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Stability-indicating spectrophotometric methods for the simultaneous determination of Lornoxicam and its oxidative degradation product. application to degradation kinetics and assay of pharmaceutical dosage forms

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ABSTRACT

Stability-indicating simultaneous spectrophotometric methods have been developed for the determination of lornoxicam (LOR) and its oxidative degradation product. To produce the degradation product, LOR was subjected to oxidation using 50% hydrogen peroxide and heating at 80°C for 20 min. Determination of LOR is based on measurement of the zero-order (^0D) amplitudes at 373 nm and the first derivative (^1D) amplitudes at 406 nm in 0.1 M hydrochloric acid solution where the oxidative degradation product does not show any interference. On the other hand, the oxidative degradation product can be estimated using its first derivative (^1D) amplitudes at 305 nm in the same solvent which represents a zero-crossing for LOR. Analytical performance of the proposed spectrophotometric procedures was validated with respect to linearity, range, precision, accuracy, selectivity, detection and quantitation limits. Calibration curves of LOR and its oxidative degradation product were linear in the range 4–24 μg/mL with correlation coefficients not less than 0.9996. The proposed methods were applied for analysis of laboratory-prepared mixtures containing different proportions of the intact drug and its degradation product. Both spectrophotometric $^0D_{373}$ and $^1D_{406}$ methods were applied for assay of LOR tablets and vials dosage forms, and they were quantified with recoveries not less than 99.1 %. The described $^0D_{373}$ and $^1D_{406}$ were utilized for investigation of LOR oxidative degradation kinetics at different temperatures. The degradation rate constants, half-lives and activation energy were calculated. It was found that the half life of LOR oxidation with 50% hydrogen peroxide at room temperature is about 10.5 hours.

Keywords: Lornoxicam; oxidative degradation; hydrogen peroxide; stability indicating spectrophotometric assay; kinetics; dosage forms

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INTRODUCTION

Lornoxicam (LOR) (Figure 1), chemically known as 6-chloro-4-hydroxy-2-methyl-*N*-2-pyridyl-2*H*-thieno[2,3-*e*][1,2]-thiazine-3-carboxamide-1,1-dioxide, is an oxicam derivative non-steroidal anti-inflammatory drug (NSAID). It is used in the management of musculoskeletal and joint disorders such as osteoarthritis and rheumatoid arthritis; it is also used in the treatment of other painful conditions including postoperative pain [1]. Several analytical methods have been reported for the quantification of LOR in its drug formulations and/or biological samples. Most of these

assay methods along with the detailed chemical and pharmacological properties of the drug are gathered and presented in its recently reported analytical profile [2].

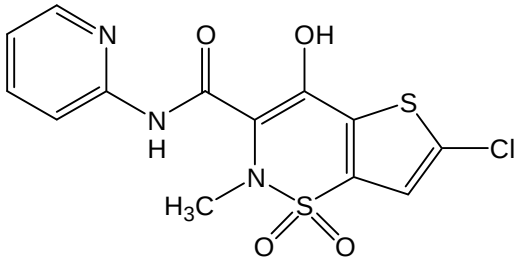

Figure 1: Chemical structure of lornoxicam (LOR)

Few reports can be found in the scientific literature for the stability-indicating determination of LOR. Spectrofluorimetric and spectrophotometric stability-indicating methods have been developed for the determination of some oxicams including LOR based on derivatization of their alkaline hydrolytic products with 7-chloro-4-nitrobenz-2-oxa-1,3-diazole (NBD-Cl) [3]. In addition, the stability-indicating determination of some oxicams including LOR in presence of their alkaline degradation products has been described using TLC and RP-HPLC methods [4]. Moreover, several RP-HPLC with UV detection methods have been reported for the assay of LOR in presence of its forced degradation products [5-8]. Finally, the forced degradation products of LOR have been characterized using hyphenated LC-MS techniques [9].

In this work, simple and direct A_{max} and first derivative spectrophotometric methods have been described for the simultaneous determination of LOR and its oxidative degradation product. The proposed spectrophtometric methods have been exploited for investigation of kinetics of the oxidative degradation of the drug; in addition, they have been applied for the assay of LOR in its pharmaceutical dosage forms.

MATERIALS AND METHODS

Instrumentation

All spectrophotometric measurements were performed using a UV-Visible spectrophotometer (UV-1800 series, Shimadzu Corporation, Kyoto, Japan) with UV Probe (version 2.32) software. The measurements were made in 1-cm quartz cells. Heating was performed on a Wisebath thermostatic water bath (WBPCP001, Daihan Scientific, Wonju-si, Gangwon-do, South Korea).

Materials and Reagents

Authentic sample of lornoxicam (LOR) (purity 101.5 %) was kindly provided by Global Napi Pharmaceutical Industries, Cairo, Egypt. Analytical grade of hydrogen peroxide (50%) and concentrated hydrochloric acid (34%) were obtained from El-Nasr Pharmaceutical Co., Cairo, Egypt. Analytical grade of methanol and dimethylformamide (DMF) (BDH Laboratory Supplies, Poole, England) were used.

Preparation of Standard and Sample Solutions

Preparation of standard stock solution

A stock standard solution containing 400 µg/mL of LOR was prepared by dissolving an accurate weight of 20 mg of the drug substance in 20 mL DMF in a 50 mL volumetric flask, then dilution to volume with methanol.

Preparation of Sample Solutions

Tablets sample solution (Xefo® Tablets)

The pharmaceutical preparation assayed in this study is Xefo® tablets (Manufactured by Multi-Apex Pharma, Cairo, Egypt for AUG Pharma, Giza, Egypt under license of NYCOMED, Austria) labeled to contain 8 mg LOR per tablet. Ten tablets were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 20 mg LOR was extracted into 20 mL DMF with the aid of shaking for 30 min then filtered into a 50 mL volumetric flask. The residue was washed with 2×10 mL portions of methanol and washings were added to the filtrate, then the solution was diluted to volume with methanol to reach a final concentration of 400 µg/mL LOR.

Vials sample solution (Xefo® Vials)
The content of one vial, containing 8 mg LOR, was reconstituted with the dilution solvent of the vial. The reconstituted solution was transferred into 10 mL volumetric flask. The vial was washed twice with methanol and washings were added to the reconstituted solution. The solution was diluted to volume with methanol to reach a final concentration of 800 ug/mL LOR.

General Procedure
Construction of calibration graphs
Working standard solutions were prepared by dilution of accurate volumes (0.1-0.6 mL) of the stock standard solution in a set of 10 mL volumetric flasks, and the flasks were completed to volume with 0.1 M HCl to obtain concentrations within the range 4-24 µg/mL LOR. For direct zero-order (^{0}D) spectrophotometric method, absorbance values of the prepared working standard solutions were measured at 373 nm against 0.1 M HCl as blank and plotted versus concentrations to obtain a linear relationship. For the first derivative (^{1}D) spectrophotometric method, the ^{1}D spectra of the working standard solutions were generated from their stored absorbance (zero-order) spectra, and the ^{1}D amplitudes were measured at 406 nm. The absolute values of the measured ^{1}D amplitudes were plotted against the corresponding concentrations to construct the calibration graph.

Procedure for analysis of pharmaceutical preparations
Aliquots of the LOR stock sample solutions were transferred into a series of 10 mL volumetric flasks, then assayed as described under "Construction of calibration graphs". Recovered concentrations for Xefo® tablets and vials were calculated from similarly treated standard solutions.

The standard addition assay was carried out by spiking sample solutions with aliquots of stock standard solutions of LOR to obtain final concentrations within the previously specified range then treated as under "Construction of calibration graphs". Recovered concentrations were calculated by comparing the analyte response with the increment response attained after addition of the standard.

Oxidative degradation of LOR
Preparation of degraded LOR solution
A degraded drug stock solution containing 400 µg/mL LOR was prepared by dissolving an accurate weight of 10 mg of the drug substance in 10 mL DMF in a 25 mL volumetric flask, followed by the addition of 1 mL 50% hydrogen peroxide and heating in a water bath at 80°C for 20 min then dilution to volume with distilled water.

Construction of calibration graph of degraded LOR
Aliquots of the degraded LOR stock solution (0.1-0.6 mL) were accurately transferred into a set of 10 mL volumetric flasks, and the flasks were diluted to volume with 0.1 M HCl to obtain concentrations within the range 4-24 µg/mL (calculated concentrations are corresponding to the intact drug). The absorbance (zero-order) spectra of the prepared degraded LOR solutions were measured against 0.1 M HCl as blank and stored, and then the first derivative (^{1}D) spectra were generated. The ^{1}D amplitudes were measured at 305 nm. The absolute values of the measured ^{1}D amplitudes were plotted against the corresponding concentrations to construct the calibration graph.

Kinetics study
Several degraded drug stock solutions each containing 400 µg/mL LOR were prepared by dissolving accurate weights of 10 mg of the drug substance in 10 mL DMF in a series of 25 mL volumetric flasks, followed by the addition of 1 mL 50% hydrogen peroxide and dilution to volume with distilled water**.** These solutions were subjected to heating at different temperatures (50, 60, 70 and 80°C). Accurate volumes (0.4 mL) of each degraded LOR stock solution were transferred into a series of 10 mL volumetric flasks at 5 min time intervals, then diluted to volume with 0.1 M HCl. The ^{0}D and ^{1}D amplitudes at 373 and 406 nm respectively were measured using 0.1 M HCl as blank, and the percentage remaining concentration of the drug was determined. Data were further processed and degradation kinetics constants were calculated.

RESULTS AND DISCUSSION

Spectral characteristics of LOR and its oxidation product
Initially, the effect of various diluting solvents on the absorption characteristics of LOR was investigated. Diluting solvents studies were 0.1 M HCl, 0.1 M NaOH and methanol. The strong absorption peak of LOR at about 370 nm

showed the highest intensity in presence of 0.1 M HCl, therefore it was adopted as optimum solvent. The characteristic profile of the zero-order absorption spectrum may represent a specific fingerprint useful for drug identification. In particular, the amplitudes at selected wavelengths can be regarded as a suitable parameter for confirmation of identity, purity and stability of the drug. Oxidative forced degradation experiments were carried out on LOR standard solution in order to produce the oxidative degradation products of the drug and test their spectrophotometric behavior using the developed method. Upon heating LOR with 50 % H_2O_2, the yellow colored solution of the drug faded gradually due to its oxidative degradation. Figure 2 represents the absorption spectra of both LOR and its oxidative degradation product in 0.1 M HCl solution. The absorption spectrum of LOR is characterized by a prominent maximum at 373 nm which completely disappeared in the spectrum of the H_2O_2 oxidation-induced degradation product. On the other hand, the absorption spectrum of the oxidative degradation product exhibited considerable UV absorption in the range 200-320 nm with a maximum at 293 nm. Obviously, the intact drug can be accurately measured at its strong absorption peak at 373 nm without any interference from the H_2O_2 oxidation-induced degradant (Figure 2).

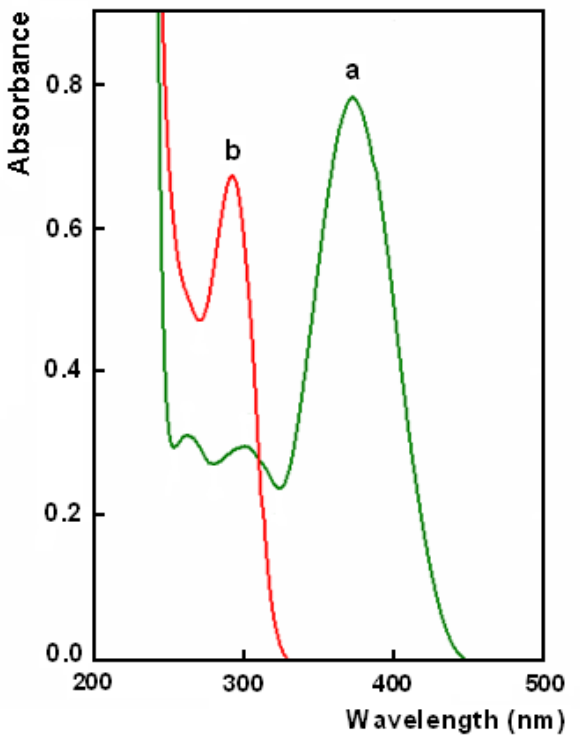

Figure 2: Absorption spectra of 12 µg/mL of both LOR (a) and its oxidative degradation product (b) in 0.1 M HCl

Furthermore, the stored absorption spectra of both the intact drug and its degradant were differentiated to produce the corresponding first-derivative (^{1}D) spectra (Figure 3). Again, LOR was selectively measured by measuring its ^{1}D amplitude at 406 nm where no contribution was found from the oxidation-induced degradant. In addition, the first-derivative (^{1}D) spectra were advantageous as they permitted the determination of the oxidation-induced product by measuring its ^{1}D amplitude at 305 nm which represented a zero crossing for LOR and hence it showed no interference (Figure 3).

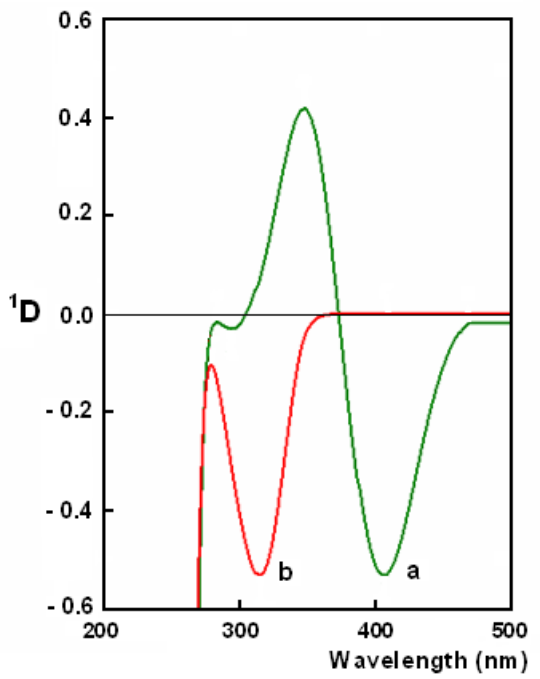

Figure 3: First-derivative (^{1}D) spectra of 12 µg/mL of both LOR (a) and its oxidative degradation product (b) in 0.1 M HCl

Validation of the proposed methods

Linearity and concentration ranges

The linearity of the proposed methods was evaluated by analyzing a series of different concentrations of LOR and its degradation product. According to the ICH guidelines [10], a minimum of 5 concentrations is recommended for establishment of linearity. The linear regression equations were generated by least squares treatment of the calibration data. Under the experimental conditions described above, the measured spectrophotometric ^{0}D amplitude at 373 nm, ^{1}D amplitude at 406 nm for LOR and ^{1}D amplitude for its oxidation product at 305 nm were found to be proportional to concentrations of the analytes (Table 1). Slopes (b), intercepts (a), correlation coefficients (r), standard deviations of the intercept (S_a), slope (S_b) and residuals ($S_{y/x}$) are given in Table 1. In addition to the correlation coefficient values which were not less than 0.9996, linearity was further evaluated by calculation of the RSD % of the slope (S_b%) for the proposed methods and they were less than 1.4%. Moreover, the ANOVA tests for the regression lines reveal high F values and low significance F (Table 1).

Table 1. Analytical parameters for the determination of LOR and its oxidative degradation product using the proposed spectrophotometric methods

Parameter	Intact LOR		Degraded LOR
	^{0}D at 373 nm	**^{1}D at 406 nm**	**^{1}D at 305 nm**
Concentration range (µg/mL)	4 - 24	4 - 24	4 - 24 (corresponding to the intact drug)
Intercept (a)	-0.0069	0.0024	0.0083
S_a	0.0121	0.0091	0.0076
Slope (b)	0.0644	0.0433	0.0377
S_b	0.0008	0.0006	0.0005
RSD% of the slope (S_b%)	1.24	1.39	1.33
Correlation coefficient (r)	0.99971	0.99964	0.99966
$S_{y/x}$	0.0129	0.0098	0.0082
F value	6919	5503	5924
Significant F	1.25×10^{-7}	1.98×10^{-7}	1.71×10^{-7}
LOD (µg/mL)	0.62	0.69	0.67
LOQ (µg/mL)	1.88	2.10	2.02

Limits of detection (LOD) and quantitation (LOQ)

According to the ICH recommendations [10], the approach based on the standard deviation of the response and the slope was used to determine the detection and quantitation limits. LOD was defined as 3.3σ/S where σ is the standard deviation of the intercept of regression line and S is the calibration graph slope. LOQ was defined as 10σ/S. The values were calculated and given in Table 1.

Accuracy and Precision

The accuracy and within-day precision (repeatability, intra-day precision) for the proposed zero-order (^{0}D) and first derivative (^{1}D) spectrophotometric methods were studied at three concentration levels of LOR within its linearity range (12, 16 and 20 µg/mL) using three replicate determinations for each concentration within one day. Similarly, the accuracy and between-day (inter-day) precision were tested by analyzing the same three concentrations using three replicate determinations repeated on three days. Recoveries were calculated using the corresponding regression equations and they were satisfactory. The percentage relative standard deviation (RSD %) and percentage relative error (E_r %) were less than 2 % proving the high precision and accuracy of the developed methods for the estimation of LOR in bulk form (Table 2).

Table 2. Precision and accuracy for the determination of LOR in bulk form using the proposed spectrophotometric methods

	Methods	Nominal value (µg/mL)	Found ± SD* (µg/mL)	RSD(%)	E_r(%)
Within-day	^{0}D at 373 nm	12	12.04 ± 0.10	0.83	0.33
		16	16.16 ± 0.08	0.50	1.00
		20	20.25 ± 0.12	0.59	1.25
	^{1}D at 406 nm	12	12.11 ± 0.11	0.91	0.92
		16	16.31 ± 0.18	1.10	1.94
		20	20.31 ± 0.17	0.84	1.55
Between-day	^{0}D at 373 nm	12	12.03 ± 0.14	1.16	0.25
		16	16.04 ± 0.22	1.37	0.25
		20	20.01 ± 0.19	0.95	0.05
	^{1}D at 406 nm	12	11.96 ± 0.19	1.59	-0.33
		16	16.14 ± 0.24	1.49	0.88
		20	20.10 ± 0.30	1.49	0.50

* *Mean ± standard deviation for three determinations.*

In addition, precision and accuracy of the proposed first derivative (^{1}D) spectrophotometric determination of oxidized LOR were evaluated. The accuracy and within-day precision were studied at three concentration levels of degraded LOR within its linearity range (12, 16 and 20 µg/mL) using three replicate determinations for each concentration within one day. The accuracy and between-day precision were tested by analyzing the same three concentrations using three replicate determinations repeated on three days. Again, recoveries, RSD % and E_r % were satisfactory as shown in Table 3.

Table 3. Precision and accuracy for the determination of degraded LOR using the proposed first derivative (^{1}D) spectrophotometric method at 305 nm

	Nominal value (µg/mL)	Found ± SD* (µg/mL)	RSD(%)	E_r(%)
Within-day	12	11.99 ± 0.03	0.25	-0.01
	16	16.07 ± 0.17	1.06	0.44
	20	19.97 ± 0.09	0.45	-0.15
Between-day	12	11.98 ± 0.14	1.17	-0.17
	16	15.96 ± 0.28	1.75	-0.25
	20	20.14 ± 0.35	1.74	0.70

* *Mean ± standard deviation for three determinations.*

Selectivity

The selectivity of the proposed methods was evaluated by preparing different mixtures of LOR and its oxidative derivative within the previously specified linearity range (4-24 µg/mL). The ratio of LOR to its oxidative derivative ranged from 1:2, 1:1 to 2:1. The synthetic mixtures were analyzed according to the previously described procedures. Satisfactory recovered concentrations, RSD % and E_r % values were obtained by employing the first derivative (^{1}D) measurements at 406 and 305 nm for LOR and its oxidative degradant respectively (Table 4). The results confirm the high selectivity, accuracy and precision of the proposed stability indicating methods for the simultaneous determination of the intact drug and its oxidative degradation product.

Table 4. Analysis of laboratory-prepared mixtures of LOR and its oxidative degradation product using the proposed first derivative (^{1}D) spectrophotometric methods

Nominal value (µg/mL)		Found ± SD* (µg/mL)		RSD(%)		Er(%)	
LOR	Degraded LOR	LOR	Degraded LOR	LOR	Degraded LOR	LOR	Degraded LOR
8	8	7.97 ± 0.11	7.98 ± 0.08	1.38	1.00	-0.37	-0.25
12	12	12.09 ± 0.09	11.99 ± 0.11	0.74	0.92	0.75	-0.08
16	16	16.15 ± 0.12	16.23 ± 0.14	0.74	0.86	0.94	1.44
4	8	4.03 ± 0.01	7.99 ± 0.14	0.25	1.75	0.75	-0.12
8	16	8.01 ± 0.12	16.18 ± 0.09	1.50	0.56	0.13	1.13
8	4	8.03 ± 0.14	3.91 ± 0.01	1.74	0.26	0.38	-2.25
16	8	15.96 ± 0.26	8.04 ± 0.12	1.63	1.49	-0.25	0.50

* *Mean ± standard deviation for five determinations.*

Stability

The stability of the working solutions in 0.1 M HCl at room temperature was examined. No spectrophotometric changes were observed within 30 min after measurement. The stock standard solution of LOR and the degraded drug stock solution were stable for at least 1 week upon storage refrigerated at 4 ºC.

Assay of pharmaceutical dosage forms

The developed spectrophotometric procedures were applied for the assay of LOR in its tablets and vials dosage forms available in the local market (Xefo® tablets and vials). Recoveries were calculated for tablets and vials using both external standard and standard addition methods. The assay results revealed satisfactory accuracy and precision as indicated from % recovery, SD and RSD% values using both direct zero-order (^{0}D) and first derivative (^{1}D) spectrophotometric methods. This is illustrated in Table 5. The good recoveries indicated the absence of any interference from commonly encountered inactive ingredients that may be present in the pharmaceutical preparations.

Furthermore, a reported reversed-phase HPLC method was adopted for the estimation of LOR in its commercial products [4]. The recoveries obtained from the proposed methods were statistically compared with those of the reported method using the one-way analysis of variance (Single factor ANOVA) [11]. The ANOVA test is useful for comparing recovery data obtained from more than two methods of analysis. The calculated F-values (2.022 and 1.504 for tablets and vials respectively) did not exceed the critical value (3.885) indicating that there were no significant differences between the proposed methods together with the reported method (Table 5). It is evident from these results that the proposed simple spectrophotometric methods are applicable to the assay of LOR in different commercial pharmaceutical preparations with a satisfactory level of accuracy and precision.

Table 5. Application of the proposed spectrophotometric methods for the determination of LOR in its commercial dosage forms

Analysis of Xefo® Tablets			
Using external standard method			
Parameter	**^{0}D at 373 nm**	**^{1}D at 406 nm**	**Reported method [4]**
% Recovery ± SD*	100.28 ± 0.94	100.54 ± 0.78	99.46 ± 0.93
RSD%	0.94	0.78	0.94
ANOVA (single factor): F = 2.022062 , F (critical) = 3.885294			
Using standard addition method			
Parameter	**^{0}D at 373 nm**	**^{1}D at 406 nm**	
%Recovery ± SD*	99.62 ± 1.39	99.13 ± 1.06	
RSD%	1.40	1.07	
Analysis of Xefo® Vials			
Using external standard method			
Parameter	**^{0}D at 373 nm**	**^{1}D at 406 nm**	**Reported method [4]**
% Recovery ± SD*	100.71 ± 1.06	99.81 ± 1.36	99.46 ± 0.93
RSD%	1.05	1.36	0.94
ANOVA (single factor): F = 1.504188 , F (critical) = 3.885294			
Using standard addition method			
Parameter	**^{0}D at 373 nm**	**^{1}D at 406 nm**	
%Recovery ± SD*	101.18 ± 0.71	101.21 ± 1.48	
RSD%	0.70	1.46	

* *Mean ± standard deviation for five determinations.*

Degradation kinetics

Kinetics experiments of the oxidative degradation of LOR were carried out using 1 mL 50% H_2O_2 at different temperatures (50, 60, 70 and 80°C). A regular decrease in the concentration of LOR with increasing time intervals was observed when measuring the absorbance at 373 nm and the first derivative (^{1}D) amplitude at 406 nm. While an increase in the trough at 305 nm in the first derivative (^{1}D) spectra was noticed indicating the formation of the oxidative degradation product. This is demonstrated in Figure 4 which represents the recorded spectra at different time intervals at 60ºC. The values obtained from calculations of the oxidation kinetics using the data of absorbance at 373 nm and the first-derivative at 406 nm were similar; therefore we selected the absorbance data to represent the kinetics study of LOR.

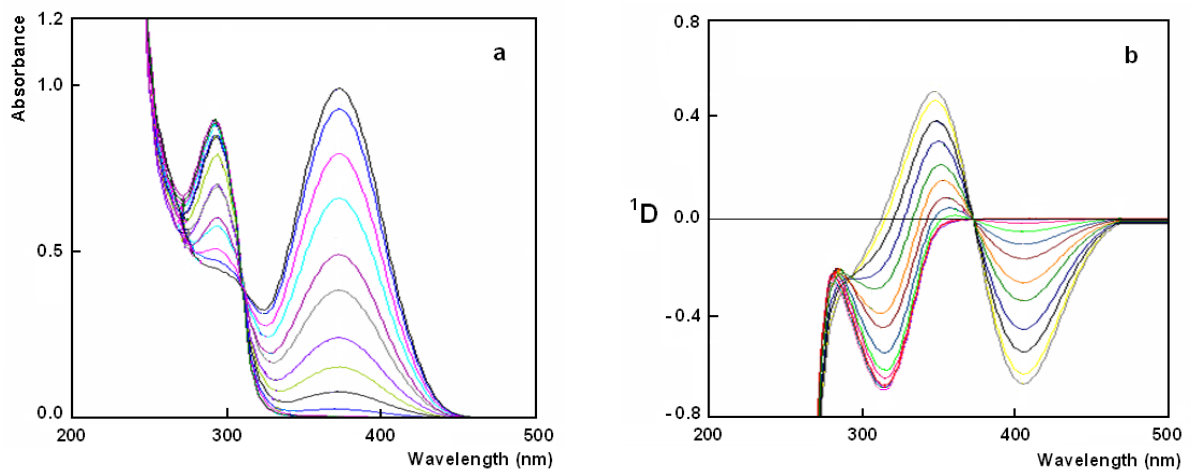

Figure 4: Absorbance (ºD) (a) and first-order derivative (^{1}D) (b) spectra for the kinetic study of 16 µg/mL LOR in 50% H_2O_2 at 60ºC

At the selected temperatures (50, 60, 70 and 80°C), the degradation process followed pseudo-first order kinetics (Figure 5). At each selected temperature, log C% values were plotted against time. From the slopes of obtained curves, it was possible to calculate the corresponding degradation rate constants (K) and half lives (t½) at each temperature, based on the following equations [12, 13]:

$$\log C\% = \log C_0\% - Kt/2.303 \quad (1)$$

$$t½ = 0.693/K \quad (2)$$

where the slope of the best-fit line = –K/2.303, C% and C_0% are the percentage drug concentrations measured at a given time t and the initial concentration respectively, K is the rate constant and t½ is the half life at each temperature. These values are gathered in Table 6.

Arrhenius equation gives the relationship between the rate constant K of a chemical reaction and the absolute temperature T, where A is the pre-exponential factor (also called frequency factor), E_a is the activation energy (kcal / mol), T is the absolute temperature (K), and R is the universal gas constant (1.987 cal / deg.mol) [14].

$$K = Ae^{-Ea/RT} \quad (3)$$

By taking the log of both sides the following equation was obtained

$$\log K = \log A - E_a / 2.303\ RT \quad (4)$$

Data obtained from the previous kinetics treatment were subjected to fitting in Arrhenius equation (4).

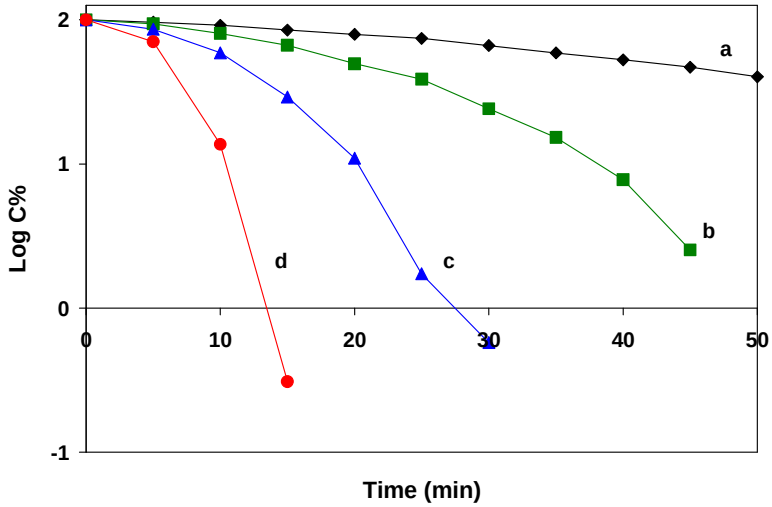

Figure 5: Pseudo-first-order plots for the percent remaining concentrations of LOR upon oxidation with H_2O_2 at various temperatures (50 (a), 60 (b), 70 (c) and 80°C (d)) versus time

Table 6. Pseudo first-order rate constants (K) and half lives (t½) for the oxidative degradation of LOR using 50% H_2O_2

^{0}D at 373 nm		
Temperature (°C)	**K (min^{-1})**	**t½ (min)**
80	0.3797	1.83
70	0.1784	3.89
60	0.0753	9.20
50	0.0182	38.08
25	0.0011	630.00 (10.50 hours)
^{1}D at 406 nm		
Temperature (°C)	**K (min^{-1})**	**t½ (min)**
80	0.3807	1.82
70	0.1949	3.56
60	0.0779	8.90
50	0.0182	38.08
25	0.0011	630.00 (10.50 hours)

Log K values were plotted against the reciprocals of the absolute temperature (1/T) to construct the Arrhenius plot [12, 13, 15]. Arrhenius equation was found to be:

$\log K = 13.672 - (4956.38 / T)$ (correlation coefficient r = 0.99169) (5)

From the slope of equation (5) the activation energy was calculated to be 22.68 kcal/mol which is the minimum energy required to start the reaction.

Arrhenius plot is presented in Figure 6. The K_{25} is used as a measure of the stability of the drug at room temperature. The log K_{25} value can be obtained by extrapolation on the Arrhenius plot as illustrated in Figure 6, however, for more accurate result, it was calculated from equation (5) where the log $K_{25} = -2.96$, and therefore K_{25} had the value of 0.0011 min^{-1}. Accordingly, it was found that half life-time (t½) of LOR in 50% H_2O_2 at room temperature is about 10.5 hrs (Table 6). It is clear from these results that LOR can be considered relatively stable at room

temperature even in a medium containing 50% H_2O_2. Again all the previously mentioned kinetics calculations were repeated using the first-order derivative (^1D) data giving the same results (Table 6).

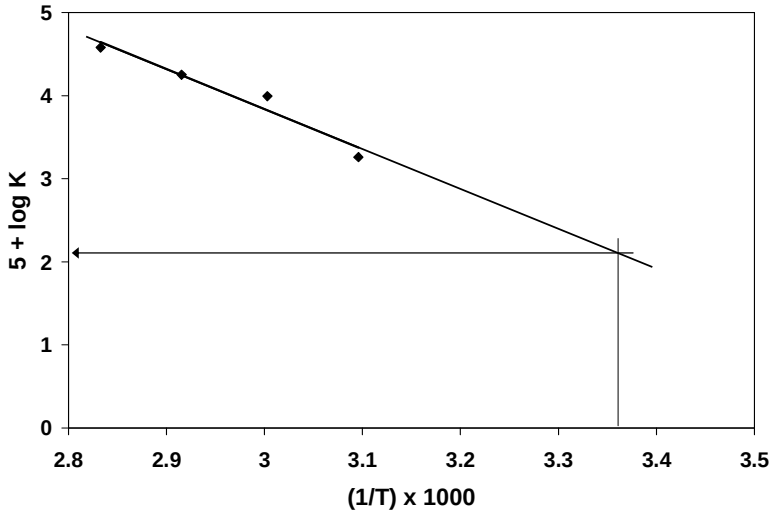

Figure 6: Arrhenius plot for the degradation of LOR in the presence of 50% H_2O_2

CONCLUSION

This study described simple, stability-indicating and reliable spectrophotometric procedures for the assay of LOR in pure form as well as in its pharmaceutical dosage forms (tablets and vials). The proposed methods are based on the simple measurement of the drug absorbance at its peak at 373 nm and measurement of the first-order derivative (^1D) amplitude at 406 nm. Both methods provide accurate and reproducible results for the determination of LOR in pharmaceutical preparations without any interference from excipients. In addition, the first-order derivative (^1D) spectra were exploited for the selective measurement of the oxidation-induced degradation product at 305 nm which represents a zero crossing for the intact drug. To our present knowledge, no reports have been found describing a spectrophotometric method for the stability indicating simultaneous determination of LOR and its oxidation-induced degradation product. Furthermore, the results showed the suitability of both ^0D and ^1D methods for kinetics study of the oxidative degradation of LOR. The degradation rate constant and half-life of LOR at room temperature were calculated. Compared with the previously reported stability-indicating chromatographic methods, spectrophotometric methods have advantages of low cost, rapid measurements and simplicity. The developed methods do not require any derivatization reactions, elaborate treatment, sophisticated experimental setup or consumption of organic solvents usually associated with HPLC and HPTLC methods of analysis. In addition, the proposed methods used only a spectrophotometer which is convenient and readily available instrument in all quality control laboratories.

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