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UV Spectrophotometric estimation of Paracetamol and Lornoxicam in Bulk drug and Tablet dosage form using Multi-wavelength method

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Abstract: A new simple, accurate, precise and economic spectrophotometric methods in UV/VIS region have been developed for the determination of Paracetamol and Lornoxicam in bulk and tablet formulations. Linearity was found over the concentration range of 2-10µg/ml for PARA and 2-14µg/ml for LOR. Interday and intraday studies showed repeatability of the method. The method has been successfully applied for the analysis of drugs in tablet formulation. Results of tablet analysis were in the range of 99.78 to 101.57 % and 98.62 to 99.84 % for PARA and LOR, which indicated repeatability of the method. The percent recoveries were found near to 100% for both the drugs indicated that the method is precise and reproducible. LOD for PARA and LOR was found to be 0.0287 µg/ml and 0.0871 µg/ml respectively. LOQ was found to be 0.2683 µg/ml and 0.0869 µg/ml respectively.
Keywords: Paracetamol, Lornoxicam, UV/Vis Spectroscopy, Multi wavelength method.

1. INTRODUCTION

Combinations of two or more drugs in the pharmaceutical dosage forms are very much useful in multiple therapies. Market survey revealed that, day by day new drugs and their combination with another drugs are being introduced in market as they have more patient compliance than a single drug. The analytical chemistry hence has challenge in developing the methods for their analysis with the help of number of analytical techniques which are available for the estimation of the drugs and their combination. Analytical monitoring of pharmaceutical product or specific ingredients within the product is necessary to ensure its safety and efficacy throughout the shelf life, including storage, distribution and use[1,10].

Paracetamol (PARA) and Lornoxicam (LOR) are recently introduced in the market as combined tablet dosage form which is widely used in the treatment of rheumatoid arthritis. PARA, chemically *N*-(4-Hydroxyphenyl)acetamide, is a centrally and peripherally acting non-opioid analgesic and antipyretic[2]. It is the first drug of choice in the treatment of rheumatoid arthritis. LOR chemically 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. LOR belongs to the chemical class of oxicams, which includes piroxicam, tenoxicam and meloxicam. LOR, which is commercially available as an 8-mg tablet, is used to treat inflammatory diseases of the joints, osteoarthritis, pain after surgery and sciatica. It works by blocking the action of cyclooxygenase (COX), an enzyme

involved in the production of chemicals, including some prostaglandins in the body[3].

Extensive literature survey reveals, there are UV, HPLC, RP HPLC, densitometric and polarographic methods reported for the estimation of PARA and LOR in pharmaceutical formulations. There is no method reported for estimation of PARA and LOR from dosage forms by multi-wavelength method[1, 4-11]. In the analysis of formulations containing two or more drugs, one drug can interfere in the estimation of another drug. To avoid this, separation of components of mixture by extraction is usually carried out which make the procedure time consuming and complicated and often lacks accuracy. The present work was undertaken to develop such method of analysis, which can estimate both the drugs in combination without prior separation which is a precise, accurate, simple, reliable and less time consuming method for estimation of drugs in tablet.

2. EXPERIMENTAL

2.1. INSTRUMENTATION

The present work was carried out on JASCO UV/Vis spectrophotometer, model no. V-550 with 1 cm matched quartz cells was used for experiments. The absorption spectra of reference and test solution were carried out in a 1 cm quartz cell over the range of 200-400 nm.

2.2. MATERIALS

A gift sample of Paracetamol was obtained from Cipla Ltd, Kurkumbh and Lornoxicam was obtained from Alkem Pharmaceuticals Ltd, Mumbai.

2.3. EXPERIMENTAL CONDITION

According to the solubility characteristics of drugs, phosphate buffer pH 6.8 was selected as solvent for analysis. From the UV scanning of both the drugs, 235nm and 376nm were the wavelengths selected for estimation of Paracetamol and Lornoxicam respectively.

2.3.1. PREPARATION OF STANDARD STOCK SOLUTION

PARA and LOR 10 mg each were accurately weighed and dissolved separately in phosphate buffer pH 6.8. Shake and sonicate it for 20 min. Adjust the final volume to 100ml with phosphate buffer pH 6.8 to get a concentration of 100µg/ml. 1ml of each from the above prepared solutions were further separately diluted to 10ml to get a concentration of 10µg/ml of each PARA and LOR. These were used as stock solutions.

2.3.2. WAVELENGTH SELECTION

The above prepared stock solutions of PARA and LOR were scanned in the range of 200-400nm to determine the wavelength of maximum absorption for both the drugs. PARA showed absorption maxima at 243nm whereas LOR showed at 376nm.

For estimation of PARA, multi-wavelength spectrophotometric method employing 235 nm and 303 nm as analytical wavelengths were used; the two wavelengths were chosen to eliminate interference of LOR at the sampling wavelength of PARA by taking the difference in the absorbance at the two wavelengths. For estimation of LOR, 376 nm was selected as the analytical wavelength, as PARA showed no absorption at this wavelength. In the multi-wavelength method developed for simultaneous estimation of PARA and LOR, the wavelengths were selected from the overlain spectra shown in Fig.No.1.

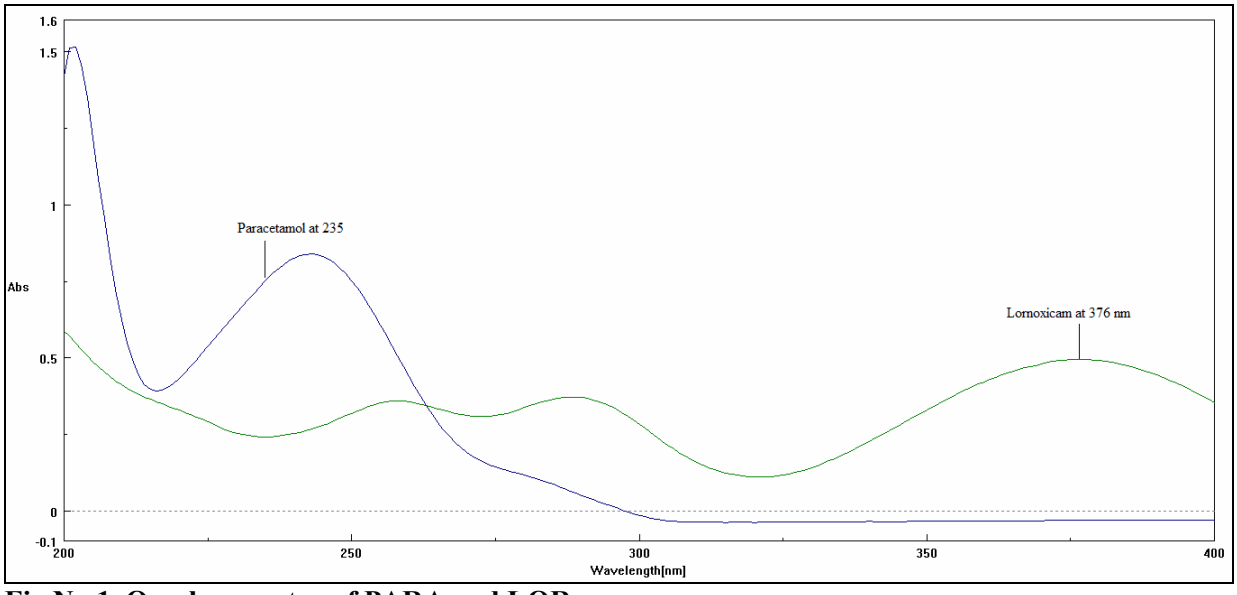

Fig.No.1. Overlay spectra of PARA and LOR

Table No. 1: Optimum parameters:

Parameters	PARA	LOR
λ_{max}	235 nm	376 nm
Beer's law limit (µg/ml)	2 – 10 µg/ml	2 – 14 µg/ml
Equation	Y= A + B*C	Y= A + B*C
Slope (B)	0.0941	0.0278
Intercept (A)	0.0114	0.0019
Correlation coefficient	$R^2 = 0.9996$	$R^2 = 0.9998$

*Y= A + B*C, where C is the concentration in µg/ml and Y is absorbance unit.

Table No. 2: Calibration curve of PARA and LOR

Conc. Of PARA (µg/ml)	Absorbance at 235 nm*	%RSD	Conc. Of LOR (µg/ml)	Absorbance at 376 nm*	%RSD
0	0	0	0	0	0
2	0.1813 ± 0.0005	0.2773	2	0.0611 ± 0.0010	1.6
4	0.3612 ± 0.0011	0.3192	4	0.1119 ± 0.0006	0.5457
6	0.5361 ± 0.0010	0.1993	6	0.1670 ± 0.0011	0.6914
8	0.7362 ± 0.0007	0.1028	8	0.2255 ± 0.0004	0.2048
10	0.9269 ± 0.0007	0.0764	10	0.2798 ± 0.0002	0.0714
12	1.1236 ± 0.0063	0.5652	12	0.3354 ± 0.0034	1.0354
14	1.3150 ± 0.0089	0.6792	14	0.3909 ± 0.0012	0.3113

Absorbance at 235/376 nm* indicates mean of 3 observations.

2.3.3. PREPARATION OF CALIBRATION CURVE

From the respective stock solution (10µg/ml) different concentration of 2, 4, 6, 8, 10, 12 and 14µg/ml PARA and LOR were prepared and scanned in UV region. Their absorbances were noted at their above selected respective λ_{max}, calibration curve were plotted as absorbance vs concentration and their linearity range was determined (Table No. 2).

2.3.4. SAMPLE PREPARATION

Twenty tablets, each containing 500 mg of Paracetamol and 8 mg of Lornoxicam were weighed and average weight was calculated. From the triturate of twenty tablets quantity equivalent to 100mg of Paracetamol and 1.6 mg of Lornoxicam was weighed, transferred to a 100 ml volumetric flask, sonicated with phosphate buffer pH 6.8, made up to volume with same phosphate buffer and filtered with Whatmann filter paper (no. 41). From this solution, appropriate volume of 2.5ml 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 LOR. Suitable aliquots were prepared, scanned in UV region and absorbance was noted at selected wavelengths.

2.3.5. METHOD VALIDATION

The developed method was validated in terms of parameters like accuracy, precision, linearity, limit of detection and limit of quantitation (**Table No. 2 – 8).**

Table No. 3. Analysis of Tablet formulation

Drug	Amount (µg/ml)		% Label claim estimated*	% RSD
	Labeled	Found		
PARA	25	25.04	100.15 ± 0.217	0.217
LOR	0.4	0.395	98.64 ± 1.4	1.43

% Label claim estimated* indicates mean of 3 observations.

Table No. 4: Recovery study

Level	% Recovery*		% RSD	
	PARA	LOR	PARA	LOR
80 %	100.33 ± 0.5766	99.84 ± 1.407	0.575	1.409
100 %	100.14 ± 0.917	99.22 ± 0.081	0.915	1.078
120 %	101.57 ± 0.545	99.13 ± 1.069	0.536	0.530

% Recovery* indicates mean of 3 observations.

Table No. 5: Results of Intraday precision

Time	% Label claim estimated*		% RSD	
	PARA	LOR	PARA	LOR
T1	100.27 ± 0.037	98.62 ± 0.107	0.0377	0.1804
T2	99.78 ± 0.247	99.55 ± 0.132	0.248	0.1329
T3	100.51 ± 0.080	99.6 ± 0.173	0.0797	0.1739

% Label claim estimated* indicates mean of 3 observations.

Table No. 6. Results of Interday precision

Day	% Label claim estimated*		% RSD	
	PARA	LOR	PARA	LOR
D1	100.38 ± 0.473	99.26 ± 0.388	0.3869	0.4765
D2	99.84 ± 0.474	99.18 ± 0.136	0.136	0.4789
D3	100.29 ± 0.813	99.21 ± 0.372	0.3706	0.8195

% Label claim estimated* indicates mean of 3 observations.

Table No. 7: Precision

Conc. (µg/ml)	Absorbance		% RSD	
	PARA	LOR	PARA	LOR
4	0.361	0.1118	0.1601	0.0893
	0.360	0.1121		
	0.360	0.1119		
8	0.7368	0.2257	0.0235	0.0767
	0.7367	0.2257		
	0.7368	0.2260		

Table No. 8. Limit of Detection and Limit of Quantitation

LOD (µg/ml)		LOQ (µg/ml)	
PARA	LOR	PARA	LOR
0.0287	0.0871	0.0869	0.2638

- **Linearity**

The linearity for spectrophotometric method was established in the concentration of 2-10µg/ml for PARA and 2-14µg/ml for LOR (Fig no. 2 & 3).

- **Recovery**

To evaluate the accuracy, precision and reproducibility of the method, known amount of pure drug was added to the analyzed sample of tablet powder and the mixture was analyzed for the drug content using the proposed method. The recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical additives and excipients. Result of recovery study has been shown in (Table 4).

- **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 LOR and PARA was added at 80%, 100% and 120% level and the contents were re-analyzed by the proposed method. The %

recovery and %RSD (Relative Standard Deviation) were calculated (Table 4).

- **Precision**

Precision studies were performed by preparing the standards three times and measuring the absorbances of drugs at 235 nm and 376 nm. Low %RSD shows that the method has good precision (Table No. 7).

- **Limit of Detection**

LOD is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. The result of LOD for PARA and LOR has been shown in Table No. 8.

- **Limit of Quantitation**

LOQ is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The result of LOQ for PARA and LOR has been shown in Table No. 8.

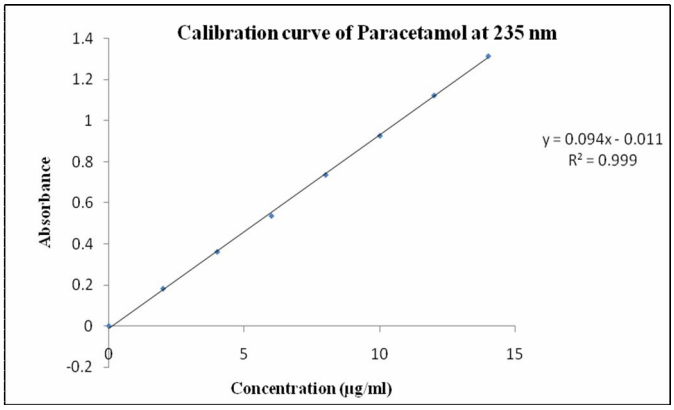

Fig. No. 2. Calibration curve of Paracetamol at 235 nm

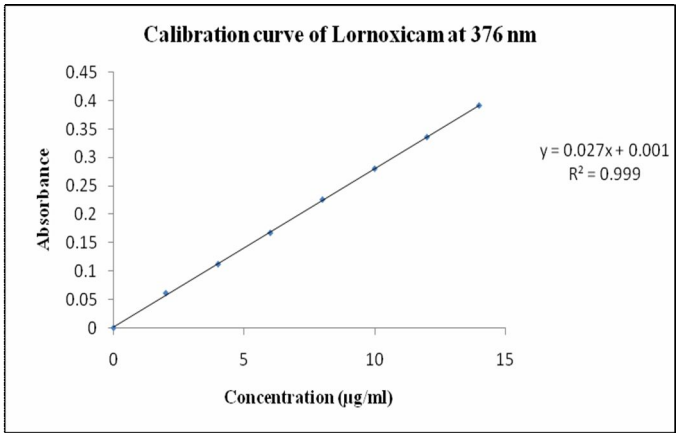

Fig. No. 3.Calibration curve of Lornoxicam at 376 nm

RESULTS AND DISCUSSION

In this method, the overlain spectra of drugs showed the λ_{max} of 235 nm and 376 nm for PARA and LOR respectively. Linear regression data showed a good linear relationship over the concentration range, 2-10 µg/ml for PARA and 2-14 µg/ml for LOR. Correlation coefficient (R^2) was found to be <1 in both the cases. The absorbances obtained were submitted in equations given in Table No. 1 to obtain concentration of drugs. The percentage drug estimated in combined dosage form was found to be 100.15 ± 0.217 % for PARA and 98.64 ± 1.4 % for LOR. The accuracy of the method was determined by performing recovery study by standard addition method. The overall results indicated percent recoveries as 100.24 ± 0.538 % and 99.29 ± 0.348 % for PARA and LOR respectively. The percent recoveries were found near to 100% for both the drugs showed the absence of interference from the commonly encountered pharmaceutical additives and excipients indicating that the method is precise and reproducible. The experiment was repeated three times in a day for precision. The method was found to be precise as % RSD for precision were < 2.
Interday and intraday studies showed repeatability of an analytical method under normal operating conditions. Results of tablet analysis showed deviation in the range of 99.78 to 101.57 % and from 98.62 to 99.84 % for PARA and LOR respectively, which indicated repeatability of the method. Lower limit of detection for PARA and LOR was found to be 0.0287 µg/ml and 0.0871 µg/ml respectively. Limit of quantitation was found to be 0.0869 µg/ml and 0.2638 µg/ml respectively.

3.CONCLUSIONS

The proposed method is simple, precise, and accurate for the rapid for determination of PARA and LOR in combined tablet dosage forms. Moreover the method is economic, simple and rapid, hence can be employed for routine analysis in quality control laboratories.

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