Original Article

A validated stability-indicating high performance liquid chromatographic method for moxifloxacin hydrochloride and ketorolac tromethamine eye drops and its application in pH dependent degradation kinetics

Abstract

Background and Aim: A fixed dose combination of moxifloxacin hydrochloride and ketorolac tromethamine is used in ratio of 1:1 as eye drops for the treatment of the reduction of post operative inflammatory conditions of the eye. A simple, precise, and accurate High Performance Liquid Chromatographic (HPLC) method was developed and validated for determination of moxifloxacin hydrochloride and ketorolac tromethamine in eye drops. **Materials and Methods:** Isocratic HPLC separation was achieved on a ACE C_{18} column (C_{18} (5 μm, 150 mm × 4.6 mm, i.d.)) using the mobile phase 10 mM potassium di-hydrogen phosphate buffer pH 4.6-Acetonitrile (75:25 v/v) at a flow rate of 1.0 mL/min. The detection was performed at 307 nm. Drugs were subjected to acid, alkali and neutral hydrolysis, oxidation and photo degradation. Moreover, the proposed HPLC method was utilized to investigate the pH dependent degradation kinetics of moxifloxacin hydrochloride and ketorolac tromethamine in buffer solutions at different pH values like 2.0, 6.8 and 9.0. **Results and Conclusion:** The retention time (t_R) of moxifloxacin hydrochloride and ketorolac tromethamine were 3.81±0.01 and 8.82±0.02 min, respectively. The method was linear in the concentration range of 2-20 μg/mL each for moxifloxacin hydrochloride and ketorolac tromethamine with a correlation coefficient of 0.9996 and 0.9999, respectively. The method was validated for linearity, precision, accuracy, robustness, specificity, limit of detection and limit of quantitation. The drugs could be effectively separated from different degradation products and hence the method can be used for stability analysis. Different kinetics parameters like apparent first-order rate constant, half-life and t_{90} (time for 90% potency left) were calculated.

Key words:
High performance liquid chromatography, ketorolac tromethamine, method validation, moxifloxacin hydrochloride, pH dependent degradation kinetics, stability-indicating method

Introduction

Moxifloxacin hydrochloride is 1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4a*S*, 7a*S*)-octahydro-6*H*-pyrrolo[3, 4*b*] pyridin-6-yl]-4-oxo-1, 4-dihydroquinoline-3-carboxylic acid hydrochloride[1] [Figure 1]. It is a newer fluoroquinolone drug indicated for the treatment of bacterial infections. Moxifloxacin hydrochloride is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV, enzymes necessary to separate bacterial DNA, thereby inhibiting cell replication.[2-4] Ketorolac tromethamine is 2-Amino-2-(hydroxymethyl) propane-1, 3-diol (1*RS*)-5-benzoyl-2, 3-dihydro-1*H*-pyrrolizine-1-carboxylate.[1] [Figure 2] It acts by blocking prostaglandin synthesis by inhibiting cyclooxygenase 1 and 2. Prostaglandins have been shown to

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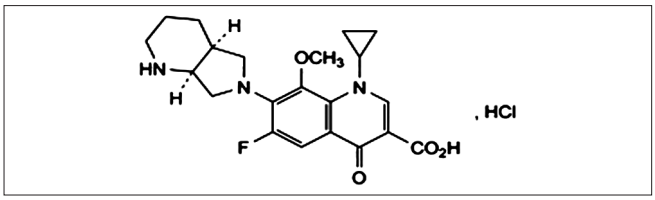

Figure 1: Moxifloxacin hydrochloride

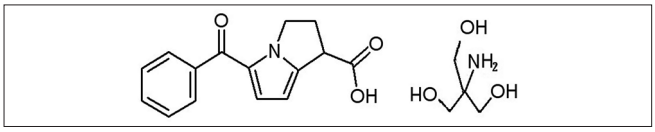

Figure 2: Ketorolac tromethamine

be mediators of certain kinds of intraocular inflammation and also produce disruption of the blood-aqueous humour barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.[5,6] A detailed survey of analytical literature for moxifloxacin hydrochloride revealed several methods based on varied techniques, viz, HPLC,[7-10] Spectrophotometry,[11,12] High-Performance Thin-Layer Chromatography (HPTLC).[13,14] Similarly, a survey of the analytical literature for ketorolac tromethamine revealed several methods like HPLC,[15,16] HPTLC,[17,18] LC/MS/MS (Liquid Chromatography-Mass Spectrometry-Tandem Mass Spectrometry),[19] capillary electro chromatography.[20] The published literature revealed spectrophotometric determination of moxifloxacin hydrochloride and ketorolac tromethamine in combination.[21,22] According to detailed survey of analytical literature none of the reported analytical procedures describes a simple and satisfactory HPLC method for simultaneous determination of moxifloxacin hydrochloride and ketorolac tromethamine in their combined dosage forms. Hence, the objective of this work was to develop simple, precise, and rapid HPLC method for combination drug products containing moxifloxacin and ketorolac tromethamine.

Materials and Methods

Instrumentation

Liquid chromatographic Shimadzu (LC-2010C_{HT}) system manufactured by Shimadzu, Kyoto, Japan, equipped with auto-sampler, UV and Photodiode Array (PDA) detector and Rheodyne injector and ACE C_{18} column (150 × 4.6 mm^2 i.d., 5 µm particle size) was used. An analytical balance (Acculab ALC-210.4, Huntingdon Valley, PA); pH meter (Thermo Electron Corp., Pune India); and sonicator (EN 30 US Enertech Fast Clean, Mumbai, India) were used.

Materials

Moxifloxacin hydrochloride and ketorolac tromethamine bulk powder were gifted by cadila health Care. Ltd. (Ahmadabad, India) and torrent pharma. Ltd. (Gandhinagar, India), respectively. The commercial Eye drops (MOXICIP-KT, 0.5 w/v% of moxifloxacin hydrochloride and 0.5 w/v% of ketorolac tromethamine) was procured from the local market. Acetonitrile (HPLC grade, Finar Chemicals Ltd., Ahmadabad, India); Water (HPLC grade, Finar Chemicals Pvt. Ltd, Ahmadabad, India); and nylon filter (Millipore Ltd., Bangalore, India) were used.

Preparation of standard stock solution

Accurately weighed quantity of 10 mg of moxifloxacin hydrochloride and ketorolac tromethamine were transferred into a 100 mL volumetric flask and dissolved in water to obtain the standard stock solution 100 µg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine.

Preparation of sample solution

An aliquot of Ophthalmic formulation (MOXICIP-KT, 0.5 w/v% moxifloxacin hydrochloride and 0.5 w/v% ketorolac tromethamine) 0.2 mL was taken in 100 mL volumetric flask and diluted to mark with water to yield 10 µg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine.

Chromatographic condition

The mobile phase was chosen after several trials with methanol, acetonitrile, water, and buffer solutions in various proportions and at different pH values. A mobile phase consisting of acetonitrile: Phosphate buffer pH 4.6 (25:75 v/v) was selected to achieve good separation and resolution. A flow rate of 1 mL/min gave an optimal signal-to-noise ratio with a reasonable separation time and run time was 13 min. Using a reversed-phase C_{18} column, the retention times for moxifloxacin hydrochloride and ketorolac tromethamine were observed to be 3.81±0.01 and 8.82±0.02 min, respectively. The wavelength was fixed at isosbetic point of 307 nm which gave good absorbance both for moxifloxacin hydrochloride and ketorolac tromethamine.

Method validation

This optimized HPLC method was validated for the parameters listed in the International Conference on Harmonization (ICH Q2 (R1)) guidelines.[23]

Linearity

Aliquots of 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, and 2.0 mL of the stock solution of moxifloxacin hydrochloride and ketorolac tromethamine were transferred into a series of 10 mL volumetric flasks and diluted to the mark with water to yield 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 µg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. The calibration curve was constructed by plotting peak areas versus concentrations, and the regression equation was calculated. Each response was an average of five determinations.

Precision

Intraday and interday precision were evaluated by determining the corresponding responses of standard solutions in triplicate on the same day (repeatability) and on different days (intermediate precision) at three concentrations of 2, 10, and 20 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. The results were reported in terms of % RSD (Relative standard deviation).

Accuracy

Accuracy was determined by calculating recovery of moxifloxacin hydrochloride and ketorolac tromethamine by the standard addition method. Known amounts of standard solutions of moxifloxacin hydrochloride (2.5, 5, 7.5 μg/mL) and ketorolac tromethamine (2.5, 5, 7.5 μg/mL) were added to a prequantified test solutions 10 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. Each solution was injected in triplicate, and the recovery was calculated by measuring peak areas and fitting these values into the regression equation of the calibration curve.

Limit of detection and limit of quantitation

LOD and LOQ were obtained by calculating using the Standard formula as per the ICH guidelines,

$LOD=3.3 \times (\sigma/S)$, $LOQ=10 \times (\sigma/S)$.

Robustness

The robustness study was performed to evaluate the influence of small but deliberate variations in the chromatographic conditions. The robustness was checked by changing the mobile phase flow rate (±0.1 mL/min); composition (±5% in organic phase); pH (±0.2 units); and temperature (±5°C).

System suitability test parameters

System suitability parameters were verified with respect to number of theoretical plates, asymmetric factor, resolution, capacity factor, and % RSD of six replicate of injection of moxifloxacin hydrochloride (10 μg/ml) and ketorolac tromethamine (10 μg/ml).

Specificity

The specificity of the method was established through the study of resolution factor of the drug peak from the nearest peak and peak purity data of the analyte peaks in forced degradation samples.

Forced degradation studies

Acid hydrolysis

Ten milliliter of a mixture of solution containing 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine in 1 M HCl was heated at 80°C for 6 h, then neutralized with 1 N NaOH after cooling and diluted with water to give 100 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. This acid degradation sample was analyzed under the optimized chromatographic conditions.

Alkali hydrolysis

Ten milliliter of a mixture of solution containing 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine in 2 N NaOH was heated at 80°C for 4 h and then neutralized with 2 N HCL after cooling and diluted with water to 100 mL to give 100 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. This alkali degradation sample was analyzed under the optimized chromatographic conditions.

Oxidative degradation

Ten milliliter of a mixture of solution containing 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine in 30% H_2O_2 was stored at room temperature for 6 h and diluted with water to 100 mL to give 100 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. This oxidative degradation sample was analyzed under the optimized chromatographic conditions.

Neutral hydrolysis

Ten milliliter of a mixture of solution containing 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine in water was heated at 80°C for 12 h and diluted with water to 100 mL to give 100 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. This thermal and aqueous degradation sample was analyzed under the optimized chromatographic conditions.

Photo degradation

Ten milliliter of a mixture of solution containing 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine in water was placed in photo-stability chamber (UV-light) for 12 h and diluted with water to 100 mL to give 100 μg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. This photo degradation sample was analyzed under the optimized chromatographic conditions.

pH dependent degradation kinetics

The pH of 2.0, 6.8, and 9.0 were used for measurement of pH degradation profile of moxifloxacin hydrochloride and ketorolac tromethamine. Accurately weighed 100 mg each of moxifloxacin hydrochloride and ketorolac tromethamine were transferred into 100 mL volumetric flask and diluted to volume with respective buffer solutions prepared as per Indian Pharmacopoeia[24] to give 1 mg/mL each of moxifloxacin hydrochloride and ketorolac tromethamine. These solutions were kept for the reflux at 60°C for different time intervals (up to 48 h). From the different pH containing stock solution (1000 μg/mL) transfer 1 mL into 10 mL volumetric flask at the specified time interval

and dilute up to mark with water (100 µg/mL) and store these solutions into refrigerator (2-8°C). Inject the stored solutions under the optimized chromatographic conditions. The concentration of remaining moxifloxacin hydrochloride and ketorolac tromethamine were calculated at each pH value and time interval.

Results and Discussion

Optimized chromatographic conditions

Different mobile phases were tried to separate moxifloxacin hydrochloride and ketorolac tromethamine. The optimum results were obtained with mobile phase consisting of acetonitrile: Phosphate buffer pH 4.6 (25:75 v/v). The t_R values of moxifloxacin hydrochloride and ketorolac tromethamine were observed at 3.81±0.01 and 8.82±0.02 min, respectively. The representive chromatogram is given in Figure 3.

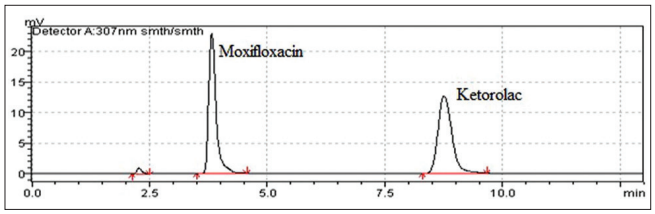

Figure 3: HPLC chromatogram of moxifloxacin (10 µg/mL) and ketorolac (10 µg/mL): Peak of moxifloxacin (t_R = 3.8) and ketorolac (t_R = 8.8)

Table 1: Linearity data for moxifloxacin hydrochloride and ketorolac tromethamine

Moxifloxacin hydrochloride		Ketorolac tromethamine	
Concentration (µg/mL)	Area*±SD	Concentration (µg/mL)	Area*±SD
2	51170±125.3	2	50425±169.19
4	101528±161.571	4	106243±270.54
6	154145±264.587	6	153740±229.14
8	214626±222.83	8	207594±559.40
10	268233±844.656	10	258892±611.74
12	330655±639.114	12	310474±607.45
14	395846±864.255	14	358228±373.55
16	451848±595.128	16	412785±648.15
18	518500±808.967	18	467216±980.82
20	572571±563.025	20	516047±969.44

*Average of five determinations and SD is standard deviation

Linearity

The response for the drugs was found to be linear in the concentration range of 2-20 µg/mL each for moxifloxacin hydrochloride and ketorolac tromethamine with correlation coefficient of 0.9996 and 0.9999, respectively. The linear regression equation obtained were y=29412x-17621 and y=25806x+293.8 for moxifloxacin hydrochloride and ketorolac tromethamine, respectively [Table 1].

Precision

The % RSD values for intraday precision study were found to be not more than 0.20% and 0.22% for moxifloxacin hydrochloride and ketorolac tromethamine, respectively, whereas % RSD values for interday precision were found to be not more than 0.25% and 0.29% for moxifloxacin hydrochloride and ketorolac tromethamine, respectively, thus confirming precision of the method [Table 2].

Accuracy

Excellent recoveries were obtained at each level of added concentrations of 25%, 50%, 75% (*n*=3). The result obtained indicated the mean recovery of 98.79-101.22% for moxifloxacin hydrochloride and 99.60-101.01% for ketorolac tromethamine [Table 3].

Limit of detection

The LOD was found to be 0.014 µg/mL and 0.021 µg/mL for moxifloxacin hydrochloride and ketorolac tromethamine, respectively [Table 4].

Limit of quantitation

The LOQ was found to be 0.042 µg/mL and 0.065 µg/mL for moxifloxacin hydrochloride and ketorolac tromethamine, respectively [Table 4].

Robustness

There were no significant differences between results obtained by applying the analytical method under established and varied conditions proving the robustness of the method [Table 5].

System suitability test parameters

The system suitability test parameters like number of theoretical plates, asymmetric factor, resolution, and capacity factor are listed in Table 6.

Table 2: Precision data for moxifloxacin hydrochloride and ketorolac tromethamine

Concentration µg/mL		Intraday precision area* ± % RSD		Interday precision area* ± % RSD	
Moxifloxacin hydrochloride	Ketorolac tromethamine	Moxifloxacin hydrochloride	Ketorolac tromethamine	Moxifloxacin hydrochloride	Ketorolac tromethamine
2	2	44097±0.15	50817±0.12	40620±0.24	49616±0.24
10	10	274371±0.20	256917±0.22	273200±0.22	255523±0.20
20	20	571165±0.13	509388±0.14	568290±0.25	501778±0.29

*Average of three determination and % RSD is relative standard deviation

Table 3: Accuracy data for analysis of moxifloxacin hydrochloride and ketorolac tromethamine

% Addition	Amt of test solution		Amt of std added		Amt recovered		% Recovery*	
	MOX	KETO	MOX	KETO	MOX	KETO	MOX	KETO
–	10	10	–	–	–	–	–	–
25	10	10	2.5	2.5	2.48	2.49	99.43	99.60
50	10	10	5	5	5.06	5.02	101.22	100.42
75	10	10	7.5	7.5	7.40	7.57	98.79	101.01

MOX – Moxifloxacin hydrochloride; KETO – Ketorolac tromethamine; *Average of three determinations

Specificity

The specificity of the method was proved by checking the peak purity of both analyte peaks in forced degradation samples which were close to 1.0 [Figure 4].

Formulation analysis

In the sample of moxifloxacin hydrochloride and ketorolac tromethamine eye drops (0.5% W/V of moxifloxacin hydrochloride and 0.5% of ketorolac tromethamine) content of moxifloxacin hydrochloride was found to be 98.46±0.39% and that of ketorolac tromethamine was found to be 101.11±0.28% [Table 7].

Table 4: Summary of validation parameters of moxifloxacin hydrochloride and ketorolac tromethamine

Validation parameter	Moxifloxacin hydrochloride	Ketorolac tromethamine
Regression equation	y=29412x–17621	y=25806x+293.8
Linearity	0.9999	0.9998
Precision (% R.S.D)		
1 Intraday (%)	0.13-0.20	0.14-0.22
2 Interday (%)	0.22-0.25	0.20-0.29
Recovery (%)	98.79-101.22	99.60-101.01
LOD	0.014 μg/mL	0.021 μg/Ml
LOQ	0.044 μg/mL	0.065 μg/mL

LOD – Limit of detection; LOQ – Limit of quantitation

Table 5: Robustness data of moxifloxacin hydrochloride and ketorolac tromethamine

Condition	Variation	Moxifloxacin hydrochloride		Ketorolac tromethamine	
		% Assay	% RSD	% Assay	% RSD
As such	-	98.46		101.11	
Temp.(30±5°C)	35°C	98.42		101.12	
	25°C	98.58		102.86	
Flow rate (1±0.1 mL/min)	1.1 mL/min	97.85		101.85	
	0.9 mL/min	99.14		102.15	
Organic phase modifier (25±5%)	27:73 (V/V)	98.72	0.69	101.15	0.84
	23:77 (V/V)	99.02		103.59	
pH (4.6±0.2)	pH 4.8	100.22		102.53	
	pH 4.4	98.88		102.85	

RSD – Relative standard deviation

Table 6: System suitability parameters of moxifloxacin hydrochloride and ketorolac tromethamine

Parameter	Moxifloxacin hydrochloride mean±SD, (*n*=6)	Ketorolac tromethamine mean±SD, (*n*=6)
Retention time	3.9±0.012	8.8±0.089
Theoretical plates	3076±12.22	4474±18.23
Tailing factor	1.41±0.01	1.12±0.02
Resolution	6.24±0.04	12.45±0.06
Capacity factor	3.5±0.2	5.3±0.1
% RSD	0.75	0.89

Table 7: Analysis of market formulation of moxifloxacin hydrochloride and ketorolac tromethamine

	Moxifloxacin hydrochloride	Ketorolac tromethamine
Lable claim (% W/V)	0.5 % W/V	0.5 % W/V
Drug content (%) ±S.D	98.46±0.38	101.11±0.28
% RSD	0.39	0.28

Forced degradation study

Acid hydrolysis

In the acid degradation study, moxifloxacin hydrochloride showed one additional peak (t_R=2.9) and ketorolac tromethamine showed one additional peak (t_R=6.9) [Figure 5].

Alkali hydrolysis

In the alkali degradation study, moxifloxacin hydrochloride showed one additional peak (t_R=2.7). However, ketorolac tromethamine showed two additional peaks (t_R=5.3 and 6.3) [Figure 6].

Oxidative degradation

In the oxidative degradation study, moxifloxacin hydrochloride showed one additional peak (t_R=2.9) and ketorolac tromethamine showed one additional peak (t_R=6.9) [Figure 7].

Neutral hydrolysis

The thermal and aqueous degradation sample showed no additional peaks [Figure 8].

Photo degradation

In the photo degradation study, moxifloxacin hydrochloride showed no additional peaks. However, ketorolac tromethamine show one additional peak (t_R=13.0) [Figure 9].

Discussion of degradation studies of moxifloxacin hydrochloride and ketorolac tromethamine

Forced degradation studies of moxifloxacin hydrochloride and ketorolac tromethamine mixture were carried out under various stress conditions. Percentage degradation of moxifloxacin hydrochloride and ketorolac tromethamine under various stress conditions was calculated and listed in Table 8. Degradation results indicated that moxifloxacin hydrochloride degraded significantly under acidic and oxidative conditions

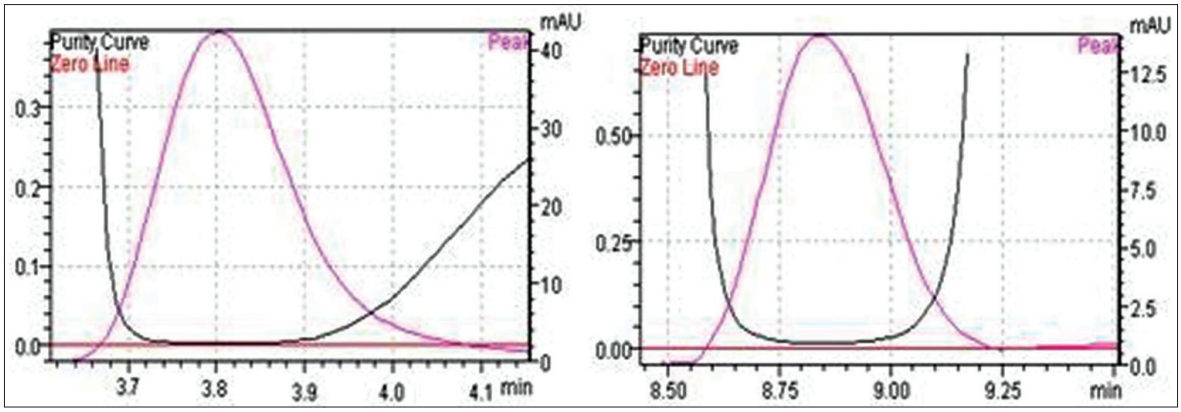

Figure 4: Peak purity spectra of moxifloxacin (a) and ketorolac (b)

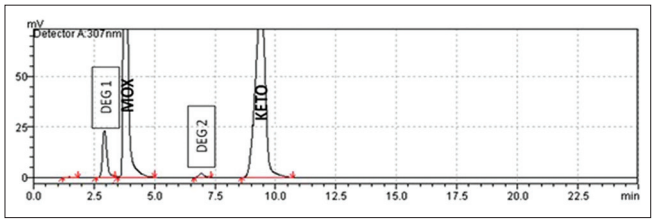

Figure 5: Chromatogram for acid hydrolysis of moxifloxacin, ketorolac and its degradants: degrade 1 (t_R= 2.9), degrade 2 (t_R= 6.9)

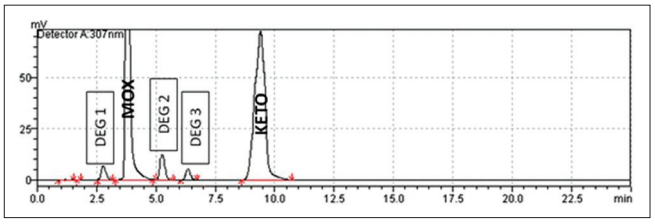

Figure 6: Chromatogram for alkali hydrolysis of moxifloxacin, ketorolac and its degradants: degrade 1 (t_R= 2.7), degrade 2 (t_R= 5.3), degrade 3 (t_R= 6.3)

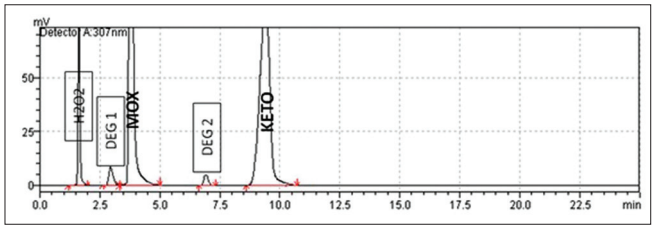

Figure 7: Chromatogram for oxidative degradation of moxifloxacin, ketorolac and its degradants: degrade 1 (t_R= 2.9), degrade 2 (t_R= 6.9)

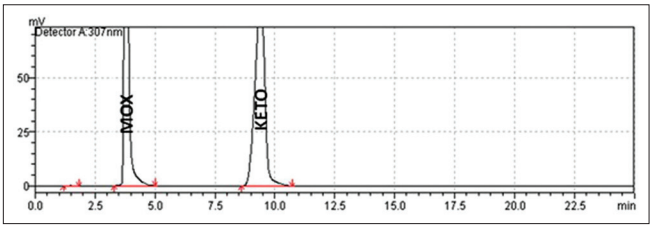

Figure 8: Chromatogram for neutral hydrolysis of moxifloxacin and ketorolac

and marginally in alkaline condition whereas ketorolac tromethamine degraded significantly under alkaline and oxidative conditions and marginally in photolytic condition.

pH dependent degradation kinetics

The pH-rate profile of degradation of moxifloxacin hydrochloride and ketorolac tromethamine in buffer solutions was studied at 60°C using the HPLC method. [Figures 10 and 11] First-order kinetics plots for the degradation of moxifloxacin hydrochloride and ketorolac tromethamine for each pH value are shown in Figures 12 and 13, respectively. The apparent first-order degradation rate constant, $t_{1/2}$ and t_{90} were calculated at all three pH values of 2.0, 6.8, and 9.0 for moxifloxacin hydrochloride and ketorolac tromethamine. [Table 9] From the degradation kinetics data, it can be concluded that the moxifloxacin hydrochloride is susceptible to acidic whereas ketorolac tromethamine is susceptible to alkaline degradation. The pH-rate profile study showed that the moxifloxacin hydrochloride and ketorolac tromethamine are most stable at pH 6.8. The results are not in full agreement with data published by S. K. Motwani *et al*. at 40°C.[14] Our result showed very high stability at pH 6.8 and much less degradation at pH 9.0 compared to published data.

Conclusion

The new HPLC method was found to be simple, precise, accurate, robust, and stability indicating for the estimation of moxifloxacin hydrochloride and ketorolac tromethamine in combined ophthalmic dosage form. Forced degradation study revealed that moxifloxacin hydrochloride degraded significantly under acidic and oxidative conditions and marginally in alkaline condition whereas ketorolac tromethamine degraded

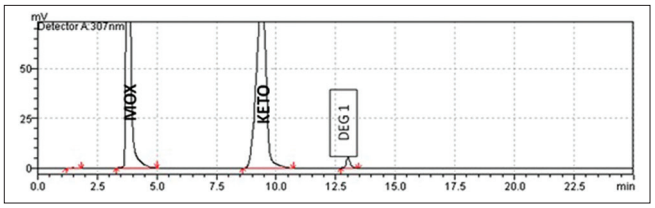

Figure 9: Chromatogram for photo degradation of moxifloxacin, ketorolac and its degradants: degrade 1 (t_R = 13.0)

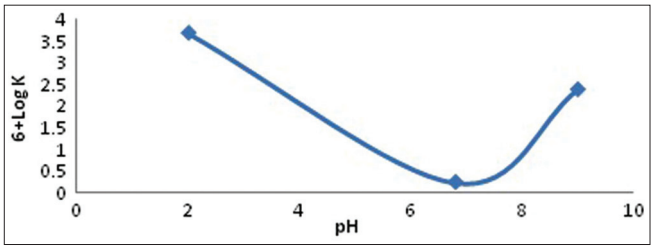

Figure 10: pH-rate profile for the decomposition of moxifloxacin at 60°C

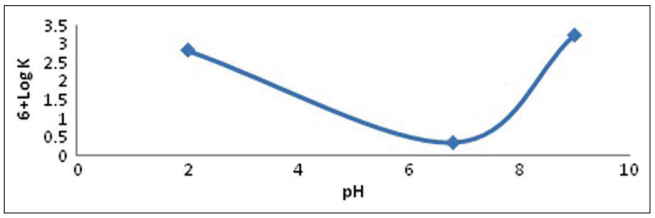

Figure 11: pH-rate profile for the decomposition of ketorolac at 60°C

Table 8: Result of degradation of moxifloxacin hydrochloride and ketorolac tromethamine

Type of degradation	Condition	No. of peak with t_R	% Degradation	Peak purity
Acid hydrolysis	1 M HCl, 80°C,6 hr	Deg. Peaks=2 t_R=2.9, 6.9	MOX: 20.12 KETO: 1.87	MOX: 0.99999 KETO: 0.99998
Alkali hydrolysis	2 N NaOH, 80°C, 4 hr	Deg. Peaks=3 t_R=2.7, 5.3, 6.3	MOX: 3.42 KETO: 22.48	MOX: 1.00 KETO: 0.99998
Oxidative degradation	30% H_2O_2, R.T, 6 hr	Deg. Peaks=2 t_R=2.9, 6.9	MOX: 6.44 KETO: 5.41	MOX: 1.00 KETO: 0.99999
Neutral hydrolysis	80°C, 12 hr	Deg. Peaks=0	MOX: - KETO: -	MOX: 1.00 KETO: 1.00
Photolytic degradation	1.2 million lux,12 hr	Deg. Peaks=1 t_R=13.0	MOX: - KETO: 5.54	MOX: 0.99999 KETO: 0.99999

MOX – Moxifloxacin hydrochloride, KETO – Ketorolac tromethamine

Table 9: Degradation rate constant (K), half-life ($t_{1/2}$) and t_{90} for moxifloxacin hydrochloride and ketorolac tromethamine

Degradation condition	Moxifloxacin hydrochloride			Ketorolac tromethamine		
	K (hr^{-1})	$t_{1/2}$ (hr)	t_{90} (hr)	K (hr^{-1})	$t_{1/2}$ (hr)	t_{90} (hr)
pH 2.0	4.93×10^{-3}	140.5309	21.0897	6.66×10^{-4}	1032.139	155.5687
pH 6.8	1.75×10^{-6}	395936.7	59419.0	2.23×10^{-6}	308875.5	46555.14
pH 9	2.43×10^{-4}	2842.277	426.546	1.66×10^{-3}	409.23	61.23

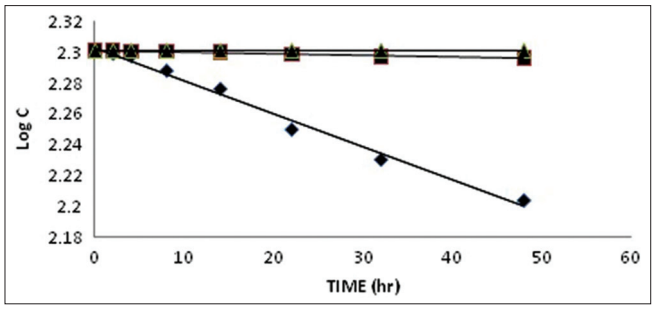

Figure 12: First-order kinetics plots for the degradation of moxifloxacin at pH 2.0(◆), 6.8(▲) and 9.0(■)

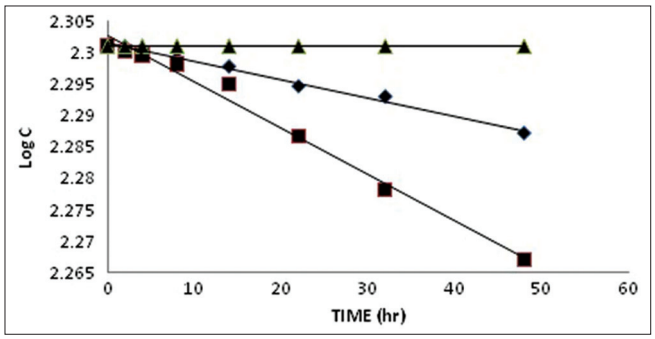

Figure 13: First-order kinetics plots for the degradation of ketorolac at pH 2.0(◆), 6.8(▲) and 9.0(■)

significantly under alkaline and oxidative conditions and marginally in Photolytic condition. The developed HPLC method adequately separated the drug from the degradation products proving the specificity of method and can be used for stability analysis. From the degradation kinetics data, it can be concluded that the moxifloxacin hydrochloride is susceptible to acidic pH whereas ketorolac tromethamine is susceptible to alkaline pH. The pH-rate profile study showed that the moxifloxacin hydrochloride and ketorolac tromethamine are most stable at pH 6.8.

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