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Research Article

First Derivative Spectrophotometric Methods for the Determination of Ketorolac Tromethamine Tablets

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Abstract

New derivative spectrophotometric methods have been developed for the assay of Ketorolac tromethamine in pharmaceutical formulations. Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug which exhibits pronounced analgesic and moderate anti-inflammatory activity. Ketorolac tromethamine was able to produce a first order derivative spectra in reagents such as phosphate buffers (pH 5.0 and 8.0), acetate buffer (pH 4.7), 0.1N NaOH and borate buffer (pH 9.0). In all these reagents the first order derivative spectra show both maxima and minima and therefore amplitude was chosen for constructing the calibration curves. Beer-Lambert's law was obeyed over the concentration range 5 - 30 µg/ml for all the methods and the methods were validated as per ICH guidelines. The methods were found to be simple, precise, accurate, economical and the methods can be successfully applied for the determination of Ketorolac tromethamine in pharmaceutical dosage forms.

Keywords: Ketorolac Tromethamine; First Order Derivative Spectroscopy; Sodium Hydroxide; Borate Buffer; Acetate Buffer; Phosphate Buffer; Validation; ICH Guidelines

Introduction

Ketorolac tromethamine synthetic pyrrolizine carboxylic acid derivative. Ketorolac tromethamine (Figure 1) is used to treat moderately severe pain and inflammation, usually after surgery. Ketorolac tromethamine is a nonsteroidal anti-inflammatory. Ketorolac tromethamine works by blocking the production of prostaglandins, compounds that cause pain, fever, and inflammation [1-3]. Literature survey reveals that Ketorolac tromethamine was estimated by various analytical methods such as HPLC [4-6], HPTLC [7,8], fluorophotometry [9], voltammetry [10], spectrophotometry [11-13] and in biological fluids such as human serum [14], human plasma [15], human eye samples [16], post mortem blood samples [17] and serum and synovial fluids [18]. In the present study the authors have proposed five UV spectrophotometric methods for the determination of Ketorolac tromethamine in pharmaceutical dosage forms and the methods were validated as per ICH guidelines [19].

Materials and Methods

Ketorolac tromethamine is available as tablets with brand name KETOROL-DT (Dr. Reddys), DENTAFORCE-DT (Mankind Pharma) and TORODENT-DT (Cipla Ltd) (Label claim: 10 mg). Ketorolac tromethamine was obtained as a gift sample from Cipla Ltd, India. Reagents such as phosphate buffer (pH 5.0) and phosphate buffer (pH 8.0), acetate buffer (pH 4.7), 0.1N NaOH and borate buffer (pH 9.0) and were prepared as per IP 2010. Double beam spectrophotometer (SHIMADZU Model No. UV - 1800) with quartz cells was used for the present study. All the solutions were scanned at 200 - 400 nm range.

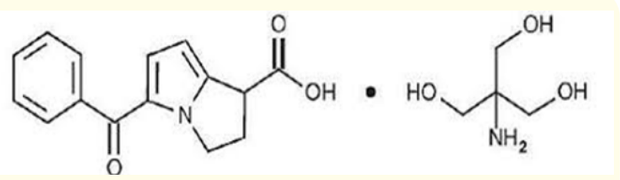

Figure 1: Structure of Ketorolac tromethamine

Procedure

25 mg of Ketorolac tromethamine was accurately weighed and transferred in to a 25 ml volumetric flask and dissolved in methanol (1000 µg/ml) and a series of dilutions were prepared with respective buffers as per the requirement.

Method validation

Linearity

A series of Ketorolac tromethamine solutions 5 - 30 µg/ml were prepared using different buffer solutions - phosphate buffer pH 5 (Method A), phosphate buffer pH 8 (Method B), acetate buffer pH 4.7 (Method C), 0.1 N NaOH (Method D) and borate buffer pH 9 (Method E) and scanned against their reagent blank at range of 200 - 400 nm. The individual zero order spectra of Ketorolac tromethamine so obtained in all the above mentioned reagents were converted into their first order derivative spectra with the help of inbuilt software of the instrument. The resultant derivative spectra have shown both maxima and minima and therefore amplitude was selected for the calculation purpose in all methods. Calibration curves were drawn by taking the concentration on the x-axis and the corresponding amplitude on the y-axis for all the methods.

Precision and accuracy

Precision was studied by measuring the derivative absorbance of six solutions (n = 6) of the same concentration (10 µg/ml) and there by mean, standard deviation and relative standard deviation were calculated. Accuracy was studied by spiking the formulation solution of a fixed concentration with pure drug solution (50%, 100% and 150%) by standard addition method and there by percentage recovery and relative standard deviation were calculated.

Assay of ketorolac tromethamine tablets

20 tablets of Ketorolac tromethamine of two different brands were procured from the local pharmacy store and powder equivalent to 25 mg of Ketorolac tromethamine was separately weighed and extracted with methanol. Further dilutions were made from this stock solution (1000 µg/ml) with respective buffers and assay was carried out for all the methods for both the brands.

Results and Discussion

New first derivative spectrophotometric methods have been developed for the determination of Ketorolac tromethamine in reagents such as phosphate buffer (pH 5.0) (Method A), phosphate buffer (pH 8.0) (Method B), acetate buffer (pH 4.7) (Method C), NaOH (Method D) and borate buffer (pH 9.0) (Method E). The present proposed methods were compared with the previously published spectrophotometric methods in table 1.

Reagent	λ_{max} (nm)	Linearity (µg/mL)	Ref
Ninhydrin	570	50-250	11
Distilled water	322	2 - 14	12
2,4-dinitrophenyl hydrazine and Tetra cyano quino dimethane	424 842	0.5 - 18.5 2.0 - 50.0	13
Phosphate buffer (pH 5.0) Phosphate buffer (pH 8.0) Acetate buffer (pH 4.7) 0.1N NaOH Borate buffer (pH 9.0)	323	5 - 30	Present methods

Table 1: Review of spectrophotometric methods.

The derivative absorption spectra of Ketorolac tromethamine were shown in figure 2 and the calibration curves were shown in figure 3. Beer-Lambert's law was obeyed over the concentration range 5 - 30 µg/ml (Table 2) in all the methods and the calibration curves were shown in figure 3. All the five methods were precise (Table 3) and accurate (Table 4) as the percentage RSD was found to be less than 2. The percentage of purity (Assay) results of Ketorolac tromethamine were shown in table 5 in the marketed formulations and is no interference of excipients was observed.

Conclusion

The five first derivative spectrophotometric methods are simple, precise, accurate and economical. The methods were validated and can be successfully applied for the determination of Ketorolac tromethamine in pharmaceutical dosage forms.

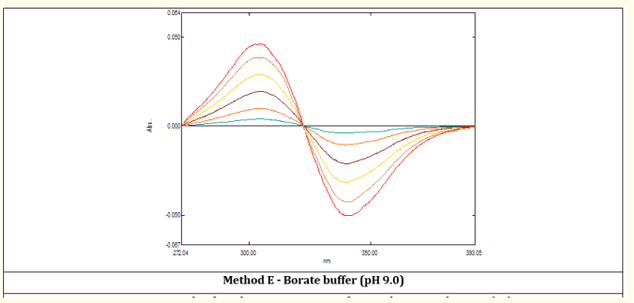

Figure 2: Overlay first derivative spectra of Ketorolac tromethamine (D_1)

Figure 3: Calibration curves of Ketorolac tromethamine (First detrivative spectroscopy)

Conc. (µg/ml)	Method A			Method B			Method c		
	Maxima	Minima	Amplitude	Maxima	Minima	Amplitude	Maxima	Minima	Amplitude
5	0.010	0.010	0.02	0.010	0.010	0.02	0.002	0.004	0.006
10	0.020	0.020	0.04	0.020	0.022	0.042	0.005	0.008	0.013
15	0.029	0.031	0.06	0.031	0.032	0.063	0.007	0.012	0.019
20	0.039	0.041	0.08	0.041	0.043	0.084	0.010	0.016	0.026
25	0.046	0.050	0.096	0.051	0.054	0.105	0.012	0.019	0.031
30	0.062	0.065	0.127	0.063	0.066	0.129	0.015	0.024	0.039
Conc. (µg/ml)	Method D						Method E		
	Maxima		Minima		Amplitude		Maxima	Minima	Amplitude
5	0.002		0.004		0.006		0.002	0.003	0.005
10	0.005		0.008		0.013		0.005	0.007	0.012
15	0.008		0.014		0.022		0.008	0.011	0.019
20	0.010		0.017		0.027		0.009	0.014	0.023
25	0.012		0.021		0.033		0.012	0.019	0.031
30	0.015		0.025		0.04		0.014	0.022	0.036

Table 2: Linearity of ketorolac tromethamine - first derivative spectroscopy (Max: Maxima; Min: Minima).

Conc. (µg/ml)	Statistical parameters: Mean ± SD (% RSD)				
	Method A	Method B	Method C	Method D	Method E
10	0.042 ± 0.0005 (0.01)	0.045 ± 0.0008 (0.01)	0.012 ± 0.0008 (0.10)	0.013 ± 0.0005 (0.03)	0.012 ± 0.0005 (0.04)
10					
10					
10					
10					
10					

Table 3: Precision study of Ketorolac tromethamine. *Mean of three replicates.

Spiked Conc.	Formulation	Total Conc.	Conc. obtained (µg/ml) [% Recovery] (RSD)				
			Method A	Method B	Method C	Method D	Method E
5	10	15	14.89	14.75	14.82	14.92	14.89
5	10	15	[99.27]	[98.33]	[98.80]	[99.47]	[99.20]
5	10	15	(0.35)	(0.29)	(0.32)	(0.73)	(0.52)
10	10	20	19.28	19.26	19.9	19.58	19.01
10	10	20	[96.4]	[96.3]	[99.5]	[97.9]	[95.05]
10	10	20	(0.36)	(0.34)	(0.29)	(0.86)	(0.34)
15	10	25	24.39	24.88	24.1	24.55	24.21
15	10	25	[97.56]	[99.2]	[96.4]	[98.2]	[96.84]
15	10	25	(0.54)	(0.19)	(0.43)	(0.99)	(0.33)

Table 4: Accuracy study of ketorolac tromethamine. *Mean of three replicates.

Brand	Method									
	Observed amount (mg)					% Recovery				
	A	B	C	D	E	A	B	C	D	E
Brand I	9.84	9.89	9.90	9.78	9.85	98.4	98.9	99.0	97.8	98.5
Brand II	9.86	9.85	9.92	9.89	9.90	98.6	98.5	99.2	98.9	99.0

Table 5: Assay of ketorolac tromethamine (Label claim: 10 mg). *Mean of three replicates.

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