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Spectrophotometric Estimation of Lornoxicam and Paracetamol Tablet dosage form using Hydrotropic Solubilizing Agent.

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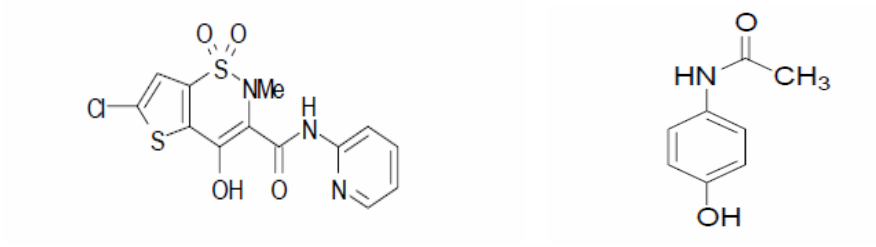
Abstract : A simple, sensitive, economical analytical methods are described for the determination of Lornoxicam and Paracetamol in bulk and tablet formulations. In the present investigation, Urea solution (Hydrotropic agent) was employed to solubilize, Lornoxicam and Paracetamol (a poorly water soluble drug), from fine powder of its tablets to carryout spectrophotometric analysis. The proposed methods namely Simultaneous Equation Method (Method 1) and Absorbance Ratio Method (Method 2). λmax for Lornoxicam and Paracetamol is 384 nm and 244 nm respectively. Both Lornoxicam and Paracetamol obey Beer's law in the concentration range of 2-10 µg/ml (r^2=0.9992) and 20-60 µg/ml (r^2=0.9990) in 8 M Urea (Hydrotropic agent) respectively. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values.
Keywords: Lornoxicam, Paracetamol, Absorbance Ratio Method, Simultaneous Equation Method, Spectrophoto - metric, Hydrotropic agent.

INTRODUCTION

Hydrotropy is a solubilization phenomenon whereby addition of large amounts of a second solute results in an increase in the aqueous solubility of another solute. A hydrotrope is a compound that solubilises hydrophobic compounds in aqueous solutions. Typically hydrotropes consist of a hydrophilic part and a hydrophobic part (like surfactants) but the hydrophobic part is generally too small to cause spontaneous self-aggregation.[1] Hydrotropes are a class of chemical compounds which effect an increased aqueous solubility by several fold to certain solutes which are sparingly soluble in water under normal conditions. This phenomenon termed Hydrotropy can be considered to be a potentially and industrially attractive technique since the observed increase in solubility is much higher than that effected by other solubilization methods. Easy recovery of dissolved solute and possible re-use of hydrotrope solutions makes this method the most attractive one particularly at industrial levels.[2] Lornoxicam (LORN) is a new nonsteroidal anti-inflammatory drug (NSAID)



[A] **[B]**

Figure No. 1 Chemical Structure of [A] Lornoxicam [B] Paracetamol.

in the enolic acid class of compound with analgesic, anti-inflammatory and antipyretic properties. Chemical Name is 6-chloro-4-hydroxy-2-methyl-3-(2-pyridyl -carbamoyl)-2H-thieno[2,3-e]-1,2-thiazine-1,1-dioxide; chlortenoxicam. Molecular weight 371.82 and melting point is 239-241°C. Lornoxicam is not official in any pharmacopoeia. It works by blocking the action of Cyclooxygenase, an enzyme involved in the production of chemicals, including some prostaglandins in the body.[3] Analytical methods have been reported for the determination of Lornoxicam includes RP-HPLC, Volatammetric, Liquid Chromatography/Electrospary Ionization/Mass Spectro -scopy, TLC-Densitometry method,[4] UV-Spectro -photometric,[5] Polarographic[6] were reported for the analysis of Lornoxicam. Paracetamol (PARA) is 4-hydroxy acetanilide, used as an analgesic and antipyretic drug and used for the treatment of pain such as headache, toothache, rheumatism and neuralgia. Molecular weight is 151.16 and melting point is 169-170.5ºC. Paracetamol is official in Indian Pharmacopoeia, British Pharmacopoeia and USP. There are many methods reported for the determination of paracetamol by Chemometric-assisted Spectrophotometric, capillary electrophoresis and hydrotropy methods, HPLC,[7] UV-Spectrophotometry,[8] RP-HPLC,[9] HPTLC,[10] Polarographic Analysis[11] from pharmaceutical preparations. However, there are no reported methods for Spectrophotometric Estimation of Lornoxican and Paracetamol Tablet Dosage Form Using Hydrotropic Solubilizing Agent.

EXPERIMENTAL

Materials and Methods

(A) Instrument

UV-Visible Spectrophotometer was purchased from Shimadzu (Model UV-1700 Pharmaspec series) which possesses a double beam double detector configuration with a 1 cm quartz matched cell. Electronic Balance was purchased from Wensar Ltd., Cyclo Mixer was purchased from REMI Instruments Limited and Centrifuge was purchased from REMI Instruments Limited.

(B) Materials

Standard gift samples of Paracetamol and Lornoxicam were procured from Burgeon Pharmaceuticals Pvt. Ltd., Mumbai. Urea was supplied from Loba Chemie Pvt. Ltd., Mumbai. The formulation of Lornocicam and Paracetamol (Lorsaid P8, Abbott Healthcare Pvt. Ltd., Mumbai) as tablet dosage containing 500 mg Paracetamol and 8 mg Lornoxicam was procured from local drug market. All the chemicals used for the study were of analytical grade.

Method 1- Simultaneous Estimation Method

Determination of λ_{max} of Drugs

Standard solution (10µg/ml) of pure Lornoxicam and Paracetamol was prepared. The pure drug solutions were scanned on UV spectrophotometer, which showed maximum absorbance at 384.0 nm and 244.0 nm for Lornoxicam and Paracetamol respectively. The UV spectra are shown in Figure No. 2 and 3.

Preparation of Standard Stock Solution

An accurately weighed powder sample equivalent to 100 mg of Lornoxicam was transferred to 100 ml of volumetric flask containing 20 ml, 8M urea solution. The flask was sonicated for about 20 min to solubilize the drug and the volume was made up to the mark with distilled water to get a concentration of 1000 µg ml^{-1}. The solution was filtered through Whatmann filter paper No 41. An accurately weighed powder sample equivalent to 100 mg of Paracetamol was transferred to 100 ml of volumetric flask

containing 20 ml 8M urea solution. The flask was sonicated for about 20 min to solubilize the drug and solution was filtered through Whatmann filter paper No 41.

Preparation of Working Standard Solution

One mililiter of standard stock solution of Lornoxicam was taken and transferred to 100ml volumetric flask and volume was made up with distilled water. Different concentration like 2, 4, 6, 8, 10 µg ml^{-1} were prepared and absorbance was recorded in UV spectrophotometer. 1 ml of standard stock solution of Paracetamol was taken and transferred to 100 ml volumetric flask and volume was made up with distilled water. Different concentration like 20, 30, 40, 50, 60 µg ml^{-1} were prepared and absorbance was recorded in UV spectrophotometer.

Preparation of the Calibration Curves of the Drug

The absorbances of each standard drug solution were taken thrice and the mean absorbance of drug was calculated for Lornoxicam and Paracetamol respectively and plotted against the concentration of the drug. The regression equation was found out by using this curve. The result of Optical Parameter of Lornoxicam and Paracetamol is shown in Table No. 1. A typical calibration curve is shown in Figure No. 4 and 5 for Lornoxicam and Paracetamol respectively.

the volume was made up to the mark with distilled water and to get a concentration of 1000 µg ml^{-1}. The

Preparation of Analysis of Tablet Formulation

Twenty tablets were accurately weighed and crushed to obtain fine powder. An accurately weight 100 mg of Paracetamol was transferred to 100 ml volumetric flask containing 20 ml 8M urea solution then flask was shaken for about ten Minutes to solubilize the drug. The volume was made up to the mark with distilled water and filtered. 10 ml filtrate was taken in 10 ml volumetric flask and the volume was made up to the mark with distilled water, further 5 ml of solution was taken and volume was made upto 10 ml. The volume was made up to final concentration. The absorbance was recorded at 244.0 nm and 384.0 nm against blank. Result of analysis of tablets formulation shown in Table No. 2.

Validation of Method—1-Simultaneous Estimation Method

Linearity

Linearity of analytical procedure is its ability (within a given range) to obtain test, which are directly proportional to absorbance of analyte in the sample. The calibration curve was ploted after analysis of five different concentrations(from 20 to 60 µg/ ml and 2 to 10 µg/ml) and absorbances for each concentration was recorded thrice and mean absorbance was calculated for Lornoxicam and Paracetamol respectively. The regression equation, correlation coefficient of the standard curve of the drug is shown in Figure No. 4 and 5 for Lornoxicam and Paracetamol respectively.

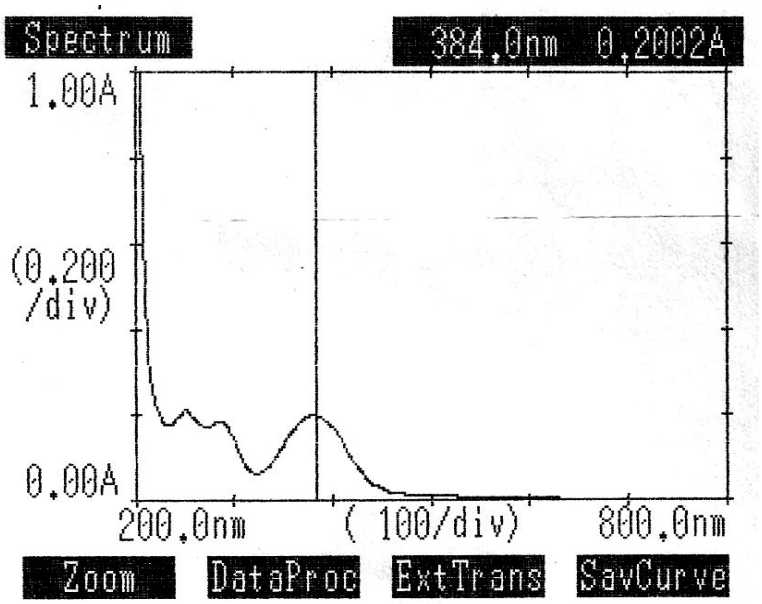


Figure No. 2 - Selection of λ_{max} of Lornoxicam.

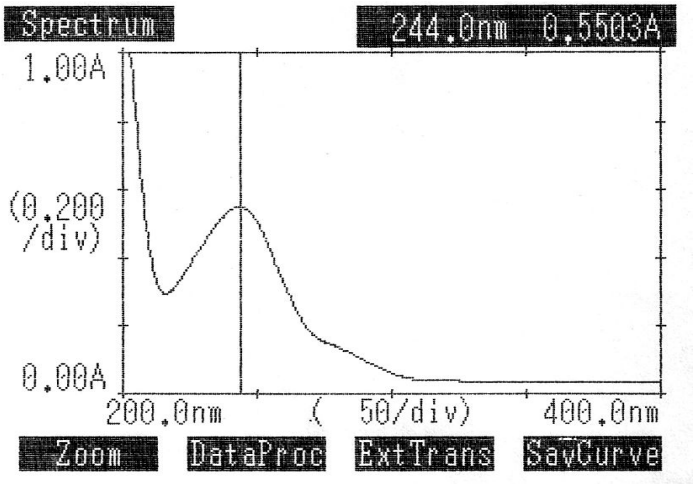


Figure No. 3 - Selection of λ_{max} of Paracetamol.

Table No. 1 - Result of Optical Parameter of Lornoxicam and Paracetamol

S.NO.	PARAMETER	LORNOXICAM	PARACETAMOL
1.	λ_{max}	384.0 nm	244.0 nm
2.	Beer's law limit (µg/ml)	2-10 µg/ml	20-60 µg/ml
3.	Regression equation	Y = 0.104 conc. + 0.0108	Y = 0.0211 conc. - 0.0039
4.	Correlation Coefficient (r^2)	0.9992	0.9990
5.	Molar Absorptivity (L mol^{-1} cm^{-1})	2.79 x 10^3	0.341 x 10^4
6.	Sandell's Sensitivity µg/ml 0.001 absorbance unit	7.52 x 10^4	0.226 x 10^4

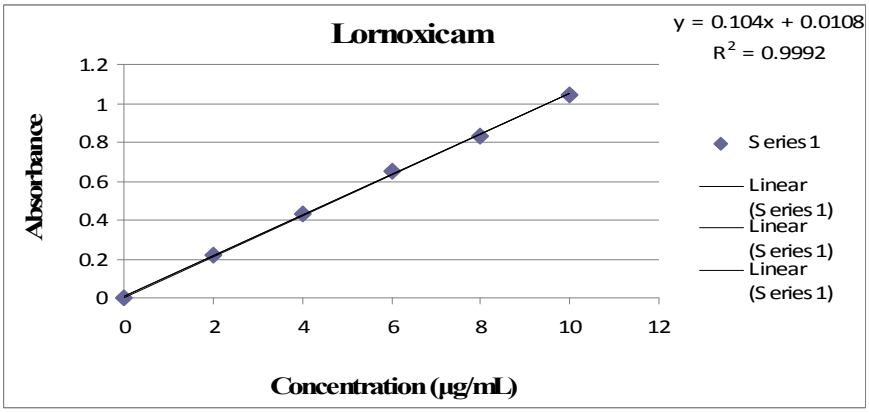


Figure No. 4 - Standard Calibration Curve of Lornoxicam.

Table No. 2 - Assay of Paracetamol and Lornoxicam in Tablet Formulation (method 1)

Brand Name	Paracetamol		Lornoxicam	
	Label Claim (mg)	% Purity	Label Claim (mg)	% Purity*
Lorsaid P 8	500	99.5 %	8	98.8%

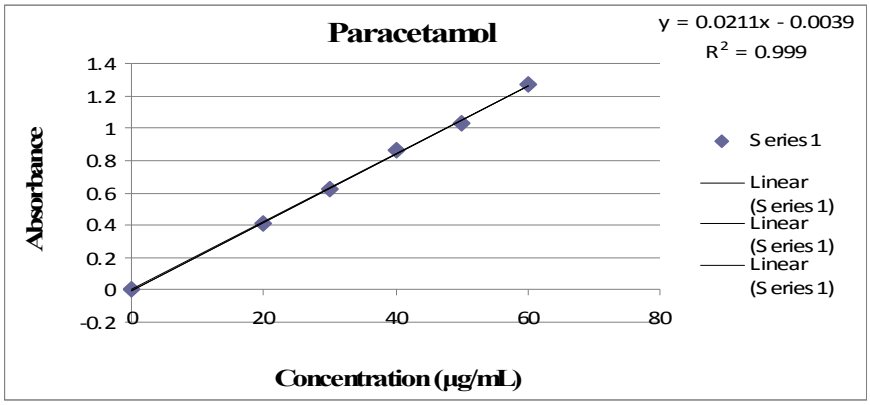


Figure No. 5 - Standard Calibration Curve of Paracetamol.

Accuracy

Recovery studies were performed to validate the accuracy of developed method. To pre-analysed sample solution, a definite concentration of standard drug (80%, 100%, and 120%) was added and then its recovery was analyzed for which result is shown in Table No. 3.

Precision

Repeatability

Standard dilutions were prepared and three replicates of each dilution were analyzed in same day for repeatability and results were subjected to statistical analysis. Standard dilutions were prepared and three replicates of each dilution were analyzed in different days and by different analysts. Statistical analysis was carried out for which result is shown in Table No.4.

Intermediate Precision

Analyst to Analyst

The intermediate precision expresses with in laboratories variation: different days, different analysts, different equipment etc. The standard dilution was prepared and three replicate of each dilution were analyzed by different analysts for all the developed methods. Result is shown in Table No.5.

Results of recovery study for PARA and LORN by simultaneous equations method (method 1)

Table No. 3 - Recovery Studies for Accuracy of Formulation (method 1)

Drug	Amount present (µg/ml)	Amount added (µg/ml)	Amount found (µg/ml)	% Recovery
PARA	25	20	19.8	99.0
	25	25	25.1	100.4
	25	30	29.9	99.6
LORN	6	4.8	4.79	99.7
	6	6	5.99	99.8
	6	7.2	7.22	100.2

Result of Precision(method 1)

Repeatability

Table No. 4 - Results of Analysis Data of Tablet Formulation

Drug	Label claim mg/tab	Amount found* mg/tab	Label claim (%)	S.D.	% RSD
PARA	500	498.99	99.79	0.107	0.115
LORN	8	7.98	99.75	0.115	0.115

Analyst to Analyst

Table No. 5- Result of Analyst to Analyst Precision (method 1)

Analyst	Label claim mg/tab		Amount found* mg/tab		Label claim (%)		S.D.		% RSD	
	PARA	LORN	PARA	LORN	PARA	LORN	PARA	LORN	PARA	LORN
1	500	8	500.10	7.93	100.02	99.12	0.264	0.150	0.132	0.154
2	500	8	498.00	7.90	99.60	98.75	0.159	0.120	0.107	0.135

Method 2 - Employing Absorbance Ratio Method (Q-Analysis)

Q-absorbance method uses the ratio of absorbance at two selected wavelengths, one at isoabsorptive point and other being the λ_{max} of one of the two components. The standard stock solution and calibration curve were prepared at described in method 1. From the overlain spectra of Paracetamol (20 µg/ ml) and Lornoxicam (10 µg/ ml), two wavelengths at 279.0 nm (isoabsorptive point) and at 384.0 nm (λ_{max} of Lornoxicam) were selected for the formation of Q-absorbance shown in Figure No. 6. The absorbances of Paracetamol 279.0 nm (isoabsorptive point) and λ_{max} of Lornoxicam at 384.0 nm and the absorptivity coefficients of each drug at both wavelengths were determined. Result of analysis of tablets formulation is shown in Table No. 6.

Validation of Method 2 - Absorbance Ratio Method (Q-Analysis)

Linearity

Linearity of analytical procedure is its ability (within a given range) to obtain test, which are directly proportional to absorbance of analyte in the sample. The calibration curve was ploted after analysis for five different concentrations (from 20 to 60 µg/ ml and 2 to 10 µg/ ml) and absorbances for each concentration was recorded three times, and mean absorbance was calculated for Lornoxicam and Paracetamol respectively. The regression equation, correlation coefficient of the standard curve of the drug is shown in Figure No.4 and 5 for Lornoxicam and Paracetamol respectively.

Accuracy

Recovery studies were performed to validate the accuracy of developed method. To pre-analysed sample solution, a definite concentration of standard drug (80%, 100%, and 120%) was added and then its recovery was analyzed and result is shown in Table No. 7.

Precision

Repeatability

Standard dilutions were prepared and three replicates of each dilution were analyzed in same day for repeatability and results were subjected to statistical analysis. Standard dilutions were prepared and three replicates of each dilution were analyzed in different days and by different analysts. Statistical analysis was carried out and result is shown in Table No. 8.

Analyst to Analyst

The intermediate precision expresses with in laboratories variation: different days, different analysts, different equipment etc. The standard dilutions was prepared and three replicate of each dilution were analyzed by different analysts for all the developed methods for which the result is shown in Table No.9.

Table No. 6 - Assay of Paracetamol and Lornoxicam in Tablet Formulation (method 2)

Brand Name	Paracetamol		Lornoxicam	
	Label Claim (mg)	% Purity	Label Claim (mg)	% Purity*
Lorsaid P 8	500	99.80	8	98.70

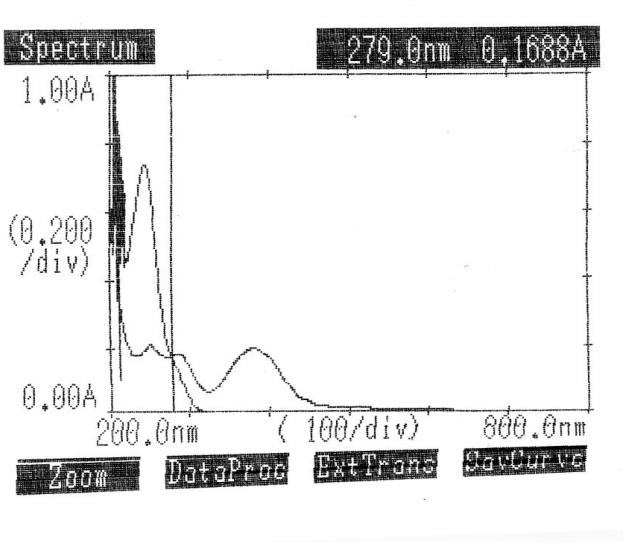


Figure No. 6 - Overlay Spectra of Lornoxicam and Paracetamol.

Results of recovery study of PARA and LORN by method 2 Absorbance Ratio method (Q-Analysis)

Table No. 7 - Recovery Studies for Accuracy of Formulation (method 2)

Drug	Amount present (µg/ml)	Amount added (µg/ml)	Amount found (µg/ml)	% Recovery
PARA	25	20	20.1	100.50
	25	25	25.3	101.20
	25	30	30.0	100.00
LORN	6	4.8	4.82	100.41
	6	6	5.95	99.16
	6	7.2	7.16	99.44

Repeatability

Table No. 8- Results of analysis Data of Tablet Formulation(method 2)

Drug	Label claim mg/tab	Amount found* mg/tab	Label claim (%)	S.D.	% RSD
PARA	500	498.50	99.70	0.712	0.714
LORN	8	7.92	99.00	0.251	0.258

Analyst to Analyst

Table No. 9 - Result of Analyst to Analyst Precision(method 2)

Analyst	Label claim mg/tab		Amount found* mg/tab		Label claim (%)		S.D.		% RSD	
	PARA	LORN	PARA	LORN	PARA	LORN	PARA	LORN	PARA	LORN
1	500	8	500.20	7.98	100.04	99.75	0.156	0.198	0.214	0.207
2	500	8	499.50	7.97	99.90	99.62	0.075	0.101	0.284	0.265

CONCLUSION

The proposed method is new, simple, cost effective, accurate, safe, and precise, Ecofriendly can be successfully employed in the routine analysis of Lornoxicam and Paracetamol in bulk and tablet dosage form. There was no interference with 8 M urea solution (as hydrotropic agent) with other excipients. Decisive advantage is that the organic solvent was precluded but not at the expense of accuracy. There is a good scope for other poorly water soluble drugs which may be tried to get solubilized in hydrotropic solubilizing agent to carry out their spectrophotometric analysis excluding the use of costlier and unsafe organic solvents.

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