

*Original Research Article***SIMULTANEOUS QUANTIFICATION OF LORNOXICAM/ PARACETAMOL TABLETS BY APPROACH OF FIRST DERIVATIVE UV-SPECTROSCOPY****Swetha Bhavani N, Hima Bindu S, Sai Supriya J, Sandya Rani CH, Panikumar D Anumolu\***

Department of Pharmaceutical Analysis, Gokaraju Rangaraju College of Pharmacy, Osmania University, Hyderabad, Andhra Pradesh-500090

**ABSTRACT**

**Background:** Derivative spectroscopy provides a greater selectivity and spectral discrimination than common spectroscopy. It is the dominant approach for resolution of one analyte whose peak is hidden by a large overlapping peak of another analyte in multi component analysis. Hence, this technique we have been successfully applied for simultaneous quantification of lornoxicam and paracetamol in combined tablets.

**Materials and Methods:** The method is based on the derivative spectrophotometric method at zero-crossing wavelengths. Two wavelengths 347 nm (zero crossing point for paracetamol) and 272.5nm (zero crossing point for lornoxicam) were selected for the quantification of lornoxicam and paracetamol respectively, using 0.01 M sodium hydroxide as solvent and Shimadzu (Japan) UV-Visible spectrophotometer (UV-1800) instrument.

**Results:** The first derivative amplitude-concentration plots were rectilinear over the range of 2-22 µg/mL and 1-75 µg/mL with detection limits of 0.06 and 0.08 µg/mL and quantification limits of 0.2 and 0.26 µg/mL for lornoxicam and paracetamol respectively. The proposed method was statistically validated as per ICH guidelines. The percentage recovery was within the range between 97-101 and % relative standard deviation for precision and accuracy of the method was found to be less than 2.

**Conclusion:** The proposed method was effectively applied to routine quality control analysis of studied drugs in their tablet formulations.

**Keywords:** Lornoxicam, paracetamol, derivative spectrophotometry.

**\*Corresponding author address: Panikumar D Anumolu** Gokaraju Rangaraju College of Pharmacy, Department of Pharmaceutical Analysis, Hyderabad, Andhra Pradesh- 500090. Email- [panindrpharma@yahoo.co.in](mailto:panindrpharma@yahoo.co.in), Tel.: 919010014734; Fax: 040-23041700

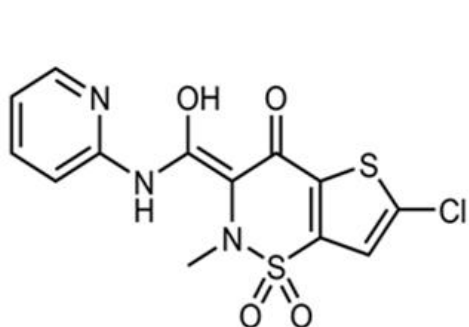
**INTRODUCTION**

Lornoxicam chemically known as 6-Chloro-4-hydroxy-2-methyl-N-2pyridinyl-2H-thieno [2,3-e]-1,2thiazine-3-carboxamide1,1-dioxide, [Figure 1] is a novel non-steroidal anti inflammatory agent with marked analgesic properties [1]. It is not official in any pharmacopeia. Paracetamol chemically *N*-(4-Hydroxyphenyl) acetamide, [Figure 2] is a centrally and peripherally acting non-opoid analgesic and antipyretic. It is official in Indian Pharmacopoeia [IP] [2], British Pharmacopoeia [BP] [3] and United States Pharmacopoeia [USP] [4]. Lornoxicam [8 mg] and

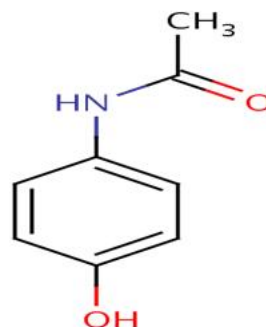
paracetamol [500 mg] have been formulated in a fixed dose tablet dosage form for the treatment of severe pains.

A detailed literature survey revealed that the few analytical methods include UV-spectrophotometry [5], high performance liquid chromatography (HPLC) [6] and HPTLC [8,9] methods available for simultaneous quantification of lornoxicam and paracetamol.

To the best of our knowledge, no method reported on the use of derivative spectrophotometry for the simultaneous quantification of lornoxicam and paracetamol in 0.01N sodium hydroxide as solvent. Moreover there was no simple, eco-friendly and economical method available for estimation of lornoxicam and paracetamol either in bulk drug or in formulation by first derivative spectroscopy using 0.01N NaOH as solvent.



**Figure 1. Chemical structure of lornoxicam**



**Figure 2. Chemical structure of paracetamol**

Derivative spectrophotometry more superior than normal spectroscopy by minimizing number of analytical problems like resolution of multicomponent systems, removal of sample turbidity, matrix back ground and enhancement of spectral details. It is the dominant approach for resolution of one analyte whose peak is hidden by a large overlapping peak of another analyte in multi component analysis [10-16]. Hence, an attempt has been made to develop a simple, eco-friendly and economical first -derivative spectrophotometric method for simultaneous quantification of lornoxicam and paracetamol either in bulk drug or in tablet dosage form using 0.01N NaOH as solvent and method was statically validated as per ICH guidelines.

## MATERIALS AND METHODS

### Instrumentation

Shimadzu (Japan) UV-Visible spectrophotometer (UV-1800) with 1cm matched quartz cells was used for spectrophotometric analysis and a calibrated electronic single pan balance (Shimadzu, Aux-220) were used during the analysis.

### Reagents and chemicals

Lornoxicam and paracetamol bulk drugs were obtained as gift samples from Dr.Reddy's laboratories Ltd, Hyderabad, India. Tablets (Lornasafe -plus and Lornoxi-P) were procured from local pharmacies. Anhydrous sodium hydroxide was purchased from Hi-media, Mumbai.

### Preparation of standard stock solutions

Each of standard lornoxicam and paracetamol (10mg) were weighed and transferred into two separate 10 mL volumetric flasks and dissolved in 0.01N NaOH. The flasks were shaken and volume was made up to the mark with 0.01N NaOH. From this 5 ml solution was diluted to 50 ml with 0.01N NaOH to obtain a standard solution of lornoxicam and paracetamol having final concentration of 100  $\mu\text{g/mL}$  of each.

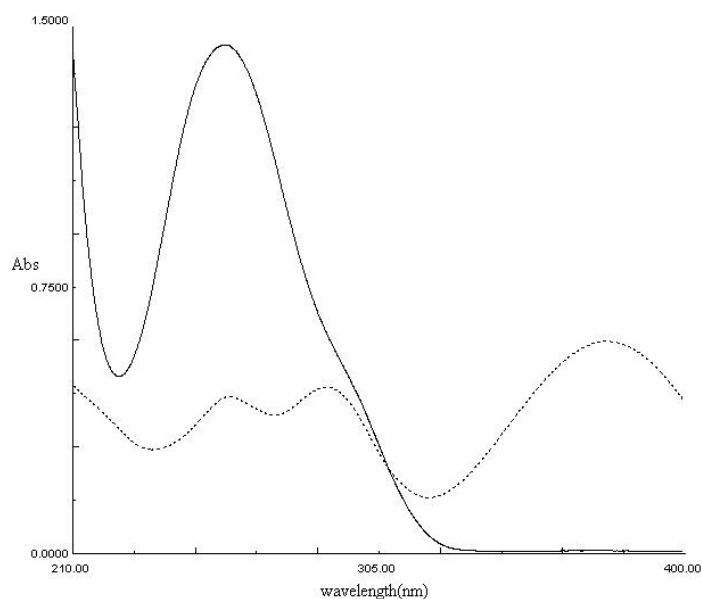


Figure 3. Normal overlaid UV spectra of lornoxicam (...) and paracetamol (--)

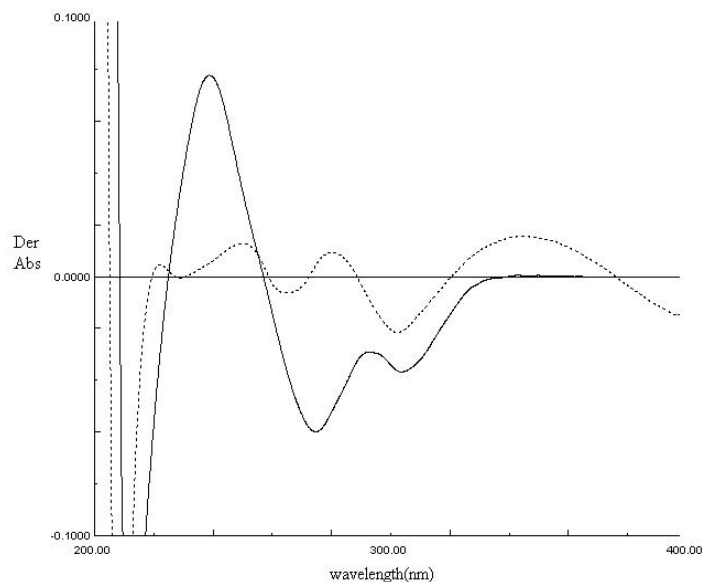


Figure 4. First order derivative UV overlaid spectrum of lornoxicam (.....) and paracetamol (--)

### **Selection of wavelengths**

Standard solution of lornoxicam (LOR) and paracetamol (PAR) were diluted appropriately with 0.01N NaOH to obtain solution containing lornoxicam(10 $\mu$ g/mL) and paracetamol (10 $\mu$ g/mL). Spectra of these diluted solutions were scanned in the spectrum mode between 200 nm to 400 nm using 0.01N NaOH as a blank. The zero-order spectra of lornoxicam and paracetamol were transformed to corresponding first-derivative spectra in the range of 200 - 400 nm. The overlaid spectra (zero and first order) lornoxicam and Paracetamol are shown in Figure 3 and 4.

### **Derivative conditions**

The overlaid zero-order spectra of standard solution of lornoxicam and paracetamol at 10  $\mu$ g/mL and spectra were found to be similar in nature and overlapping. It was observed that lornoxicam and paracetamol contribute significantly below 300 nm wavelength for absorbance. Hence, the derivative graphical method was used to estimate lornoxicam and paracetamol in presence of each other. First-order derivative spectra of lornoxicam and paracetamol were overlapped. The wavelength 347 nm was selected for the quantification of lornoxicam (where the derivative response for paracetamol was zero). Similarly, 272.5nm was selected for the quantification of paracetamol (where the derivative response for was zero). Characteristic wavelengths (zero-crossing points) for lornoxicam and paracetamol were confirmed by varying the concentrations of both drugs.

### **Calibration curves for lornoxicam and paracetamol**

The standard solution of lornoxicam and paracetamol were used to prepare two different sets of working standard solutions of lornoxicam (0.2-4.2  $\mu$ g/mL) and paracetamol (1-75  $\mu$ g/mL).The first-derivative spectra were recorded using the prepared solutions against 0.01N NaOH as blank. The values of first-derivative absorbance were plotted against corresponding concentrations to construct the calibration curves.

### **Determination of Lornoxicam and paracetamol in their combined dosage form (assay)**

Twenty tablets of each marketed formulation (Lornoxi-P and Lornasafe-plus), each containing 8 mg of lornoxicam and 500mg of paracetamol were taken and accurately weighed. Average weight was determined and crushed into fine powder. An accurately weighed quantity of powder equivalent to 8 mg lornoxicam and 500mg paracetamol was transferred to volumetric flask of 10 mL capacity, Volume was made up to the mark with 0.01N NaOH. The above solution was filtered through whatmann filter paper (No.41).The filtrate was further diluted to obtain sample solutions of concentrations within linearity range. The derivative absorbance of sample solutions were measured at selected wavelengths used for the quantification of lornoxicam and paracetamol.

### **Method validation**

The method was validated for accuracy, precision, specificity, linearity, LOD and LOQ by the following procedures [17].

### **Accuracy**

The accuracy of the method was determined by calculating recoveries of lornoxicam and paracetamol by the method of standard additions. Known amounts of lornoxicam and paracetamol (80%, 100% and 120%) levels were added to a pre quantified sample solutions. The

recovery was verified by estimation of drug in triplicate preparations at each specified concentration level and calculated % RSD.

### **Precision**

The intra-day and inter-day precision of the proposed first-derivative spectrophotometric simultaneous method was determined by estimating the corresponding response three times on the same day (intra- day) and for three consecutive days (inter-day) for three different concentrations of lornoxicam (0.2, 2.2 and 4.2  $\mu\text{g/mL}$ ) and paracetamol (1, 45 and 75  $\mu\text{g/mL}$ ). The results are reported in terms of relative standard deviation (% RSD).

### **Selectivity**

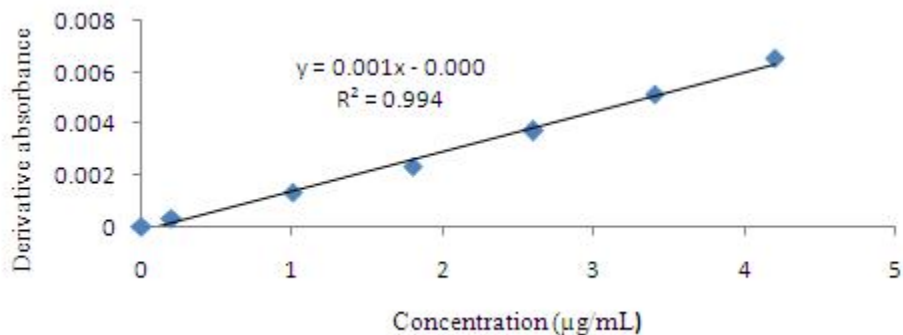
Selectivity is the ability of the method to accurately measure a compound in the presence of other components such as impurities, degradation products and matrix components. The selectivity of the proposed method was evaluated through the analysis of a placebo solution, which was prepared with the common excipients of the pharmaceutical formulation. Thus, the mixture of component inert was prepared in their usual concentration employed in tablets (concentrations were determined based in Handbook of Pharmaceutical Excipients <sup>[18]</sup> and calculated for medium weight of content). The developed method was applied in order to check if any component of the formulation could generate a response with emission band similar to the drugs.

### **Sensitivity**

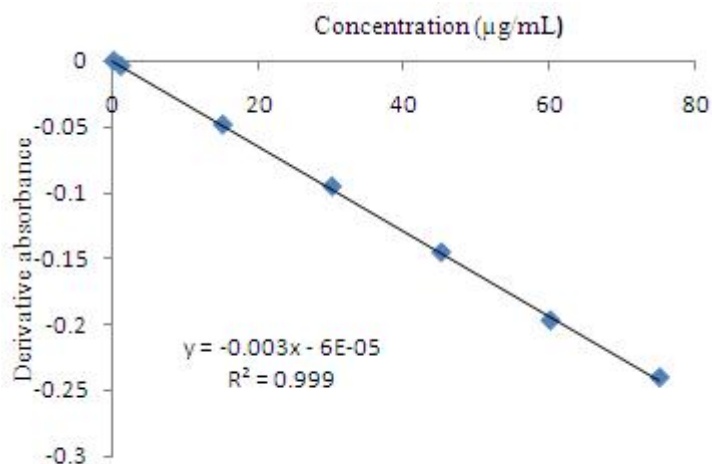
The sensitivity of the method was determined with respect to LOD and LOQ. The LOD and LOQ were separately determined based on standard calibration curve.

## **RESULTS AND DISCUSSION**

A simple, eco-friendly and economic first derivative spectrophotometric method was developed for the simultaneous quantification of lornoxicam and paracetamol bulk drug and formulations using 0.01N NaOH as solvent and was also validated as per ICH guidelines. The calibration curves shows that, the developed method was linear in the concentration range of 0.2-4.2  $\mu\text{g/mL}$  and 1-75  $\mu\text{g/mL}$  for lornoxicam and paracetamol. [Figure 5 & 6] Limit of detection and limit of quantification values were indicated that the method shows high sensitivity. The optimized conditions for developed method are shown in Table 1. No significant difference between intra-day and inter-day precision, revealed that the method is reproducible (Table 2). The % recovery was within the range between 97-101 (Table 3) and %RSD for commercial formulation was shown less than 2 (Table 4). This indicates that the method is accurate and reliable.



**Figure 5 Calibration plot for lorinoxicam**



**Figure 6 Calibration plot for paracetamol**

**Table 1: Optimum conditions for proposed method**

Parameter	Lornoxicam	Paracetamol
Absorption maxima (nm)	347	272.5
Beer's Law Limit(µg/mL)	0.2-4.2	1 – 75
Slope	0.001	-0.003
Intercept	0	0
Correlation coefficient	0.994	0.999
Regression equation	$y = 0.001x + 0.0$	$y = -0.003x - 0.00005$
LOD (µg/mL)	0.06	0.08
LOQ (µg/mL)	0.2	0.26

LOD- Limit of detection; LOQ- Limit of quantification

**Table 2: Precision of the method**

Concentration (mcg/ml)	Intra-day precision		Inter-day precision	
	Concentration estimated ( $\mu\text{g/mL}$ ) (AM $\pm$ SD) *	% RSD	Concentration estimated ( $\mu\text{g/mL}$ ) (AM $\pm$ SD) *	%RSD
Lornoxicam				
0.2	0.25 $\pm$ 0.004	1.6	0.26 $\pm$ 0.002	0.76
2.2	2.24 $\pm$ 0.015	0.66	2.22 $\pm$ 0.026	1.17
4.2	4.50 $\pm$ 0.05	1.11	4.34 $\pm$ 0.08	1.84
Paracetamol				
1	1.22 $\pm$ 0.003	0.25	1.12 $\pm$ 0.004	0.35
45	45.14 $\pm$ 0.116	0.25	45.02 $\pm$ 0.129	0.28
75	75.32 $\pm$ 0.272	0.36	75.24 $\pm$ 0.358	0.47

\*Average of three determinations and % RSD is relative standard deviation.

**Table 3: Accuracy of the method (Recovery studies)**

Formulation	Recovery level (%)	Recovery of analyte	Theoretical content (mg)	Amount found (mg)* (Mean $\pm$ SD)	Recovery (%)	% RSD
Lornoxi-P	0	LOR	2	2.1 $\pm$ 0.015	105	0.714
		PAR	125	125.1 $\pm$ 0.145	100.08	0.115
	80	LOR	3.6	3.5 $\pm$ 0.045	97.2	1.285
		PAR	225	224.5 $\pm$ 0.34	99.77	0.151
	100	LOR	4	4.2 $\pm$ 0.009	105	0.214
		PAR	250	250.24 $\pm$ 0.98	100.09	0.393
120	LOR	4.4	4.4 $\pm$ 0.01	100	0.272	
	PAR	275	275.12 $\pm$ 1.25	100.04	0.456	
Lornasafe -plus	0	LOR	2	2.2 $\pm$ 0.01	110	0.56
		PAR	125	125.04 $\pm$ 0.25	100.03	0.201
	80	LOR	3.6	3.4 $\pm$ 0.00	94.4	0.24
		PAR	225	225.05 $\pm$ 0.55	100.02	0.247
	100	LOR	4	3.7 $\pm$ 0.02	92.5	0.67
		PAR	250	250.12 $\pm$ 0.35	100	0.142
120	LOR	4.4	4.3 $\pm$ 0.01	97.7	0.34	
	PAR	275	274.9 $\pm$ 0.85	99.9	0.309	

LOR-lornoxicam; PAR- paracetamol; \* Average of three determinations and SD- standard deviation.

**Table 4: Analysis of commercial tablets (assay)**

Formulation	Lornoxicam				Paracetamol			
	Label claim (mg)	Amount found (mg) (AM ± SD)	% Recovery	% RSD	Label claim (mg)	Amount found (mg) (AM ± SD)	% Recovery	% RSD
Lornoxi-p	8	8.4 ± 0.011	105	0.13	500	500.16±0.25	100.03	0.05
Lornasafe-plus	8	8.2 ± 0.102	102	1.24	500	500.04 ±0.56	100	0.11

AM- Arithmetic mean

## CONCLUSION

A simple, eco-friendly, sensitive and economic first derivative spectrophotometric method has been proposed for simultaneous quantification lornoxicam and paracetamol in pure form and in tablet dosage forms by using 0.01N NaOH as solvent. The assay values were in good concurrence with their respective labeled claim, which suggested no interference of formulation excipients in the estimation and obtained results from validation proved the proposed method was scientifically sound. Therefore, the developed method can be readily adopted by pharmaceutical quality control laboratory for routine analysis.

## ACKNOWLEDGEMENT

The authors are thankful to the management and Prof.C.V.S.Subrahmanyam, Principal, Gokaraju Rangaraju College of Pharmacy

## REFERENCES

1. Maryadele. JO.Neil. The Merck index, an encyclopedia of chemicals, drugs and biologicals. 14<sup>th</sup> ed. Merck & Co, INC, White house station 2006.1269.
2. Indian pharmacopoeia, Vol.3.The Indian pharmacopoeia commission, Ghazianad 2007. 1514.
3. British pharmacopoeia, Vol.2. British pharmacopoeia commission, UK 2008.1653.
4. United States of Pharmacopoeia-National Formulary, The official compendia of standards. Asian edition, USP Convention, Inc., Rockville: 2003. 129.
5. Lakshmi sivasubramanian, Lakshmi KS, Tintu T. Simultaneous spectrophotometric estimation of paracetamol and lornoxicam in tablet dosage form. Int J. Pharma sci 2010; 2(4):165-168.
6. Santosh NM, Surekha SN, Swaroop RL, Jaiprakash NS. Simultaneous estimation of paracetamol and lornoxicam by RP-HPLC method from combined dosage form. Der pharmacia sinica 2011; 2(5):138-144.

7. Savitha SY, Anuradha SJ, Janhavi RR. Simultaneous determination of paracetamol, lornoxicam and chlorzoxazone in tablets by high performance thin layer chromatography. *Der pharma chemica* 2012; 4(5):1798-1802.
8. Raja T, Lakshmana Rao A. Validated HPTLC method for simultaneous quantification of paracetamol and lornoxicam in bulk drug and pharmaceutical formulation. *Int J. Pharm Biomed Res* 2012; 3(3):162-166.
9. Dhara JP, Vivek PP. Simultaneous determination of paracetamol and lornoxicam in tablets by thin layer chromatography combined with densitometry. *Int J. ChemTech Res* 2010; 2(4):1929-1932.
10. Haripriya A, Sirisha N, Vishali S, Ramakrishna K, Panikumar AD. Validated eco-friendly derivative spectrophotometric method for valsartan and hydrochlorothiazide combined tablet dosage form. *Asian J. Research Chem* 2012; 5(8):1074-1077.
11. Mark H, Workman J. Derivatives in spectroscopy. *Spectroscopy*.2003; 18 (4): 32-37.
12. Basilio M. Derivative spectrophotometry in the analysis of mixtures of cefotaxime sodium and cefadroxil monohydrate. *J Pharm Biomed Anal*.2003; 32: 257-267.
13. Beckett AH, Stenlake JB. *Practical pharmaceutical chemistry*, the athlone press 2007; 4: 269-299.
14. Sriphong L, Chaidedgumjorn A, Chaisuroj K, Derivative spectrophotometry applied to the determination of triprolidine hydrochloride and pseudoephedrine hydrochloride in tablets and dissolution testing. *Engineering and technology* 2009; 55: 573 – 577.
15. Jiignesh Dilipbhai Patel, Bhavik Patel A, Bhuvan Raval P, Vipul Vaghela M, Development and validation of derivative spectrophotometry method for simultaneous estimation of drotaverine hydrochloride and mefenamic acid in their combined dosage form. *Journal of pharmacy research* 2010; 3(1): 566-569.
16. Dahivelkar PP, Mahajan VK, Bari SB, Shirkhedkar AA, Fursule RA, Surana SJ. Simultaneous derivative and multi-component spectrophotometric determination of drotaverine hydrochloride and mefenamic acid in tablets, *Indian journal of pharmaceutical sciences* 2007; 69 (6): 812-814.
17. International Conference on Harmonization, Harmonized Tripartite Guideline, Validation of Analytical Procedures, Text and Methodology, Q2 (R1), November 2005.
18. Raymond CR, Paul JS, Sian CO. *Hand Book of Pharmaceutical Excipients*, Pharmaceutical press and American pharmacists association, 2007.