
For determining the concentration of drugs by Vierodt's method, following equation was used. $C_X = (A_2 a_{y1} - A_1 a_{y2}) / (a_{X2} a_{y1} - a_{x1} a_{y2})$, $C_Y = (A_1 a_{X2} - A_2 a_{X1}) / (a_{X2} a_{y1} - a_{x1} a_{y2})$, where C_X and C_Y are concentration of Lornoxicam and paracetamol, respectively, a_{X1} and a_{X2} are the absorptivity values of Lornoxicam at 289.4nm and at 257 nm, respectively. a_{y1} and a_{y2} are the absorptivity values of paracetamol at 289.4nm and at 257 nm, respectively. A_1 and A_2 are the absorbances of the diluted mixture sample at 289.4nm and 257nm respectively. Equation used

C_X = A2 x 612.3 – A_1 x 615.47 / -307154.1 -----(1)
C_Y = A_1 x 506.4 – A_2 x 1002.45 / - 307154.1 ---(2)

Where, Molar absorptivities determined for lornoxicam at 289.4nm and 257 nm are 615.47 and 612.13, respectively, and molar absorptivities determined for paracetamol at 257 nm and 289.4nm are 1002.45 and 506.4, respectively.

Application of Proposed Method to Synthetic Mixture

The synthetic mixture of lornoxicam and paracetamol was prepared in ratio of 1**:**6.25. Accurately weighed 4 mg of lornoxicam and 25 mg of paracetamol were transferred to 100 ml volumetric flask, and 70 ml of 0.05 N sodium hydroxide was added. Common excipients, such as starch, magnesium stearate and lactose which were used in tablet formulation, were added in this mixture and sonicatad for 20 minutes. This solution was filtered through the Whatmann filter paper No. 41 and residues were washed with 0.05 N sodium hydroxide. The filtrate and washings were combined and volume was made-up to 100 ml with 0.05 N sodium hydroxide.
5 ml from above stock solution is transferred to 100 ml volumetric flask and dilute to 100 ml with 0.05 N sodium hydroxide to get final concentration as 2 ppm of lornoxicam and 12.5 ppm of paraceamol.

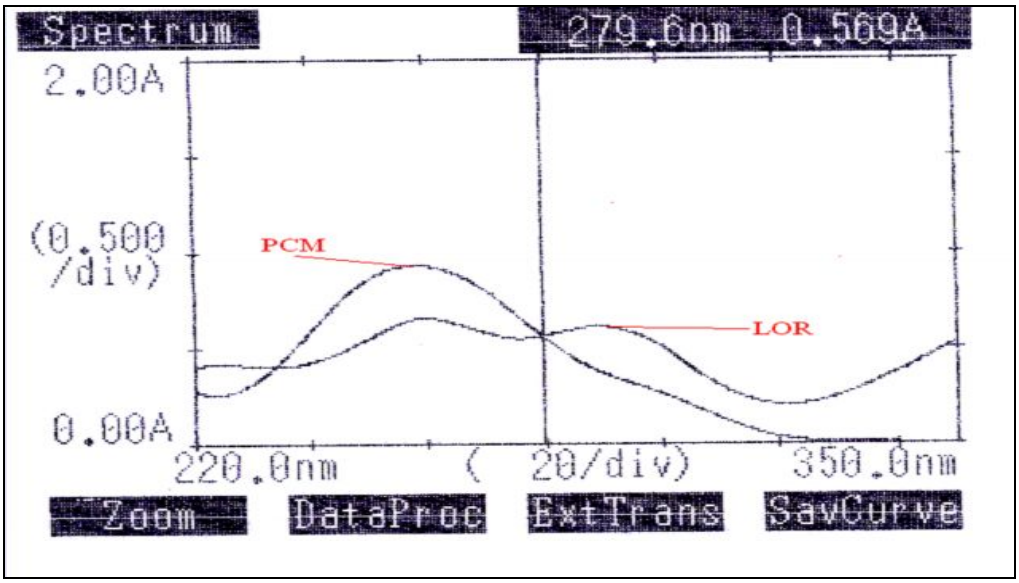


Figure 1: Overlain spectra showing λ max. of Lornoxicam (289.4nm) and Paracetamol (257nm).

Table 1: Data of recovery study of LOR and PCM by simultaneous equations method

Drug	Amount taken (µg/ml)	Amount added (µg/ml)	Amount found (µg/ml)	% Recovery ± S.D (n=3)
LOR	2	2	3.93	98.25 ± 0.23
	2	4	6.16	102.66 ± 0.86
	2	6	8.11	101.34 ± 1.13
PCM	12.5	6.25	18.79	100.02 ± 0.02
	12.5	12.5	25.67	102.69 ± 0.65
	12.5	18.75	30.66	98.11 ± 1.43

Table 2: Optical & regression characteristic & validation parameters for LOR & PCM

Parameters	LOR		PCM	
	257nm	289.4 nm	257nm	289.4 nm
Beer's Law Limit (µg/ml)	2 -12	2 - 12	2 -30	2 -30
Molar Absorptivity ($1mole^{-1}cm^{-1}$)	2.1 X 10^{-1}	2.4 X 10^{-1}	1.7 X 10^{-1}	1.2 X 10^{-1}
Sandell's sensitivity ($\mu g/cm^2$/0.001absorbance unit)	1770.5714	1549.25	889.1765	1259.6667
Regression equation (y* = mx + c) Slope (m) Intercept (c)	 0.071 -0.0489	 0.142 -0.045	 0.089 0.090	 0.044 0.016
Correlation Coefficient (r^2)	0.9996	0.9990	0.9992	0.9998
Standard Deviation (S.D)	0.0029	0.0031	0.013	0.006
Relative Standard Deviation (RSD or %CV)	0.7189	0.989	1.133	0.995
LOD (µg/ml)	0.136	0.133	0.163	0.102
LOQ (µg/ml)	0.402	0.407	0.496	0.309
Precision Intra-day (n=5) (% CV) Inter-day (n=5) (% CV)	 0.52-1.23 0.28-1.78	 0.43-1.83 0.48-1.59	 0.81-1.36 0.63-1.79	 0.34-1.96 0.78-1.78

y* =a + bc Where, 'c' is the concentration and 'y' is the absorbance

Table 3: Absorbances for synthetic mixture in 1: 6.25 (LOR: PCM) ratio

Conc. (μg/ml)	WL. (nm)	Absorbance			Mean ± S.D. (N=5)
		A	B	C	
2 : 12.5	257	0.975	o.981	0.977	0.977 ± 0.0030
	289.4	0.542	0.548	0.549	0.546± 0.0037

RESULTS AND DISCUSSION

To study the linearity, accuracy and precision of the proposed method, the recovery studies were carried out by adding a known quantity of standard to the pre analyzed sample and the % recovery was calculated and shown in [Table 1]. The regression analysis of the calibration curves and the optical characteristics such as Beer's law limits, molar absorptivities and sandell's sensitivities are presented in [Table 2]. Absorbance of the sample solutions at 289.4nm and 257 nm were measured and from the absorbance values, the concentration of drugs in the sample solution was determined by Vierodt's method and result of synthetic mixture are shown in [Table 3].

The proposed Vierodt's method is simple, accurate and economical for routine analysis of two drugs without prior separation. The amount found was in good agreement with the label claim synthetic mixture containing common tablet additives. The value of the standard deviation was satisfactorily low indicating the reproducibility and accuracy of the proposed method.

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