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# Development and Validation of Analytical Methods for the Simultaneous Estimation of Lornoxicam and Paracetamol from their Pharmaceutical Dosage Forms.

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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 288.0 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 2-14 µg/ml for Paracetamol and 2-14 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 288.0 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 sciatica10. It works by blocking the action of cyclooxygenase, an enzyme involved in the production of chemicals, including some prostaglandins in the body [11-18]. Extensive literature survey reveals, none of the method is available that is based on estimation of Paracetamol and Lornoxicam by simultaneous equation method.

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Aim of present work was to develop simple, precise, accurate and economical Spectrophotometric methods for simultaneous determination of binary drug formulation[19].
The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[20]

## Materials and Methods
**Apparatus:** SHIMADZU-UV Spectrophotometer (Double Beam) With UV-Detector (C-1700).
**Reagent:** 0.1N Sodium hydroxide, API Lornoxicam & Paracetamol.
**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 2-14µg/ml of PARA. The stock solution of LOX dilutions of 2-14µg/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, 2) and LOX (fig 3, 4) as absorbance Vs

Concentration. From the overlain spectra (Fig 5) of two wave lengths, 257.0 nm and 288.0 nm were selected and absorptivity values E (1%, 1cm) of both the drugs at both wavelengths were determined for formation of simultaneous equation [Table 1 and 2].

**C1 = (A2ay1 – A1ay2)/ (ax2ay1- ax1ay2) --- (1)**

**C2 = (A1ax2 – A2ax1)/ (ax2ay1- ax1ay2) --- (2)**

**Analysis of Formulation**

**Preparation of standard solution**

Stock solution of Lornoxicam (100 µg/ml), Paracetamol (100 µg/ml) and their mixtures were prepared in 0.1N sodium hydroxide. From the respective stock solutions, different concentrations of Lornoxicam (2- 14 µg/ml), Paracetamol (2- 14 µg/ml) and mixtures of Lornoxicam and Paracetamol were prepared and scanned in UV region.

**Preparation of sample solution**

Twenty tablets, each containing 500 mg of Paracetamol and 8 mg of Lornoxicam were weighed and average weight was calculated. Quantity equivalent to 100mg of Paracetamol and 1.6 mg of Lornoxicam were weighed, transferred to a 100 ml volumetric flask, extracted and made upto volume with 0.1N sodium hydroxide and filtered with Whatmann filter paper (no. 41). From this solution, 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. Suitable aliquots were prepared, scanned in UV region and absorbances were noted at selected wavelengths [Table 3].

**Validation of the Method**

The developed method was validated in terms of parameters like accuracy, precision, linearity and stability studies.

**Accuracy**

In order to ensure the suitability and reliability of proposed method, recovery studies were carried out. To an equivalent quantity of formulation powder, a known quantity of standard Lornoxicam and Paracetamol added at 50% and 100% level and the contents were re-analysed by the proposed method. The % recovery and %RSD were calculated [Table 4].

**Precision**

Precision studies were performed by preparing the standards six times and measuring the absorbances of drugs at 257 nm and 288 nm. Low %RSD shows that the method has good precision. [Table 5].

**Stability:**

Stability studies of the drug solutions were carried out and they were found to be stable at room temperature and refrigerated condition for about 7 hours [Table 6].

## Results and Discussion:

In this simultaneous equation method, the overlain spectra of drugs showed the λmax of 257.0 nm and 288.0 nm for PARA and LOX respectively. Both the drugs obeyed linearity range 2-14 µg/ml and 2-14 µg/ml respectively and correlation coefficient (r2) 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 combined dosage form was found to be 98.67± 0.45 %for PARA and 97.50 ± 0.35 % 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 six times in a day for precision. The method was found to be precise as % RSD for precision were < 2.

## 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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**Table 1: Absorbances and absorptivity of Lornoxicam at selected wavelengths.**

| Conc. (µg/ml) | 257 nm | | | 288 nm | | |
|---|---|---|---|---|---|---|
| | Abs. | Absorpti-vity | Avg. Absorpti - vity | Abs. | Absorpti-vity | Avg. absorpti-vity |
| 2.0 | 0.095 | 0.049 | 0.055 | 0.099 | 0.047 | 0.055 |
| 4.0 | 0.220 | 0.055 | | 0.222 | 0.055 | |
| 6.0 | 0.324 | 0.057 | | 0.344 | 0.054 | |
| 8.0 | 0.440 | 0.058 | | 0.465 | 0.055 | |
| 10.0 | 0.551 | 0.057 | | 0.577 | 0.055 | |
| 12.0 | 0.661 | 0.057 | | 0.689 | 0.055 | |
| 14.0 | 0.762 | .0.056 | | 0.796 | 0.055 | |

**Table 2: Absorbances and absorptivities of Paracetamol selected wavelengths.**

| Conc. (µg/ml) | 257 nm | | | 288 nm | | |
|---|---|---|---|---|---|---|
| | Abs. | Absorpti-vity | Avg. Absorpti - vity | Abs. | Absorpti-vity | Avg. Absorpti-vity |
| 2.0 | 0.15 | 0.075 | 0.073 | 0.07 | 0.035 | 0.032 |
| 4.0 | 0.288 | 0.072 | | 0.128 | 0.032 | |
| 6.0 | 0.454 | 0.075 | | 0.200 | 0.033 | |
| 8.0 | 0.603 | 0.075 | | 0.268 | 0.033 | |
| 10.0 | 0.741 | 0.074 | | 0.324 | 0.032 | |
| 12.0 | 0.873 | 0.072 | | 0.387 | 0.032 | |
| 14.0 | 1.032 | 0.073 | | 0.458 | 0.032 | |

**Table 3: Analysis of formulation.**

| Drug | Amount(µg/ml) | | % label claim | %RSD* |
|---|---|---|---|---|
| | Labeled | Found | | |
| Para | 25 | 24.67 | 98.67 | 0.4532 |
| Lorno | 0.4 | 0.39 | 97.50 | 0.3467 |

**Table 4: Recovery studies.**

| Level | % Recovery | | % RSD* | |
|---|---|---|---|---|
| | Para | Lorno | Para | Lorno |
| 50% | 99.47 | 99.23 | 0.645 | 0.812 |
| 100% | 99.16 | 98.93 | 0.589 | 0.791 |

**%RSD* of six observations**

**Table 5: Precision studies.**

| Conc. (µg/ml) | Absorbances | | | | % RSD | | | |
|---|---|---|---|---|---|---|---|---|
| | Para | | Lorno | | Para | | Lorno | |
| | 257 nm | 288 nm | 257 nm | 288 nm | 257 nm | 288 nm | 257 nm | 288 Nm |
| Para - 8.0 Lorno - 8.0 | 0.601 | 0.268 | 0.441 | 0.464 | 0.1354 | 0.0475 | 0.1245 | 0.1622 |
| | 0.602 | 0.267 | 0.440 | 0.464 | | | | |
| | 0.603 | 0.266 | 0.441 | 0.465 | | | | |
| | 0.603 | 0.268 | 0.441 | 0.466 | | | | |
| | 0.602 | 0.265 | 0.440 | 0.465 | | | | |
| | 0.603 | 0.268 | 0.440 | 0.465 | | | | |

**Table 6: Stability studies.**

| Concentration (µg/ml) | Time (min) | Absorbances of the drug (257nm) at Room temp | | Absorbances of the drug (257nm) at Refrigerated condition | |
|---|---|---|---|---|---|
| | | Para | Lorno | Para | Lorno |
| Para – 8.0 Lorno - 8.0 | 0 | 0.601 | 0.441 | 0.603 | 0.440 |
| | 60 | 0.598 | 0.430 | 0.600 | 0.435 |
| | 180 | 0.565 | 0.419 | 0.591 | 0.425 |
| | 300 | 0.545 | 0.413 | 0.582 | 0.417 |
| | 420 | 0.505 | 0.401 | 0.569 | 0.399 |
| | 540 | 0.465 | 0.381 | 0.534 | 0.371 |

**Fig. 1:** Calibration graph of Paracetamol at 257 nm.

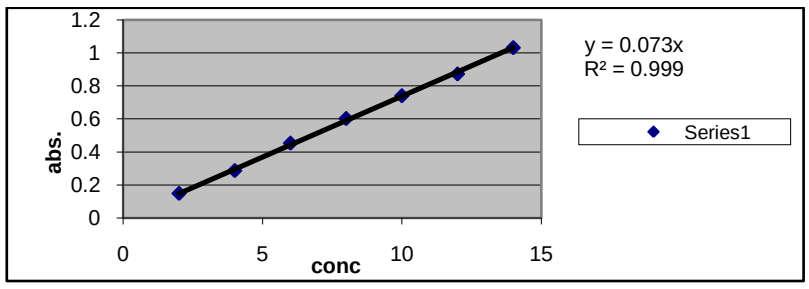


**Fig. 2:** Calibration graph of Paracetamol at 288 nm.

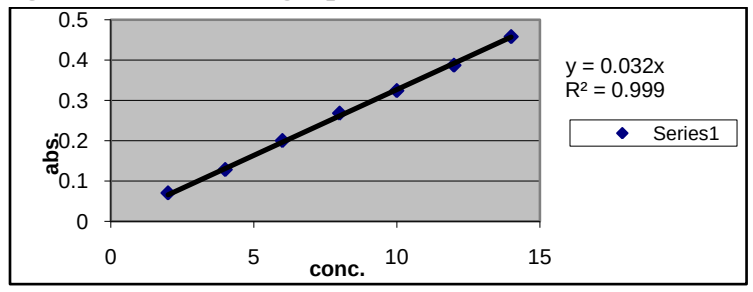


**Fig. 3:** Calibration graph of Lornoxicam at 257 nm.

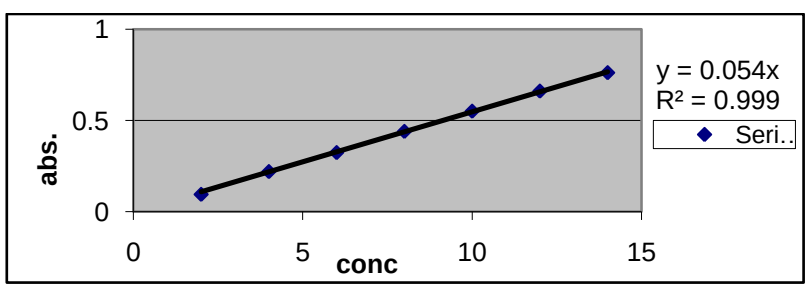


**Fig. 4:** Calibration graph of Lornoxicam at 288 nm.

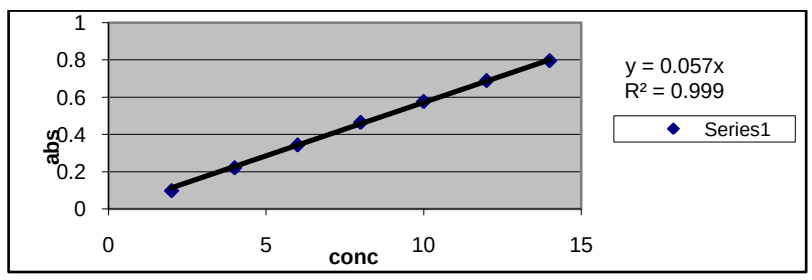


**Fig. 5:** Overlain UV spectra of Lornoxicam and Paracetamol in 0.1N sodium hydroxide.