

RESEARCH ARTICLE

Development and Validation of FTIR Spectroscopic Method for the Quantitative Estimation of Lornoxicam in Tablet Dosage Form

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ABSTRACT

Lornoxicam is available in the market as a solid dosage form, particularly tablets. Liquid chromatography has been the recommended assay procedure for lornoxicam in various pharmacopeias. While going through the literature, it was observed that for the analysis of lornoxicam, no FTIR based method was found. The present study involves the development of a novel, rapid, superior, labor-free, non-destructive, and economic FTIR-based analytical technique for the analysis of lornoxicam in both bulk and tablet formulations. International Council validated the method for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines Q2A and Q2B in accordance with the United States Food and Drug Administration (USFDA) guidance and by United States Pharmacopoeia (USP). FTIR based method is extremely precise, quite linear, very accurate, and has adequate ruggedness. The developed method can be of potential use in the routine quantitative drug analysis of lornoxicam in the pharmaceutical industry for quality control purposes.

Keywords: Lornoxicam, FTIR, method, Validation, Estimation, Tablets.

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INTRODUCTION

Fourier transform infrared spectroscopy (FTIR) is a rapid, superior, labor-free, non-destructive investigative spectroscopic technique that is widely applicable for the routine analysis of pharmaceuticals and also in new drug research that needs no or minimal sample pre-treatment.¹ Traditionally, FTIR analysis is carried out by transmission measurement technique using the transparent pellets of the sample with the halide salts. Because of the availability of newer sampling techniques in handling samples, FTIR is gaining more attention from analytical researchers for the quantitative analysis of solid-state samples.² Using this method, pharmaceutical samples can be scanned at a high resolution and high wavelength accuracy. Moreover, statistical examination based on the spectral information obtained can be automatically done for the selection of the FTIR region, which is most appropriate for the quantitative determination.³

Quantification of some pharmaceuticals has been reported in the literature using FTIR spectroscopy either by measuring the transmission of analyte in potassium bromide or in chloroform.⁴ An easy infrared spectroscopic

method can be very helpful for regular analysis of bulk and formulation samples as compared to the costly, skillful, and lengthy analytical methods.⁵ Quantitative evaluation of drugs by means of solid sampling (KBr disc method), the FT-IR spectroscopy has been described recently. On the other hand, the solid sampling technique has the drawback of inappropriate distribution of the drug throughout the KBr pellet but can be eliminated by careful mixing.⁶

Lornoxicam (6-chloro-3-[hydroxyl(pyridin-2-ylamino)methylene]-2-methyl-2,3-dihydro-4H-thieno[2,3-e] [1,2]thiazin-4-one 1,1-dioxide) (Figure 1) is an analgesic and anti-inflammatory drug, belonging to the imperative class of non-steroidal anti-inflammatory drugs (NSAIDs) that is used primarily for the treatment of osteoarthritis and rheumatoid arthritis.⁷ It is available in the market in solid dosage forms, particularly tablets. Liquid chromatography has been the recommended assay procedure for lornoxicam in various pharmacopeias.⁸⁻¹⁰ However, several reports have been validated for the quantitative analysis of lornoxicam in numerous pharmaceutical dosage forms (tablet¹¹, powder for injection¹²) as single drug product¹³ as well as combined drug

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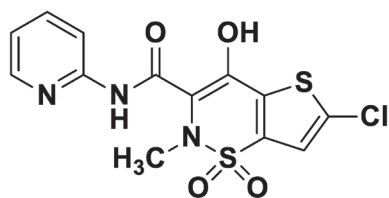


Figure 1: Structure of lornoxicam

products (paracetamol)¹⁴ by using RP-HPLC. In addition to it, the analysis of combined drug products with paracetamol by UV-vis spectrophotometry has also been reported by researchers.¹⁵ The analyses of lornoxicam in human plasma and synovial fluid by RP-HPLC¹⁶ and LC-MS¹⁷ have also been reported.

While going through the literature, it was observed that for the analysis of lornoxicam, no FTIR based method was found. The present study involves the development of a novel FTIR based analytical technique for the analysis of lornoxicam in both bulk and tablet formulations. International Council validated the method for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines Q2A and Q2B and in accordance with the United States Food and Drug Administration (USFDA) guidance and by United States Pharmacopoeia (USP).

MATERIALS AND METHODS

Chemicals

Lornoxicam was obtained as a generous gift sample from Prayosha Healthcare Pvt. Ltd., Ankleshwar, Gujarat, India. Commercially available tablets (Lornoxi[®]-8; 8 mg of lornoxicam) used in the study were purchased from a local medical store in Nagpur, Maharashtra, India. Potassium bromide (KBr) was purchased from Merck Pvt. Ltd., Mumbai, Maharashtra, India and analytical grade chemicals were obtained from LobaChemie Pvt. Ltd., Mumbai, Maharashtra, India.

Instrumentations

The study was performed on a Shimadzu[®] Fourier Transform Infrared Spectrophotometer (8400s, Kyoto, Japan). The infrared spectrum of the pure oxycam derivative, lornoxicam, over a frequency range of 4000 to 400 cm⁻¹ was obtained using the KBr pellet method to identify the characteristic absorption peak corresponding to the stretching variations of different functional groups. A resolution of 4cm⁻¹ was selected and the number of the scan was kept 40. Shimadzu[®] Analytical Balance (AW220) was utilized for weighing the chemicals. BioTechnics[®] Hot Air Oven (BTI-26) was employed for the research work.

Preparation of Stock Sample

Accurately weighed 50 mg of lornoxicam was transferred into a 100 mL conical flask and dissolved with 20 mL of chloroform. Further, the content was sonicated for 20 minutes duration and filtered through a Whatman filter paper no. 41. The collected

clear filtrate was evaporated in a hot air oven and the dried residue was collected. About 30 mg of the dried residue was weighed and made up to 300 mg with KBr to achieve a final concentration of 100 µg/mg.

Preparation of Standard Calibration Curve

From the stock sample, 7.5, 15, 22.5, 30, and 37.5 mg of lornoxicam were accurately weighed and to this, KBr was added to make the total content of 150 mg. This gave the resultant concentration of 2.5, 5, 7.5, 10, 12.5, 15, and 17.5 µg/mg. The absorbance was calculated considering the percentage transmission of the carbonyl group centered at 1643.24 cm⁻¹ using the following formula:

$$A = 2 - \log \% T \text{ ----- (1)}$$

Sample analysis (Formulation): Extraction of drug from tablet matrix

Tablet powder equivalent to 50 mg of lornoxicam was accurately weighed, extracted with 50 mL of chloroform, sonicated for 30 minutes duration, and filtered through Whatman filter paper no. 41. The clear filtrate was evaporated in a hot air oven and the dried residue was collected. The extraction procedure was repeated 5 times. 30 mg of residual drug was weighed accurately and made up to 300 mg with KBr. From this mixture, 15 mg was weighed and made up to 150 mg with KBr. The sample pallets for lornoxicam were prepared and analyzed by the FTIR spectrometer. The absorbance was calculated considering the percentage transmission of carbonyl group centered at 1643.24 cm⁻¹ for lornoxicam, using the following formula (1).

Method Validation

Linearity and range

Accurately weighed quantities of drug powder equivalent to 80, 90, 100, 110, and 120 of the label claim were taken and dilutions were prepared appropriately to obtain a concentration in the range of 80 to 120% of the test concentration. The prepared samples were analyzed by the FTIR spectrometer and the obtained absorbance corresponding to the concentration of the drug (µg/mg) was plotted. The linearity was expressed in the regression coefficient value (r²).¹⁸

Accuracy

The multi-level recovery studies were performed to check the accuracy of the proposed method. The accuracy corresponds to the immediacy between the detected values during the analytical study and the reference standard value. The accuracy was assessed as the percentage relative standard deviation (%R.S.D.) and the mean percentage recovery.¹⁹ In this study, different concentrations (80, 100, and 120%) of the pure drug were added to a known pre-analyzed formulation sample and the total concentration was determined using the proposed method. The percent recovery of the added pure drug was calculated using the formula (2).

$$\% \text{Recovery} = \text{-----} (2)$$

Where A is the % drug concentration after standard drug addition, B is the % drug concentration in pre-analyzed formulation, and C is the % drug added in the formulation sample.

Precision

The precision of an analytical method refers to the degree of agreement among the individual results when the method is applied repeatedly to the multiple readings of a homogenous sample. It is expressed as S.D. or R.S.D. of the series of measurements where values <2% are considered as an acceptable limit. It was ascertained by the replicate estimation of the drugs by the proposed method.²⁰⁻²²

Ruggedness

The studies of ruggedness were carried out under two different conditions: inter-day and intra-day. The inter-day study was performed by applying the proposed method on the same sample of formulation on different days. The intra-day study was performed by applying the proposed method on the same sample of formulation on the same day at three hours intervals.²³⁻²⁵

RESULTS AND DISCUSSION

By using a range of 5 different concentrations of pure drugs standard calibration curve was plotted and the percentage estimation of tablet formulation was carried out using the equation obtained from the standard calibration curve. The standard calibration curve in the range of 2.5 to 17.5 µg/mg presented an enhancement of 0.221 to 2.0 with reduced %transmittance from 60 to 1 (Table 1). It was observed that with the increasing concentration, the %transmittance value of the selected peak centered at 1643.24 cm⁻¹ for lornoxicam was decreased. A high degree of linearity ($y = 0.114x + 0.014$) was observed in the entire range with r² value of 0.995 (Figure 2). The FTIR spectra-based representation of the standard calibration curve in the range of 2.5 to 17.5 µg/mg is provided in Figure 3.

For the qualitative analysis, the extraction of the drugs from the marketed formulation was carried out in chloroform and residue was used for FTIR analysis. The ketonic group (C = O) was selected for further quantitative analysis of drugs, as it shows a prominent change in %transmittance by changing the

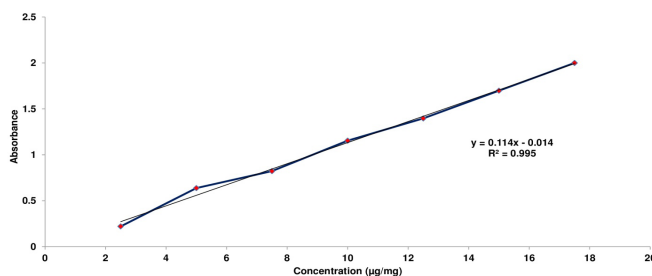


Figure 2: Standard calibration curve of lornoxicam

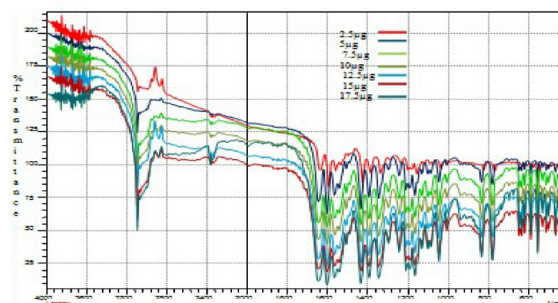


Figure 3: Spectral representation of standard calibration curve for lornoxicam

concentration. The infrared spectrum of lornoxicam extracted from the tablet dosage form is given in Figure 4.

The linearity of the method was studied by analyzing the standard samples at 5 different concentration levels ranging from 80 to 120% w/w. The calibration curve of lornoxicam showed a very high degree of linear constitution ($y = 0.0114x + 0.0074$) with r² value of 0.997 (Figure 5). It was observed that with the increasing concentration, the % transmittance value of lornoxicam decreased while the absorbance was seen to get increase simultaneously (Table 2). The FTIR spectra-

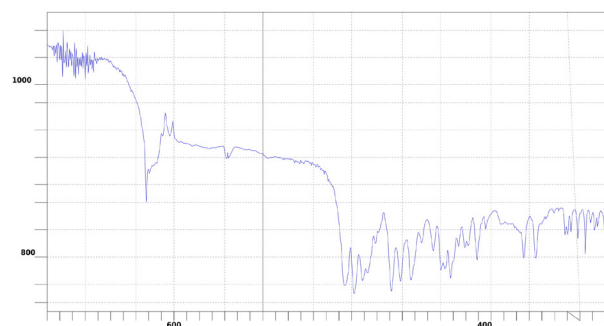


Figure 4: Infrared spectrum of lornoxicam extracted from tablet dosage form

Table 1: Standard calibration curve of lornoxicam

Concentration (µg/mg)	%Transmittance	Absorbance
2.5	60	0.221
5	23	0.638
7.5	15	0.823
10	7	1.154
12.5	4	1.397
15	2	1.698
17.5	1	2.0

Table 2: Linearity and range study of lornoxicam

%Label claim	%Transmittance	Absorbance
80	11	0.958
90	9	1.045
100	7.5	1.124
110	5.8	1.236
120	4	1.397

Table 3: Accuracy study of lornoxicam

%Recovery level	Equivalent weight of mixture (Tablet powder) (μg)	%drug found on reanalyzed basis	Amount of pure drug added (μg)	%Transmittance	Absorbance	%Recovery
80	10	99.82	8	0.9	2.045	100.98
100	10	101.40	10	0.5	2.301	102.91
120	10	98.85	12	0.3	2.522	101.99
Mean	101.69					
\pm S.D.	0.864					
C.V.	0.894					
%R.S.D.	0.00894					

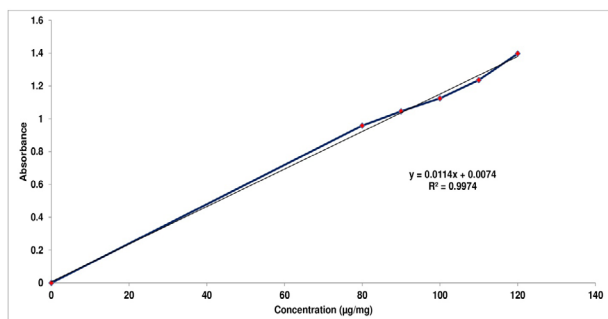


Figure 5: Linearity and range study of lornoxicam

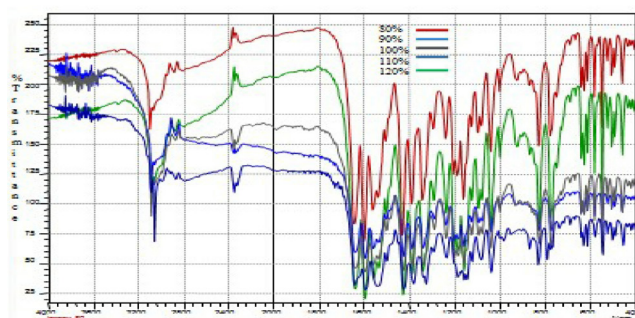


Figure 6: Spectral representation of linearity for lornoxicam

Table 4: Results of precision study for lornoxicam

Sample	%Transmittance	Absorbance	%Estimation
Tablet powder equivalent to 10 $\mu\text{g}/\text{mg}$	7.5	1.123	99.82
	7.2	1.142	101.40
	7	1.113	98.85
	7.3	1.136	100.8
	7.5	1.123	99.82
Mean	100.152		
\pm S.D.	0.899		
C.V.	0.897		
%R.S.D.	0.00897		

based representation of the linearity curve in the range of 80 to 120% is provided in Figure 6.

The recovery was estimated from the calibration curve, where the slope and Y-intercept of the graph were employed in

Table 5: Results of inter-day study for lornoxicam

Days	%Transmittance	Absorbance	%Estimation
Day 1	7.5	1.123	99.82
Day 2	7.2	1.142	101.40
Day 3	7.7	1.113	98.85
Mean	99.87		
\pm S.D.	1.062		
CV	1.063		
R.S.D.	0.0106		

the accuracy range from 80, 100, and 120% w/w, respectively. The mean percentage recovery (%R.S.D.) for lornoxicam was found to be 0.00894 (Table 3). The value was perceived to fall within the acceptable pharmacopeia prescribed limit of $\pm 2\%$, which was an indication of the good accuracy of the developed FTIR method. The % recovery value nearer to 100% also represented a high accuracy of the proposed FTIR method.

Precision was determined by studying the repeatability of the proposed FTIR method. The repeatability results in a specific precision under the same working condition over a short interval of time. The %R.S.D. of the analyzed concentration from the regression equation was taken as a parameter for judging the system precision where the value of 0.00897 indicated that it falls within the acceptable pharmacopeia prescribed limit of $\pm 2\%$ (Table 4). The % estimation value nearer to 100% also represented a high precision of the proposed FT-IR method.

Ruggedness studies were performed by preparing and analyzing different samples from an independent stock sample. The study was carried out on different days (Inter-day) and the same day (Intra-day) by different analysts. Inter-day and intra-day variations were taken into account to determine the ruggedness of the proposed FTIR method. In the ruggedness study, %R.S.D. values were less than 2% in all the cases, indicating that this method is excellently stable (Table 5).

Multiple time (n=5) analysis of tablet dosage form was carried out and the mean, SD, and RSD were calculated where it was found that all observations were within range. On analysis of the formulation (Lornoxi[®]-8 tablets - 10 $\mu\text{g}/\text{mg}$) by the FTIR method, the amount of lornoxicam present in the tablet was found to be 100.152% (Table 6). The assay concluded that the developed FTIR-based method precisely

Table 6: Results of estimation of lornoxicam in marketed formulation

Product name	Amount found (%w/w) ^a
Lornoxi [®] -8 tablets (10 µg/mg)	± 0.899 ^b

^amean value of 5 estimations; ^b standard deviation

and accurately determines the content of drug present in the tablet formulation.

CONCLUSION

The proposed FTIR spectroscopy method was found to be very simple, rapid, promising, and economical for the direct determination of lornoxicam in both bulk and pharmaceutical formulations. The greatest advantage identified in this method was the avoidance of other complicated procedures such as the use of multivariate analysis, chemometric or internal standard, etc., as well as avoiding the use of very complex systems such as LC-MS or RP-HPLC, etc. Hence, it can be concluded that this FTIR-based method can be of potential use in the routine quantitative drug analysis of lornoxicam in the pharmaceutical industry for quality control purposes.

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