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NEW ANALYTICAL METHODS FOR THE SIMULTANEOUS DETERMINATION OF LORNOXICAM AND PARACETAMOL IN TABLETS

Mukthinuthalapati Mathrusri Annapurna*, Malineni Sushmitha and Vellanki S. V. Sevyatha

Department of Pharmaceutical Analysis & Quality Assurance, GITAM Institute of Pharmacy,

GITAM University, Visakhapatnam-530045, India

Email: mathrusri2000@yahoo.com

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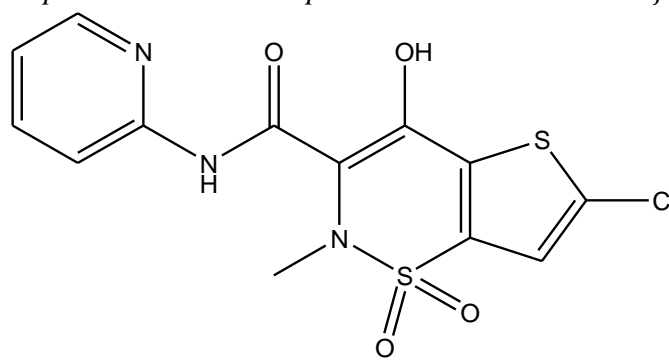
Abstract

Two simple spectrophotometric methods have been developed for the simultaneous determination of Lornoxicam and Paracetamol by in tablet dosage forms and validated. In first method i.e. simultaneous equation method, the absorption maxima of the two drugs were selected where as in the second method (Q-Analysis), one of the drugs absorption maxima and the osbestic point were selected for the quantification of Lornoxicam and Paracetamol. Beer's law was obeyed over the concentration range 0.1-40µg/ml for both Lornoxicam and Paracetamol. The proposed methods were validated and are applicable for the simultaneous analysis of Lornoxicam and Paracetamol in tablets.

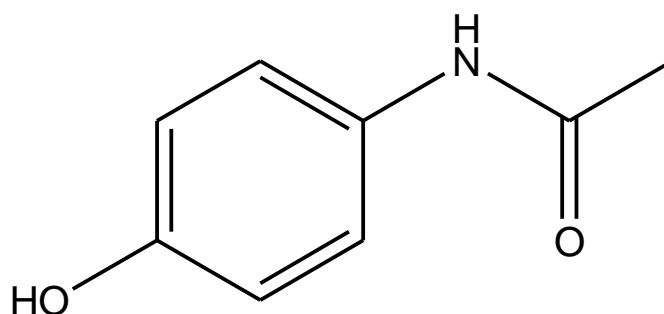
Key Words: Paracetamol, Lornoxicam, Spectrophotometry, Simultaneous equation method, Q-Analysis Validation.

Introduction

Lornoxicam [LCM] is chemically it is (3E)-6-chloro-3- [hydroxyl (pyridin-2-ylamino)methylene] -2-methyl-2, 3-dihydro-4H-thieno [2,3-e] [1,2] thiazin-4-one 1,1-dioxide¹⁻². It is a non-steroidal anti-inflammatory drug with analgesic, anti-inflammatory and antipyretic properties. Paracetamol [PCT] is also a widely used analgesic and antipyretic. It is chemically it is N-(4-hydroxyphenyl) acetamide³. The combination of Lornoxicam and Paracetamol is very much effective in relieving symptoms of osteoarthritis, rheumatoid arthritis etc (Figure 1). Literature survey reveals UV spectroscopic⁴⁻¹⁴, HPLC¹⁵⁻²⁵, LCMS²⁶ and HPTLC²⁷⁻²⁸ methods for the simultaneous estimation of LCM and PCT in combination. The present aim for the simultaneous determination of LCM and PCT using the Spectrophotometric method and to validate the method as per ICH guidelines.²⁹



[A]



[B]

Figure 1: Structures of Lornoxicam [A] and Paracetamol [B]

Materials and Methods

Instrumentation

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with software UV Probe was employed with spectral bandwidth of 1nm and wavelength accuracy of $\pm 0.3\text{nm}$ with a pair of 10mm path length matched quartz cells. For scanning, the wavelength range selected was 400nm to 200nm with medium scanning speed. All weights were taken using electronic balance (Shimadzu, Japan). All experiments were performed at room temperature (25 ± 1)°C.

Chemicals and reagents

LCM and PCT were obtained as gift samples from Dr. Reddy's Labs(India). Methanol, boric acid and Sodium hydroxide (NaOH) were purchased from Merck (India). All chemicals were of analytical grade and used as received. The combined dosage form of LCM and PCT is available as tablets with brand names Camri plus (Cadila Healthcare, India), Flexilor P (Glenmark Pharmaceuticals, India) Lornac-P (Active Healthcare, India)and Lorna-P (Adcock Ingram Healthcare Pvt. Ltd., India) consisting of LCM and PCT with label claim 8 mg, 500 mg respectively.

Preparation of phosphate buffer (pH-7.0)

27.218 gm of potassium dihydrogen phosphate was dissolved in water and the pH was adjusted to 7.0 with 0.2M

sodium hydroxide (about 29.1ml) and diluted with water in a 1000ml volumetric flask.

Preparation of Standard Stock Solution

The standard stock solution of was prepared by dissolving 10mg of the standard Lornoxicam standard in 10ml volumetric flask containing Sodium hydroxide and then make up the volume to with methanol. Similarly, the stock solution of Paracetamol was prepared by dissolving accurately weighed 10 mg Paracetamol in 10ml volumetric flask with methanol and the working standard solutions of these drugs were prepared by dilution from their stock solutions with phosphate buffer (pH 7.0) solution.

Preparation of Sample Stock Solutions

Twenty tablets were weighed and crushed to a fine powder and powder equivalent to 25mg of Paracetamol was dissolved in methanol in a 25ml volumetric flask with the help of NaOH and sonicated. The resultant solution was filtered through Whatmann filter paper No.41 and diluted with phosphate buffer solution so that LOR: PCT are present in the ratio 0.8:50asintablets.

Procedure

Method A: Simultaneous Equation Method

The absorption spectrum shows that Lornoxicam has λ_{\max} at 376 nm whereas Paracetamol has at 243 nm respectively. For the simultaneous equation method, two wavelengths i.e. λ_{\max} of the two drugs were selected and the absorbance as well as the absorptivity values were calculated from their individual spectra. Absorbance was noted against each concentration at 376 and 243 nm for both the drugs from their individual spectra and their absorptivity values were calculated.

Method B: Absorbance ratio Method (Q Analysis)

Lornoxicam has shown λ_{\max} at 376 nm and Paracetamol at 243 nm respectively in their absorption spectra. Three isosbestic (iso-absorptive) points were observed at 212.74, 218.57 and 261.76 nm in the overlay spectra of Lornoxicam and Paracetamol. For the Q-analysis method, two wavelengths such as λ_{\max} one of the drugs and the isosbestic point were selected and the absorbances as well as the absorptivity values were calculated from their individual spectra.

By using the simultaneous equation method and absorbance ratio method Lornoxicam and Paracetamol were determined in bulk and in its pharmaceutical formulations (Tablets) using phosphate buffer (pH 7.0) and the proposed method was statistically validated.

Validation

Linearity

A series of solutions of Lornoxicam and Paracetamol (0.1-40 µg/ml) were prepared separately and scanned against the reagent blank i.e. phosphate buffer pH 7.0 and the absorbance was noted at the selected wavelengths for both the methods i.e. simultaneous equation method and absorbance ratio method (Q-analysis) and ϵ values were calculated. A graph was drawn by taking the concentration of the drug solution on the x-axis and the corresponding absorbance values on the y-axis at the selected wavelength.

Precision

The intra-day and inter-day precision studies of the method was performed at three different concentration levels (15, 20 and 30 µg/mL) at three different intervals on the same day (Intra-day) and on three different days (Inter-day) respectively and the %RSD was calculated.

Accuracy: Recovery studies were carried out by the standard addition method for the determination of accuracy of the proposed methods A and B. 80%, 100%, and 120% of pure bulk samples of Lornoxicam and Paracetamol were added to that of the pre-analyzed formulation and the % recovery as well as the % RSD were calculated.

Assay of Lornoxicam and Paracetamol combined dosage forms (Tablets)

Different brands of tablets containing Lornoxicam and Paracetamol were procured from the local pharmacy store and 20 tablets of each brand were weighed and powdered and powder equivalent to 12.5 mg of Hydrochlorothiazide was dissolved in a 100 ml volumetric flasks containing methanol and sonicated for 30 minutes. The solution was filtered and further diluted with phosphate buffer pH 7.0 and the two methods were applied for the assay of Lornoxicam and Paracetamol.

Results and Discussion

The authors have developed two spectrophotometric methods, simultaneous equation method (Method A) and Q – Analysis (Method B) for the simultaneous determination of Lornoxicam and Paracetamol in phosphate buffer pH 7.0.

Method A: Simultaneous Equation Method

For the simultaneous determination of two drugs by simultaneous equation method, specific absorptive values of the two drugs at the selected wavelengths were determined. The overlay absorption spectrum of Lornoxicam and Paracetamol was shown in Figure 2. The absorption spectrum Lornoxicam has shown λ_{\max} at 376 nm and that of Paracetamol at 243 nm respectively.

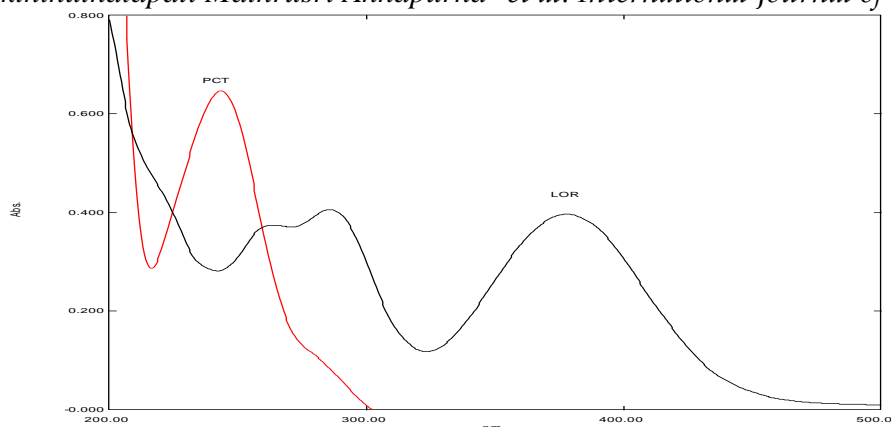


Figure 2: Absorption Spectrum of Lornoxicam (10 µg/ml) and Paracetamol (10 µg/ml) in phosphate buffer (pH 7.0)

The specific absorptivity value of a drug is the absorbance of the drug shown by a 1%, i.e. g/100ml solution and the absorptivity values obtained were incorporated in the simultaneous equations.

At 243 nm, $A_1 = 702.83 C_{PCT} + 225.07 C_{LOR}$

At 376 nm, $A_2 = -0.99 C_{PCT} + 436.870 C_{LOR}$

where A_1 and A_2 are absorbance's of the mixture solution at 243 nm and 376 nm, respectively; 702.83 and -0.99 are the absorptivity's of PCT at 243nm and 376 nm, respectively and 225.07 and 436.870 are the absorptivity's of LOR at 243nm and 376 nm, respectively; C_{PCT} and C_{LOR} are the concentrations of Lornoxicam and Paracetamol, respectively in g/100ml.

Method B: Absorbance ratio Method (Q Analysis)

Lornoxicam and Paracetamol show λ_{max} at 243 nm and 376 nm respectively. Three isosbestic (iso-absorptive) points were observed at 212.74, 218.57, 261.76 nm in the overlay absorption spectrum of Lornoxicam and Paracetamol (Figure 2). The absorptivity values obtained at the selected wavelengths were incorporated in the following equation.

$$C_x = \frac{Q_m - Q_y / Q_x - Q_y \times A_1 / a_{x1}}$$

$$C_y = \frac{Q_m - Q_x / Q_y - Q_x \times A_2 / a_{y1}}$$

' C_x ' = the concentration of Paracetamol

' C_y ' = the concentration of Lornoxicam

' A_1 ' = the absorbance at iso-absorptive wavelength 261.76 nm.

' A_2 ' = the absorbance at wavelength 243 nm.

' a_{x1} ' = the mean absorptivity of Paracetamol at 261.76 nm.

' a_{y1} ' = the mean absorptivity of Lornoxicamat 243 nm.

Q_m = the ratio of absorbance of sample solution at 261.76 & 243 nm.

Q_x = the ratio of absorptivity of Paracetamol at 261.76 & 243 nm.

Qy = ratio of absorptivity of Lornoxicamat 261.76 & 243nm.

Validation

Linearity

Lornoxicam and Paracetamol have shown linearity over the concentration range 0.1-40 µg/ml in phosphate buffer (p^H 7.0) in both simultaneous equation method and absorbance ratio method. The calibration curves of Lornoxicam and Paracetamol were shown in Figure 3 and 4 respectively.

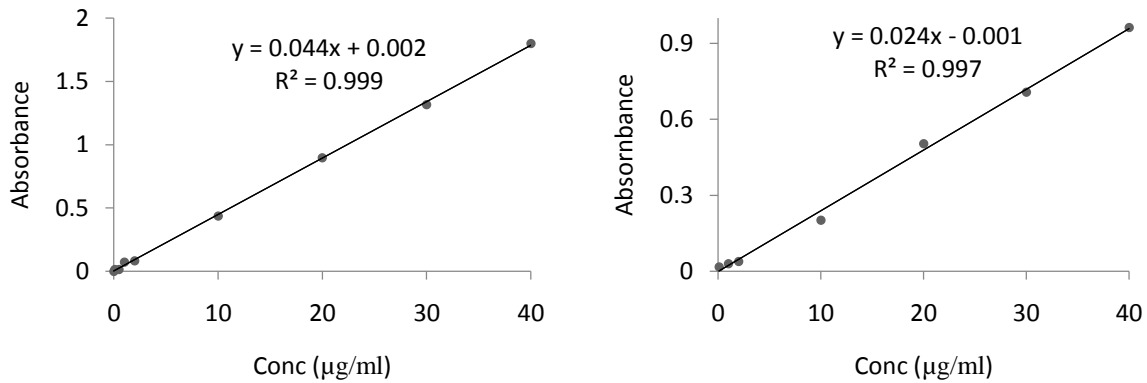


Figure 3: Calibration curve of Lornoxicam at A) 376 nm B) 243 nm.

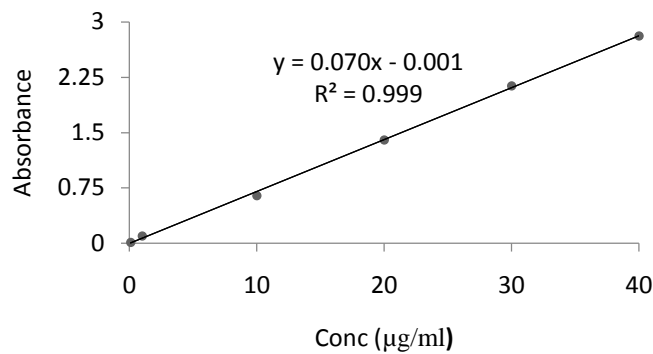


Figure. 4: Calibration curve of Paracetamol at A) 243 nm.

The precision and accuracy results were shown in Table 1 and 2 and the percentage RSD was found to be less than 2.0 indicating that the methods are precise and accurate. The assay results of Lornoxicam and Paracetamol tablets were shown in Table 3.

Table 1: Precision study of LOR and PCT.

Drug	Conc. µg/ml	Intra-day precision				Inter-day precision			
		Method A		Method B		Method A		Method B	
		*Conc. obtained (µg/ml) ± SD (RSD)	*% Recovery	*Conc. obtained (µg/ml) ± SD (RSD)	*% Recovery	*Conc. obtained (µg/ml) ±SD (RSD)	*% Recovery	*Conc. obtained (µg/ml) ± SD (RSD)	*% Recovery
LOR	10	9.93±0.02 (0.18)	99.4	9.91±0.068 (0.68)	99.1	9.94±0.06 (0.65)	99.4	9.9±0.09 (0.99)	99.0

PCT	20	19.86±0.3 (1.54)	99.3	19.90±0.07 (0.36)	99.5	19.82±0.19 (0.98)	99.1	19.81±0.5 2 (1.2)	99.1
	30	29.85±0.4 (1.34)	99.5	29.94±0.5 (1.74)	99.8	29.7±0.25 (0.84)	99.0	29.82±0.2 6 (0.92)	99.4
	10	9.98±0.05 (0.51)	99.8	9.97±0.03 (0.35)	99.7	9.94±0.09 (0.98)	99.4	9.91±0.08 (0.88)	99.1
	20	19.84±0.1 0 (0.52)	99.2	19.92±0.02 (0.1)	99.6	19.78±0.06 (0.3)	98.9	19.92±0.4 0 (1.12)	99.6
	30	29.82±0.3 0 (1.00)	99.4	29.82±0.26 (0.88)	99.4	29.88±0.1 (0.33)	99.6	29.76±0.2 (1.02)	99.2

*Mean of three replicates

Table 2: Accuracy study of LOR and PCT.

Drugs	Spiked Conc (µg/ml)	Formulation Conc. (µg/ml)	Method A		Method B	
			%RSD	">%Recovery	%RSD	">%Recovery
LOR	0.16 (80%)	0.2	1.00	98.72	0.65	99.67
	0.2 (100%)	0.2	1.01	99.01	0.45	98.97
	0.24 (120%)	0.2	0.92	99.21	0.98	98.76
PCT	10 (80%)	12.5	1.16	98.68	0.76	99.65
	12.5 (100%)	12.5	0.91	98.90	0.77	99.53
	15 (120%)	12.5	0.88	99.29	0.67	98.75

*Mean of three replicates

Table 3: Assay of Lornoxicam and Paracetamol Tablets.

Formulation Brand	Drug	Label claim(mg)	Method A		Method B	
			*Amount found	*Recovery (%)	*Amount found	*Recovery (%)
I	LOR	8	7.92	99.0	7.87	98.38
	PCT	500	496	99.2	497.56	99.51
II	LOR	8	7.94	99.75	7.88	98.50
	PCT	500	498.05	99.61	498.40	99.68

*Mean of three replicates

Conclusion

The proposed method is simple, precise and accurate and can be applied for the simultaneous determination of Lornoxicam and Paracetamol in pharmaceutical formulations successfully.

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Corresponding Author:

Mukthinuthalapati Mathrusri Annapurna*,

Email: mathrusri2000@yahoo.com