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Research Article

DEVELOPMENT AND VALIDATION OF UV-SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF PARACETAMOL AND LORNOXICAM IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

A simple and sensitive spectrophotometric method has been developed for simultaneous determination of Paracetamol and Lornoxicam in a binary mixture. In the proposed method, the absorbances were measured at 257.0 nm and 287.0 nm corresponding to the absorbance maxima of Paracetamol and Lornoxicam in 0.1 N Sodium Hydroxide respectively. Linearity range was observed in the concentration range of 5-30 µg/ml for Paracetamol and 2-10 µg/ml for Lornoxicam. Concentration of each drug was obtained by using the absorptivity values calculated for both drugs at two wavelengths, 257.0 nm and 287.0 nm and solving the simultaneous equation. Developed method was applied to laboratory mixture and its marketed formulation. The method was validated statistically and recovery study was performed to confirm the accuracy of the method. The method was found to be rapid, simple, accurate and precise.

Key words: Lornoxicam, Simultaneous equation, Sodium Hydroxide (NaOH), Paracetamol.

INTRODUCTION

Paracetamol (PARA), chemically 4-hydroxy acetanilide, is a centrally and peripherally acting non-opioid analgesic and antipyretic[1-3]. Literature survey reveals, there are UV and HPLC methods reported for the estimation of PARA in Pharmaceutical formulations[4-9].

Lornoxicam (LOX) 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. LOX belongs to the chemical class oxicams, which includes piroxicam, tenoxicam and meloxicam. LOX, which is commercially available as an 8-mg tablet, is used to treat inflammatory diseases of the joints, osteoarthritis, pain after surgery, and sciatica[10]. It works by blocking the action of cyclooxygenase, an enzyme involved in the production of chemicals, including some prostaglandins in the body[11-13].

Extensive literature survey reveals, none of the method is available that is based on estimation of Paracetamol and Lornoxicam by simultaneous equation method. Aim of present work was to develop simple, precise, accurate and economical Spectrophotometric methods for simultaneous determination of binary drug formulation[14]. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[15].

MATERIALS

Spectrophotometric analysis was carried out on double beam spectrophotometer (Systronic 2201) with a fixed slit width (3 nm) using a pair of 1 cm matched quartz cells. Pure drug sample PARA was kindly gifted by Ajantha Pharmaceuticals, Jalgoan. Sodium Hydroxide was procured from Merck Chemical Corporation, Mumbai. Commercial pharmaceutical preparation (Paracetamol-Lornoxicam, Ravenbhel Pharmaceutical Pvt. Ltd) was procured from commercial source. All the reagents are of analytical grade.

METHOD

1. Study of overlain spectra and selection of wavelength

PARA and LOX 100 mg each were accurately weighed and dissolved separately in 100 ml 0.1 N NaOH Shake it up to the 15 min until clear solution appeared. From the above solution 10ml were diluted upto 100ml with 0.1 N NaOH to make concentration of PARA and LOX of 100 µg/ml which is

used as a stock solution. The stock solution of Paracetamol dilute with 0.1 N NaOH to obtain 5-25 µg/ml of PARA. The stock solution of LOX dilutions of 2-10µg/ml were made with 0.1 N NaOH. Absorbance of both dilutions were determined (Table 1). Calibration curve were plotted of both that is PARA (Fig 1) and LOX (fig 2) as absorbance Vs Concentration. From the overlain spectra (Fig 3) of two wave lengths, 257.0 nm and 287.0 nm were selected and absorptivity values E (1%, 1cm) of both the drugs at both wavelengths were determined for formation of simultaneous equation.

$C_1 = (A_2ay_1 – A_1ay_2)/ (ax_2ay_1 - ax_1ay_2)$ --- (1)

$C_2 = (A_1ax_2 – A_2ax_1)/ (ax_2ay_1 - ax_1ay_2)$ --- (2)

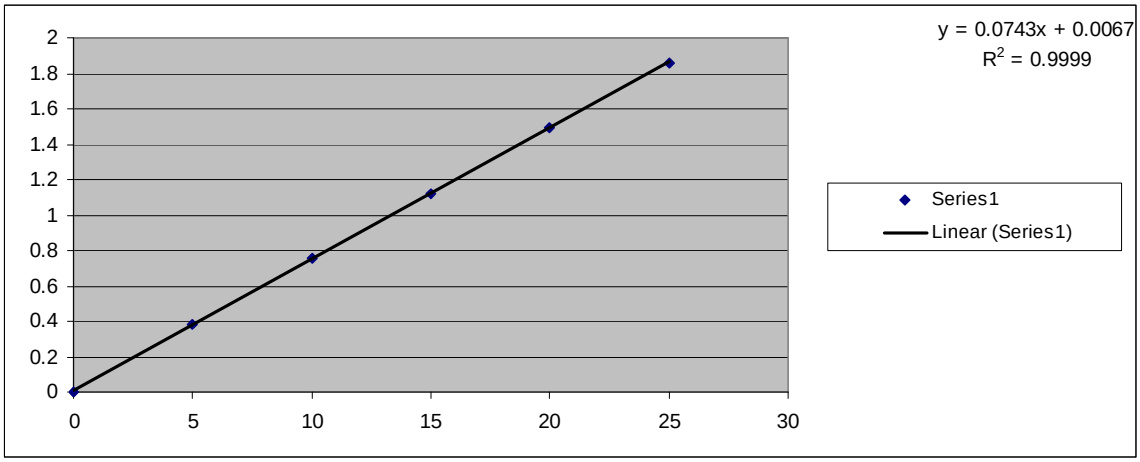


Fig1. Calibration Curve of Paracetamol by the Proposed Method.

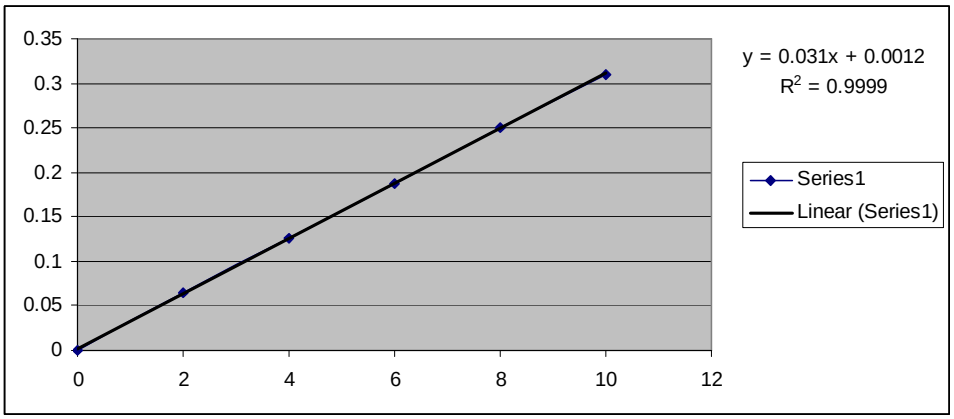
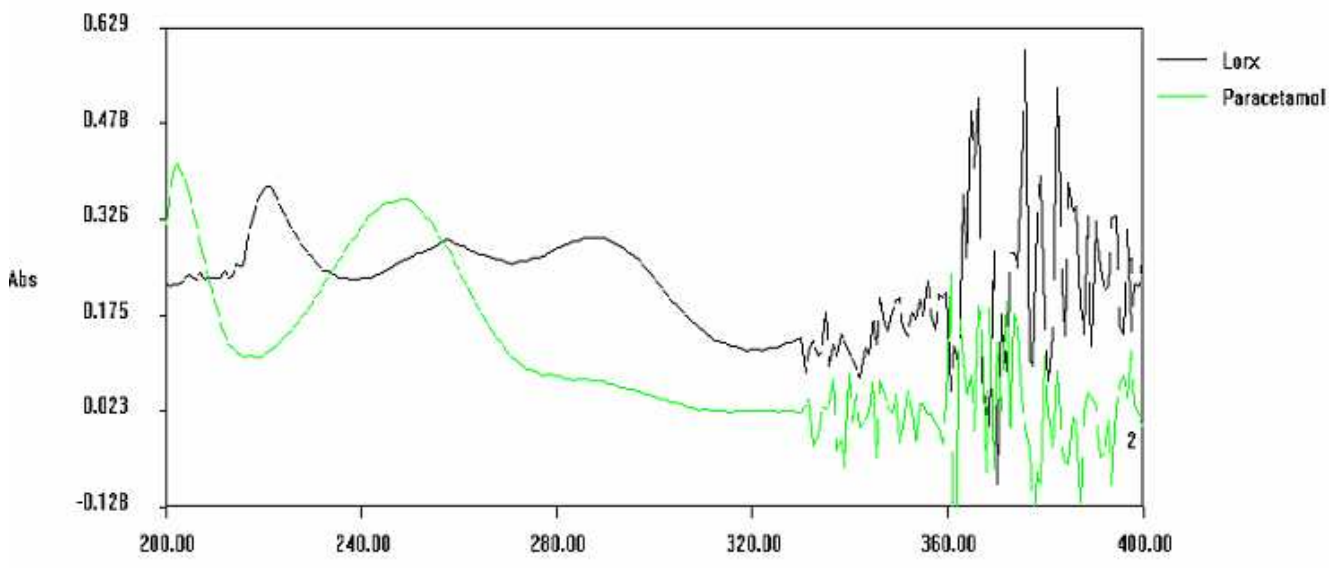


Fig. 2 Calibration Curve of Lornoxicam by the Proposed Method.



Wavelength in nm

Fig. 3 Overview of Paracetamol and Lornoxicam Spectra

Table 1. Linearity Study of PARA and LOX

Sr. No.	Concentration of PARA	Absorbance Mean ± S. D.	R.S.D.	Concentration of LOX	Absorbance Mean ± S. D.	R.S.D.
1	5	0.38± 0.0017	0.46	2	0.06 ±0.001	1.30
2	10	0.75± 0.0011	0.15	4	0.12± 0.001	0.90
3	15	1.11± 0.0015	0.14	6	0.18 ± 0.001	0.53
4	20	1.49± 0.0019	0.13	8	0.25± 0.001	0.51
5	25	1.49± 0.0019	0.10	10	0.31 ± 0.0008	0.26

2. Analysis of laboratory mixture

Accurately weighed 125 mg of PARA and 2 mg of LOX were transferred to 100 ml volumetric flask, dissolved in 0.1 N NaOH and volume was adjusted up to the mark with same solvent. Then, take 50ml in that solution and dilute it to the 100ml. Appropriate aliquot 1ml was transferred to 10 ml volumetric flask and volume was adjusted up to the mark with same solvent to get concentration

25µg/ml of PARA and 0.4 µg/ml of LOX. The absorbances of solutions were recorded at 257.0 nm and 287.0 nm against blank. Concentration of each drug was obtained by solving the simultaneous equation [Table 2].

Table 2. Results of Analysis of Laboratory Mixture (PARA: LOX 25: 0.4)

Amount taken PARA [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
25	25.01	100.04
25	25.01	100.04
25	25.00	100.02
25	25.00	100.03
25	25.00	100.02
Mean ± S.D.	25.00±0.002	100.03±0.01
% R.S.D.	0.01	0.01
Amount taken LOX [µg/ml]	**Amount found [µg/ml**	**Amount found [%]**
0.4	0.40	100.35
0.4	0.39	99.46
0.4	0.40	100.18
0.4	0.40	100.27
0.4	0.40	100.18
Mean ± S.D.	0.40 ±0.001	100.09±0.359
% R.S.D.	0.35	0.35

3. Application of proposed method for analysis of tablet formulation

Twenty **'LORNOCAM PLUS 8'** tablets (containing 500 mg of PARA and 8 mg of LOX**)** were weighed and ground to fine powder. A quantity of sample equivalent to 500 mg of PARA and 8 mg of LOX was transferred into 100 ml volumetric flask containing 0.1 N NaOH, sonicated for 10 min; the

volume was made up to the mark and filtered through Whatmann filter paper (no. 41). An appropriate volume of this solution was transferred to 10 ml volumetric flask, dissolved and volume was adjusted to mark. The absorbances of the solutions were measured at 257.0 nm and 287.0 nm against blank. Concentration of each drug was obtained by solving the simultaneous equation [Table 3].

Table 3. Application of Proposed Method to Tablet Formulation

Amount taken PARA [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
25	25.00	100.01
25	25.01	100.04
25	25.00	100.03
25	25.00	100.02
25	25.01	100.04
Mean ± S.D.	25.00±0.003	100.03±0.01
% R.S.D.	0.01	0.01
Amount taken LOX [µg/ml]	**Amount found [µg/ml]**	**Amount found [%]**
0.4	0.40	100.99
0.4	0.39	99.46
0.4	0.40	100.27
0.4	0.40	100.18
0.4	0.40	100.35
Mean ± S.D.	0.40± 0.002	100.25± 0.54
% R.S.D.	0.54	0.54

4. Validation of proposed method

The method was validated in terms of accuracy, precision and ruggedness

4.1 Accuracy

To assess the accuracy of proposed method, recovery experiment was performed. To the preanalyzed sample solution of PARA and LOX, a known amount of standard drug solution was added that is 5 µg/ml and 0.2 µg/ml respectively and absorbance were recorded. The % recovery was then calculated [Table 4].

Table 4. Results of Recovery Study

Drugs	Excess Drug added [µg/ml, n=3]	Amount recovered [µg/ml]	% Recovery	% R.S.D.
PARA	0	5	100	0.03
	5	4.99	99.80	0.02
	5	4.98	99.79	0.12
	5	4.99	99.94	0.17
LOX	0	0.2	99.79	0.43
	0.2	0.20	100.12	0.83
	0.2	0.20	100.17	0.88
	0.2	0.19	99.69	0.72

4.2 Precision

Precision of the method was asessed by repeatability; determined by analyzing 25 µg/ml of PARA and 0.4 µg/ml LOX of drug solutions for five times; results were recorded [Table 5].

Precision method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 20, 25 and 30 µg/ml of PARA and 2, 4 and 6 µg/ml of LOX for three times in the same day. Inter-day precision was determined by analyzing the same concentration range of solutions daily for three days, results were recorded [Table 6].

Table 5. Result of Intra-Day and Inter-Day Precision

Drug	Concentration [µg/ml]	Intra-day amount found [µg/ml n=3]	% R.S.D.	Inter-day amount found [µg/ml n=3]	% R.S.D.
PARA	20	99.91±0.11	0.11	99.84±0.16	0.16
	25	99.85±0.14	0.14	99.92±0.10	0.10
	30	99.87±0.17	0.17	99.88±0.13	0.13
LOX	0.2	99.41±0.89	0.90	100.02±0.30	0.30
	0.4	100.10±0.73	0.73	99.90±0.49	0.49
	0.6	100.02±0.35	0.35	100.20±0.57	0.57

Table 6. Results of Repeatability Study

Drug	Amount taken [µg/ml, n=3]	Amount found[µg/ml]±S.D.	% R.S.D.
PARA	25	25.00 ±0.004	0.01
LOX	0.4	0.40 ±0.0008	0.21

4.3 Ruggedness

Ruggedness of the method was determined by analysis of aliquots from homogeneous slot by two analyst using same operational and environmental conditions [Table 7].

RESULTS AND DISCUSSION

In this simultaneous equation method, the overlain spectra of drugs showed the λ_{max} of 257.0 nm and 287.0 nm for PARA and LOX respectively. Both the drugs obeyed linearity range 5-30 µg/ml and 2-10 µg/ml respectively and correlation coefficient (r^2) were found to be <1 in both cases. The absorptivity values were calculated and along with absorbances, these values were submitted in equation (1) and (2) to obtain concentration of drugs. The percentage purity of drugs in binary mixture was found to be 100.03 ± 0.01 % for PARA and 100.09 ± 0.35 % for LOX. The percentage purity of drugs in combined dosage form was found to be 100.03 ± 0.01 % for PARA and 100.25 ± 0.54 % for LOX. The accuracy of the method was determined by performing recovery study by standard addition method. The % recoveries were found near to 100 % for PARA and LOX. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The method was found to be precise as % RSD for intra-day and inter-day precision were < 2. The method was found to be rugged as the percentage purity of the drugs determined by two different analysts were 100.04 ±0.20 for PARA, 100.15±0.15 for LOX and 99.89±0.18 for PARA, 100.19±0.16 for LOX.

CONCLUSION

The proposed method is simple, precise, and accurate for the rapid for simultaneous determination of PARA and LOX in combined tablet dosage forms and this method may be successfully applied in control laboratories for their determination in combined dosage form.

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