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Simultaneous Estimation of Ketorolac Tromethamine and Omeprazole by Ultraviolet Spectroscopy

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ABSTRACT:

A spectrophotometric method for the simultaneous estimation of Ketorolac Tromethamine and Omeprazole in their combined dosage form have been developed and validated for linearity, accuracy, precision, ruggedness and repeatability. Simultaneous equation method involves the measurement of absorbance at two wavelengths 318nm (λmax of KETO) and 304nm (λmax of OMEZ) in methanol. Both drugs shows linearity in the concentration range of 2-18 µg/mL for Ketorolac Tromethamine and 2-20 µg/mL for Omeprazole. The accuracy and precision of the method was determined and validated statistically. Developed method shows good reproducibility and recovery with % RSD less then 2. Developed simultaneous equation method was found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Ketorolac Tromethamine and Omeprazole in combined dosage form.

KEYWORDS: Omeprazole, Ketorolac tromethamine, Simultaneous equation method.

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INTRODUCTION:

Multi-drug administration is often associated with clinically significant interaction, especially of narrow therapeutic index drugs, either at pre-absorption or post-absorption stage.[1] This can limit the desired therapeutic effect of either of the drug molecules. The present study was aimed to develop simple, rapid and precise spectrophotometric method for simultaneous estimation of Omeprazole and Ketorolac Tromethamine(KETO).[2] Chemically Omeprazole (OMZ)[3] is 5-methoxy -2-(4-methoxy-3 - 5- dimethyl – 2 – pyridinyl methyl sulfinyl)-3H-benzimidazole. It is used as an anti ulcerative (proton pump inhibitor). Omeprazole is racemate (both R & S forms). In acidic condition of the stomach both (R & S forms) are converted to achiral products which reacts with the cystine group in H+/K+. ATPase there by destroying the ability of the parietal cells to produce Gastric acid. Literature survey revealed that validation of spectrophotometric determination of Omeprazole and pantoprazole sodium via their metal chelates and only Omeprazole formulation determined by spectrophotometric method. Omeprazole is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United State Pharmacopoeia (USP). The IP[4] , BP[5] and USP[6] describe HPLC method for estimation of omeprazole. Ketorolac Tromethamine, [2] has anti-inflammatory and analgesic activity. Chemically it is 5-benzoly-2,3-dihydro-1H-pyrrolizine-1-carboxylicacid,2-(hydroxymethyl)-1,3-propanediol and official only in USP. Literature survey showed that very few analytical methods have been reported for the estimation of ketorolac tromethamine and omeprazole in single or in combination. The aim of present work is to develop a simple, rapid, precise and selective spectrophotometric method for the estimation of Omeprazole and Ketorolac tromethamine in dosage form.

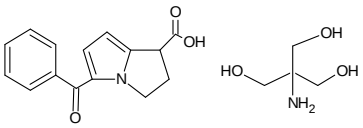

Fig.01. Chemical structure of Keterolac

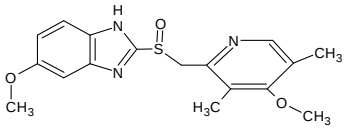

Fig.02. Chemical Structure of Omeprazole

MATERIALS AND METHODS:

Instrument:

PC based UV-Vis. double beam spectrophotometer, model analytical SPECTRO 2080 with 1 cm quartz cells were used.

Chemicals and reagents:

The gift sample of Ketorolac tromethamine and Omeprazole were obtained from Shreeji pharma, Vadodara, Gujarat, India. Methanol was of analytical grade.

Preparation of solutions:

Standard stock solution of KETO and OMEZ were prepared separately to the concentration of 1mg/mL in methanol. Suitable aliquots were pipeted out from standard stock solution to obtained working standard solution of KETO and OMEZ, 6 µg/mL and 12 µg/mL, respectively. Both solutions were scanned over a range of 318 nm to 304 nm in the spectrum mode and the overlain spectra of two were recorded. From the overlain spectra, wavelengths 318 and 304 nm were selected for the formation of simultaneous wave equations. For construction of calibration curves, two series of different concentrations in range of 2-10 µg/mL for KETO and 4-20 µg/mL for OMEZ were prepared from stock solution. The calibration curves were plotted at 318 and 304 nm. The absorptivity (A1%, 1cm) of the drugs at selected wavelengths was determined. These calculated values were the mean of five independent determinations.

Analysis of laboratory mixture by proposed method:

In order to see the feasibility of proposed method for simultaneous estimation of KETO and OMEZ, the method was first tried for estimation of drugs in standard laboratory mixture. Accurately weighed quantities KETO (6mg) and OMEZ (12mg) were taken in a volumetric flask (100mL) and dissolved in methanol. The volume was made up to the mark by methanol filter through whatman filter paper. The aliquot portions of this stock solution were further diluted with solvent to get final concentrations KETO (6µg/mL) and OMEZ (12µg/mL) and the absorbance were measured at 318 nm and 304 nm respectively against methanol as blank. The quantitative estimation of the drugs were carried out by solving simultaneous equation,

$$Cx = (A_2ay_1 - A_1ay_2)/ (ax_2ay_1 - ax_1ay_2) \quad (1)$$

$$Cy = (A_1ax_2 - A_2ax_1)/ (ax_2ay_1 - ax_1ay_2) \quad (2)$$

Where A_1 and A_2 are absorbance's of mixture at 318 and 304nm, respectively ax_1 and ax_2 are absorptivities of x at 318 and 304 nm, respectively, ay_1 and ay_2 are absorptivities of y at 318 and 304 nm, respectively and Cx is the concentration of KETO and Cy is the concentration of OMEZ.

Table 1: Analysis of KETO and OMEZ in laboratory mixture

Sr.no.	Amt taken (µg/ml)	Amt found(µg/ml)*	(%) Amt found ±SD
1	KETO (6µg/ml)	5.98	99.40 ± 0.52
2	OMEZ (12µg/ml)	11.99	99.84±0.32

*mean of 5 estimation.

Validation of proposed method:

The proposed analytical method was validated as per recommendations of USP and ICH guidelines for the parameters like recovery, precision, ruggedness and repeatability.

Recovery study:

The accuracy of an analytical method is closeness of test results obtained by that method to the true value. The accuracy of an analytical method should be established across its range. A known amount of standard solution of pure drugs KETO and OMEZ were added to preanalysed sample solution KETO 6 µg/mL and OMEZ 12 µg/mL. These solutions were subjected for analysis. The lower the values of relative standard deviation (RSD) indicate the method is accurate. Recovery studies were carried out at 3 levels 80% , 100% , 120 % for both the drugs using methanol as solvent.(Table 2)

Precision:

The precision of an analytical method is the degree of agreement among the individual test results when the method is applied repeatedly to multiple samplings of a homogeneous sample. Variation of results within the same day (intra day), variation of results between days (inter day) were analyzed. Intra day precision was determined by analyzing, the 2, 6 and 10µg/mL of KETO and 4, 12 and 20µg/mL of OMEZ concentrations for three times in the same day. Inter day precision was determined by analyzing, the same concentrations of drugs daily for three days.(Table 3)

Ruggedness:

The ruggedness of analytical method is the degree of reproducibility of test results obtained by the analysis of the same sample under a variety of conditions, such as different laboratories, different analysts, different instruments, and different lots of reagent. Ruggedness of the proposed method is determined by analysis of aliquots from homogenous slot by two analyst using same operational and environmental conditions and the results are reported in Table 4.

Repeatability:

Repeatability was determined by analyzing KETO (6µg/ml) and OMEZ (12µg/mL) concentration of drug solutions for six times and results are reported in Table 5.

RESULT AND DISCUSSION:

Table 2: Recovery study data

Drug	No.of preparations	Concentration (µg/lml)			
		Sample Solution	Pure Drug	% Recovery	%RSD
Ketorolac tromethamine	80%	6 µg/ml	4.6 µg/ml	99.56%	0.18%
	100%	6 µg/ml	6 µg/ml	99.90%	
	120%	6 µg/ml	7.2 µg/ml	99.84%	
Omeprazole	80%	12 µg/ml	9.6 µg/ml	100.92%	0.30%
	100%	12 µg/ml	12 µg/ml	100.63%	
	120%	12 µg/ml	14.4 µg/ml	101.23%	

Recovery studies were carried out by adding a known amount of standard solution of pure drugs (KETO and OMEZ) to a preanalysed sample solution (KETO 6µg/ml and OMEZ 12µg/ml). These solution were subjected to analysis. The study showed the result with in acceptable limit of above 99% and below 102% and lower value of RSD indicates the proposed method is accurate.(Table 2).

Table 3: Precision study data

Precision Data						
Sr No.	**Drug**	**Concentration**	**Intraday**	**%RSD**	**Interday**	**%RSD**
1	Ketorolac tromethamine	2 µg/ml	1.8	0.6384	1.93	0.7193
		6 µg/ml	6.03	0.2613	6.1	0.4075
		10 µg/ml	9.88	0.7543	9.95	0.6946
2	Omeprazole	4 µg/ml	3.6	0.6653	3.78	0.6145
		12 µg/ml	11.89	0.1621	11.97	0.4389
		20 µg/ml	20.31	1.0870	20.19	0.9094

Precision studies were carried out using parameters like intra-day and inter-day analysis precision. The study showed the result with in acceptable limit, i.e % RSD below 2.0, indicating that the method is reproducible.(Table 3)

Table 4: Ruggedness data

Ruggedness Data					
Drug	**Amount Taken**	**Analyst 1 (µg/ml)**	**%RSD**	**Analyst 2 (µg/ml)**	**%RSD**
Ketorolac tromethamine	6 µg/ml	6.08	0.3996	5.99	0.4154
Omeprazole	12 µg/ml	11.93	0.6548	12.02	0.5864

Ruggedness studies were carried out using only 1 parameter, i.e. different analyst. Result showed that the % RSD was less then 2, for different analyst. This study signifies the ruggedness of the method under varying conditions of its performance.(Table 4)

Table 5: Repeatability data

Repeatability Data			
Drug	**Amount Taken**	**Amount found (µg/ml)**	**%RSD**
Ketorolac tromethamine	6 µg/ml	6.05	0.94
Omeprazole	12 µg/ml	11.94	0.75

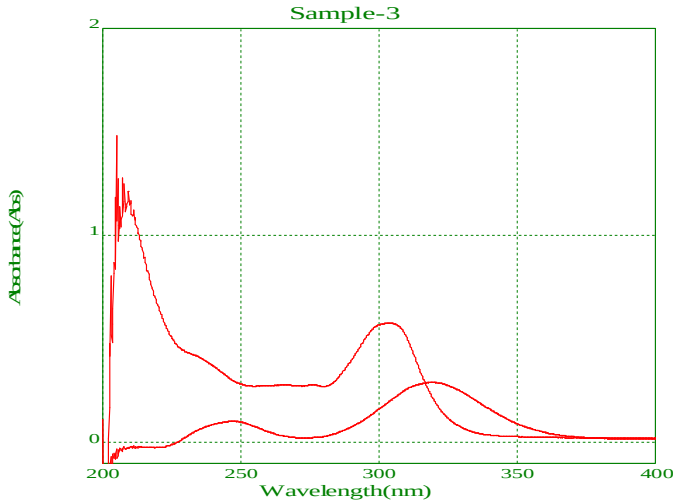

Figure 03: Overlain spectra of Ketorolac tromethamine and Omeprazole

Ketorolac Tromethamine is an anti-inflammatory agent and also has analgesic activity. It acts by inhibiting cyclooxygenase enzyme and prostaglandin synthesis. Gastric ulceration is side effect associated with application of ketorolac tromethamine. Omeprazole is an antacid, used to reduce acidity and gastric ulceration. literature survey also revealed that no methods are reported for the simultaneous estimation of KETO and OMEZ in their combined dosage form. Hence, an attempt has been made to develop the spectrophotometric method for simultaneous estimation of Ketorolac Tromethamine and Omeprazole in oral dosage form. The overlain spectra of both drugs showed good absorbances at 318 and 304 nm, hence these wavelengths were selected for estimation of KETO and OMEZ. Linearity of both KETO and OMEZ were obeyed in the concentration range of 2-10 µg/mL and 4-20 µg/mL with the correlation coefficient 0.9983 and 0.9982, respectively. The absorptivities was then calculated and substituted in equation 1 and 2 to obtained concentration of both drugs.

CONCLUSION:

The developed spectroscopic method was validated and the statistical validation was performed with the simplicity and ease of operation ensures that the validated method can successfully used for routine analysis of Ketorolac Tromethamine and Omeprazole in bulk and tablet dosage form.

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