Original Article

Development and validation of spectrophotometric method for simultaneous estimation of paracetamol and lornoxicam in different dissolution media

Abstract

Background: Paracetamol and lornoxicam in combined tablet dosage form are available in the market. This combination is used to treat inflammatory diseases of the joints, osteoarthritis and sciatica. Spectrophotometric and high performance liquid chromatography (HPLC) methods have been reported for their simultaneous estimation in tablet dosage form in specific solvent. This paper presents simple, accurate and reproducible spectrophotometric method for simultaneous determination of paracetamol and lornoxicam in tablet dosage form in different dissolution media. The reported method is helpful in determination of paracetamol and lornoxicam during dissolution study. **Materials and Methods:** Simple, sensitive, accurate and economical spectrophotometric method based on an absorption correction equation was developed for the estimation of paracetamol and lornoxicam simultaneously in tablet dosage form in different dissolution media at different pH. **Results:** Paracetamol showed absorption maxima at 243 nm in 0.1N HCland phosphate buffer pH 6.8, while lornoxicam showed absorption maxima at 374 nm in 0.1N HCland phosphate buffer pH 6.8. The linearity was obtained in the concentration range of 4-12 µg/ml for paracetamol and 4-16 µg/ml for lornoxicam. **Discussion:** The concentrations of the drugs were determined by an absorption correction equation method. The results of analysis have been validated statistically by recovery studies.

Key words: Absorption correction method, dissolution media, lornoxicam, paracetamol

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INTRODUCTION

Lornoxicam is 6-chloro-4-hydroxy-2-methyl-N-2-pyridinyl-2H-thieno-[2, 3-e]-1, 2-thiazine-3-carboxamide 1, 1-dioxide; is a novel non-steroidal anti-inflammatory drug (NSAID) with marked analgesic properties. It is not official in any pharmacopoeia, but listed in the MerkIndex.[1] Lornoxicam belongs to the chemical class oxicams, which includes piroxicam, tenoxicam and meloxicam. Lornoxicam, which is commercially available as an 8-mg tablet and 16-mg SR tablet, is used to treat inflammatory diseases of the joints, osteoarthritis, and pain after surgery, and sciatica. It works by blocking the action of cyclooxygenase, an enzyme involved in the production of chemicals, including some prostaglandins in the body. Paracetamol, chemically 4-hydroxy acetanilide, is a centrally and peripherally acting non-opioid analgesic and antipyretic. It is official in Indian Pharmacopoeia,[2] British Pharmacopoeia[3] and United States Pharmacopoeia.[4] Literature survey reveals simultaneous spectrophotometric method[5,6] and RP-HPLC method[7,8] for their determination. The literature survey revealed that there is no simultaneous estimation for dissolution profile of paracetamol and lornoxicam in dissolution media. This paper presents simple, accurate and reproducible an absorption correction method for simultaneous determination of paracetamol and lornoxicam in tablet dosage form in different dissolution media.

The reported method is helpful in determination of paracetamol and lornoxicam during dissolution study.

MATERIALS AND METHODS

Materials

Lornoxicam was received as gift sample from Cirex Pharmaceuticals Ltd., Andhra Pradesh, India. Paracetamol was received from RecspeedPharma, Ahmedabad, India. The tablets (referred as T1) of the said combination were purchased from local pharmacy (The label claim for T1 was to contain 8mg of lornoxicam and 500mg of paracetamol). All the chemicals used were of either pharmaceutical or analytical grade.

Instrument

All the absorbance measurements were made on double beam UV visible spectrophotometer (Shimadzu, Kyoto, Japan, model UV – 1800) with matched quartz cuvettes.

Methods

Preparation of standard drug solution

The stock solution (100 µg/ml) of lornoxicam was prepared by dissolving accurately about 10mg of drug in 20 ml N, N-dimethyl formamide and the volume was made up to 100 ml with 0.1N HCl. The stock solution (100 µg/ml) of paracetamol was prepared by dissolving accurately about 100mg of drug in 10ml 0.1N HCl and the volume was made up to 100ml with 0.1N HCl. The same stock solutions were made in phosphate buffer pH 6.8.

Study of Beer - Lambert's law

A stock solution of each drug having a concentration of 1000 µg/ml was prepared by dissolving paracetamol and lornoxicam separately in 0.1N HCl and N, N-dimethyl formamide, respectively. Aliquots of the stock solutions were further diluted in 0.1N HCl and were scanned in the wavelength range of 200-400nm. Overlain spectra are presented in Figure 1. The two wavelengths selected for determination were 243 and 374nm, the maximum absorbance wavelength (λ_{max}) of paracetamol and lornoxicam, respectively. Paracetamol and lornoxicamshowed significant absorption at 243 nm, but at the λ_{max} of lornoxicam (374 nm) paracetamol showed practically no absorption. Beer's law was obeyed over the concentration range 4-12 µg/ml at 243 nm by paracetamol and over the concentration range 4-16 µg/mL at 243 and 374 nm by lornoxicam. The

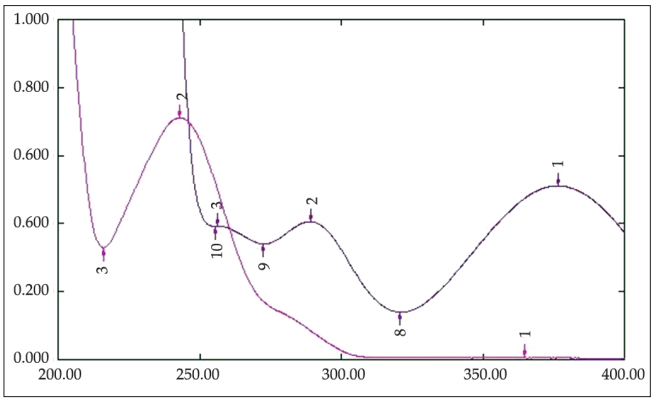

Figure 1: Overlain spectra of paracetamol and lornoxicam

absorptivity values at 243 and 374 nm for both the drugs were determined by measuring absorbance values for working standards of paracetamol and lornoxicam. The determination of lornoxicam was done at 374 nm using its absorptivity value, since there was no interference of paracetamol. An accurate determination of paracetamol was achieved after correction for absorbance by lornoxicam at 243 nm.

Determination of E (1%, 1cm) value at selected wavelength

The E (1%, 1cm) value of lornoxicam and paracetamol were calculated at λ_{max} in the respective media. The absorption correction equations were formed using calculated absorptivity values for each media. The equations for 0.1N HCl (Eqns. 1 and 2) and phosphate buffer pH 6.8 (Eqns. 3 and 4) are given below.

$$C_X = A_1/511.79 \quad \text{(1)}$$

$$C_Y = A_2 - 1092.30 \times Cx/669.90 \quad \text{(2)}$$

Where, A_1 and A_2 are the absorbance of samples at 374 and 243 nm in 0.1N HCl, respectively. C_X and C_Y are the concentration of lornoxicam and paracetamol, respectively.

$$C_X = A_1/507.44 \quad \text{(3)}$$

$$C_Y = A_2 - 1272.87 \times Cx/720.27 \quad \text{(4)}$$

Where, A_1 and A_2 are the absorbance of samples at 374 and 243 nm in phosphate buffer pH 6.8, respectively. C_X and C_Y are the concentration of lornoxicam and paracetamol, respectively.

Assay of standard laboratory mixture

The laboratory mixtures of different concentration of both drugs were prepared from stock solution in

their respective media. Their absorbance value at the two selected wavelength was recorded [Figure 2] and quantitative estimation of the drugs was carried out by solving absorption correction equation. The recovery study was performed by standard addition method where 5µg/ml of lornoxicam was added to pre-analyzed solutions containing both the drugs. The percentage recovery was calculated from the added amount for lornoxicam. The results of the recovery study of the physical mixtures are shown in Table 1.

Assay of tablet formulation

Twenty tablets were weighed and finely powdered. An accurately weighed quantity of the powder equivalent to 500 mg paracetamol and 8 mg of lornoxicam was taken in 100 ml volumetric flask and dissolved in 20 ml of N,N-dimethyl formamide; it was further diluted up to the mark with 0.1N HCl. The solution was filtered and a filtrate was further diluted to obtain sample solutions of concentrations within Beer-Lambert's range. The absorbance of sample solutions were measured at selected wavelengths for the estimation of paracetamol and lornoxicam. The results of the assay are shown in Table 2.

In vitro dissolution studies

The *in vitro* drug release rate method of combined tablet is not official. It was carried out using USP dissolution testing apparatus II (paddle type) at 50 rpm. The dissolution test was performed using 750 ml of 0.1 N HCl (pH 1.2) for 2 h at 37 ± 0.5°C and then 250 ml of 0.2 M tri sodium phosphate ($Na_3PO_4.12H_2O$) was added and pH is adjusted to 6.8 as described in the USP 26/NF monograph.[9] Dissolution test was carried out using 0.1N HCl (pH 1.2) for first 2 h and then the pH is adjusted to 6.8 for the rest of the period. The temperature of the dissolution medium is maintained at 37 ± 0.5°C. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at regular intervals and replaced with the same volume of pre-warmed fresh dissolution medium. The samples were filtered through a 0.45 µm membrane filter and diluted to a suitable concentration with respective media. The amount of drug release was determined from the standard calibration curve of pure drug.[10] The results of *in vitro* dissolution are shown in Table 3 and Figure 3.

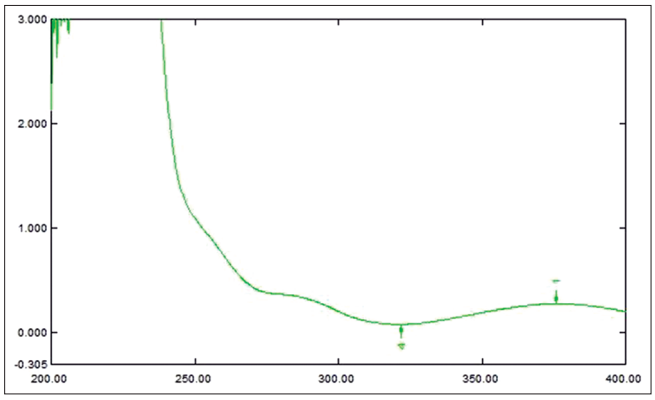

Figure 2: Spectrum of mixtures of paracetamol and lornoxicam

Validation of analytical method

To study the accuracy and precision of the proposed method, recovery studies were carried out by addition of known amount of standard drug solutions of paracetamol and lornoxicam to pre-analyzed tablet solution. The resulting solutions were then analyzed by proposed method. Results of recovery studies were found to be satisfactory as shown in Table 1.

RESULTS AND DISCUSSION

The proposed method was found to be simple, accurate and reproducible for routine simultaneous estimation of paracetamol and lornoxicam in different dissolution media. The proposed method is based on spectrophotometric absorption correction method for simultaneous estimation of paracetamol and lornoxicam in different dissolution media. The standard deviation, percentage recovery indicates precision and accuracy of the method. Since no any

Table 1: Recovery study of the physical mixtures

Media	Physical mixtures		With standard addition of 5 µg/ml	Conc. of lornoxicam	% Recovery	Conc. of paracetamol	% Recovery
	Lornoxicam	Paracetamol					
0.1 N HCl	0.40µg/ml	12.5µg/ml	5.40µg/ml	5.45µg/ml	100.94%	12.70µg/ml	101.60%
	0.32µg/ml	10.0µg/ml	5.32µg/ml	5.32µg/ml	100.00%	10.60µg/ml	106.00%
	0.24µg/ml	7.5µg/ml	5.24µg/ml	5.18µg/ml	98.81%	7.90µg/ml	105.33%
	0.16µg/ml	5.0 µg/ml	5.16µg/ml	5.06µg/ml	101.22%	5.40µg/ml	108.00%
Phosphate buffer pH 6.8	0.40µg/ml	12.5µg/ml	5.40µg/ml	5.40µg/ml	100.00%	13.10µg/ml	104.00%
	0.32µg/ml	10.0µg/ml	5.32µg/ml	5.32µg/ml	100.00%	10.37µg/ml	103.00%
	0.24µg/ml	7.5µg/ml	5.24µg/ml	5.26µg/ml	100.42%	7.97µg/ml	106.00%
	0.16µg/ml	5.0 µg/ml	5.16µg/ml	5.20µg/ml	100.77%	5.20µg/ml	104.06%

Table 2: Assay of the marketed products

Formulation	Simultaneous equation method	
	% label claim*	% Recovery*
Lornoxicam	8 mg	103.00
Paracetamol	500 mg	102.40

*Indicates mean of three determinations

Table 3: Dissolution profile of the marketed product

Time	% Release for paracetamol	% Release for lornoxicam
0 min.	0	0
15 min.	65.06	21.60
30 min.	78.12	53.34
60 min.	85.67	72.61
120 min.	98.48	90.95
180 min.	99.20	97.12

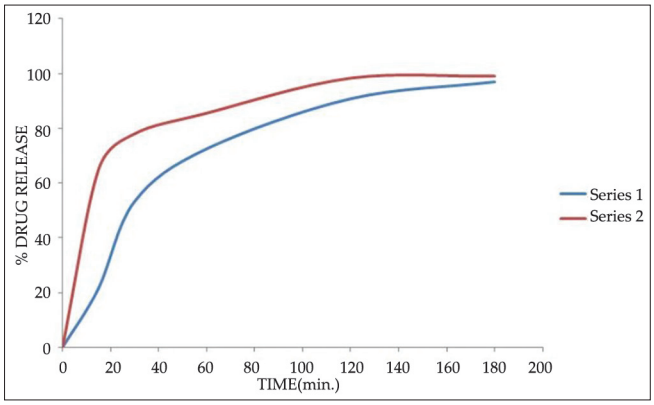

Figure 3: Dissolution profile of the marketed preparation (Series 1: Lornoxicam; Series 2: paracetamol)

method is available for determining paracetamol and lornoxicam in combined dosage form during dissolution study, this method is very useful for those who want to study release pattern of the formulation containing both the drugs.

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