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SIMULTANEOUS ESTIMATION OF DICLOFENAC SODIUM AND ESOMEPRAZOLE MAGNESIUM TRIHYDRATE IN BULK DRUG AND IN SYNTHETIC MIXTURE BY SPECTROPHOTOMETRY

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Keywords:

Diclofenac Sodium, Esomeprazole Magnesium trihydrate, Simultaneous equation method (Vierodt's method), Absorbance ratio method (Q-method)

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ABSTRACT: Two simple, rapid, precise and accurate spectrophotometric methods have been developed for simultaneous estimation of Diclofenac Sodium (DIC) and Esomeprazole Magnesium Trihydrate in bulk drugs and synthetic mixture. Method A, Simultaneous equation method (Vierodt's method) applies measurement of absorptivities at two wavelengths, 280.00 nm, (λ_{max} of Diclofenac Sodium) and 301.00 nm,((λ_{max} of Esomeprazole Magnesium Trihydrate) in zero order spectra. The concentrations can be calculated from the derived equations. Method B, Absorbance ratio method (Q-method) involves formation of Q-absorbance equation at 302.80 nm (isoabsorptive point) and 280.00 nm (λ_{max} of Diclofenac Sodium) in zero order spectra. Developed methods were validated according to ICH guidelines. The calibration graph follows Beer's law in the range of 2.0 to 10.0 µg/ml for Esomerazole Magnesium Trihydrate and 5.0 to 25.0 µg/ml for Diclofenac Sodium with R^2 value greater than 0.999. Accuracy of all methods was determined by recovery studies and showed % recovery between 98 to 102%. Intraday and inter day precision was checked for both methods and mean %RSD was found to be less than 2 for both the methods. The methods were successfully applied for estimation of Diclofenac Sodium and Esomeprazole Magnesium Trihydrate in Synthetic mixture.

INTRODUCTION: Esomeprazole Magnesium Trihydrate (ESO) is chemically Magnesium, bis{5-methoxy-2[(S)-{(4-methoxy-3,5-dimethypyridine-2-yl)methane}sulfinyl]- 1H-1, 3-Benzimidiazole, trihydrate (**Fig. 1**), is a Proton Pump inhibitor for the Symptometic treatment of Hyperacidic condition.

QUICK RESPONSE CODE

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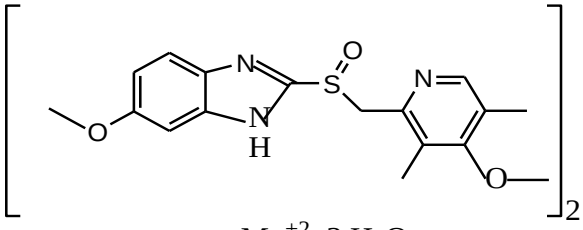
Esomeprazole Magnesium trihydrate is official in Indian Pharmacopoeia 2010 which describes liquid chromatography for its estimation [1]. Diclofenac Sodium (DIC) is Chemically sodium 2-[(2, 6-dichlorophenyl)-amino]phenylacetate (**Fig. 2**), is a broadly used non-steroidal anti-inflammatory drug for the treatment of inflammatory conditions such as rheumatoid arthritis, osteoarthritis and ankylosing spondilytis. Diclofenac Sodium is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). IP, BP, USP describes potentiometric titration for its estimation [2, 3, 4].



Mg^{+2}. 3 H_2O

FIG. 1: ESOMEPRAZOLE MAGNESIUM TRIHYDRATE

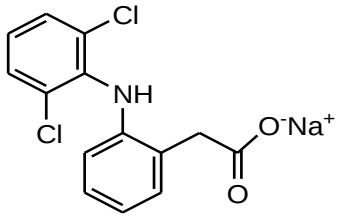


FIG. 2: DICLOFENAC SODIUM

Objective of Study: Survey of literature revealed that numbers of method have been reported in literature for the individual analysis of Esomeprazole Magnesium Trihydrate and Diclofenac sodium by UV spectrophotometric and RP-HPLC method. UV spectrophotometric method available in literature for simultaneous determination of Diclofenac Sodium with other drugs like Paracetamol, Misoprostol and Thiocolchicoside Nimesulide [5, 6, 7, 8]. RP-HPLC method available in literature for simultaneous determination of Esomeprazole Magnesium trihydrate with Itopride.[9] However, to best of our knowledge, there is no reported uv-spectrophotometric method available for simultaneous estimation of Esomeprazole Magnesium Trihydrate and Diclofenac Sodium.

The aim of the present work was to develop easy, economic, accurate, specific and precise spectrophotometric methods for simultaneous estimation of Esomeprazole Magnesium trihydrate and Diclofenac Sodium in bulk drugs and synthetic mixture and validation of newly developed analytical methods.

MATERIALS AND METHODS:

Apparatus and Software: Shimadzu UV-1700 double beam spectrophotometer connected to a computer loaded with Shimadzu UV Probe 2.10 software was used for all the spectrophotometric measurements. The absorbance spectra of the reference and test solutions were carried out in 1cm quartz cells over the range of 200-400 nm. The samples were weighed on electronic analytical balance (A×120, shimadzu).

Reagents and Chemicals:

Solvent: Methanol: Water, Methanol analytical reagent grade (Spectrochem Pvt. Ltd, Mumbai, India), Water- single distilled water.

Diluent: Methanol: Water, Methanol analytical reagent grade (Spectrochem Pvt. Ltd, Mumbai, India), Water- single distilled water.

Year of Experiment: 2012.

Site- Quality Assurance Laboratory, Centre of Relevance and Excellence in Novel Drug Delivery System, G. H. Patel Building, Donor's Plaza, The Maharaja Sayajirao University of Baroda, Fatehgunj, Vadodara – 390 002, Gujarat, India.

Preparation of Stock Solution: Accurately weighed 25 mgs of ESO and DIC separately and transferred to two separate 25 ml volumetric flasks, dissolved with the use of methanol : water (50:50) and volume was made up to the mark with methanol : water (50:50) to obtain stock solution of ESO (1000 µg/ml) and DIC (1000 µg/ml)

Preparation of Working Standard Solutions: From the above solution, standard stocks solutions of ESO (50 µg/ml) and DIC (50 µg/ml) were prepared by transferring 2.5 ml aliquots to 50 ml volumetric flasks and making up the volume with methanol : water (50:50).

Preparation of Calibration Curve of Standard ESO and DIC: From working std. solution of ESO (50 µg/ml) 0.4, 0.8, 1.2, 1.6 and 2.0 ml were transferred to 10 ml volumetric flasks and volume were made up to the mark with methanol : water (50:50). This gives 2.0 to 10 µg/ml of ESO. From working std. solution of DIC (50 µg/ml) 1.0, 2.0, 3.0, 4.0 and 5.0 ml were transferred to 10 ml volumetric flasks and volume were made up to the mark with methanol: water (50:50). This gives 5.0 to 25.0 µg/ml of DIC.

Preparation of Sample Solution: The Combined Dosage Formulation of DIC and ESO is of Orbit life Science Pvt Ltd., which is not yet available in market, so a laboratory sample was prepared using the excipients mentioned in the literature [10, 11] and by following the standard procedure [12], formula for laboratory sample used for analysis was,

TABLE 1: FORMULA FOR THE LABORATORY SAMPLE

Sr No.	Chemical	Quantity (mg)
1	Diclofenac Sodium	100
2	Esomeprazole Magnesium Trihydrate	40
3	Anhydrous lactose	70
4	Eudragit-S	30
5	Glyceryl monostearate	8
6	Aerosil	2
Total		**250**

Synthetic mixture was weighed and dissolved in methanol: water (50: 50) to make up the volume 100 ml, the solutions were further diluted with methanol: water (50: 50) to obtain the final solutions in the concentration range of 2 to 10 µg/ml for ESO and 5 to 25 µg/ml for DIC for recovery study.

Method A:

Simultaneous equation method (Vierodt's method): If a sample containing two absorbing drug (X and Y) each of which absorbs at λ_{max} of other. It may possible to determine both drugs by the technique of simultaneous equations (Vierodt's method) provided that certain criteria apply. The information required is the aborptivities of X at and λ1 and λ2 ax1 and ax2 respectively (a) The aborptivities of Y at and λ1 and λ2 ay1 and ay2 respectively (b) The absorbances of the diluted sample at λ1 and λ2, A1 and A2 respectively.

Let Cx and Cy be the concentrations of X and Y respectively in the diluted sample. Two equations are constructed based upon the fact that at λ1 and λ2 the absorbance of the mixture is the sum of the individual absorbance of X and Y. From the stock solutions, working standard solutions of ESO (50 µg/ml) and DIC (50µg/ml) were prepared. By appropriate dilutions, the solutions with concentrations 2.0-10 µg/ml (for ESO) and 5.0-25.0 µg/ml (for DIC) were prepared and scanned between 200 to 400 nm **(Fig. 3).**

Calibration curve of absorbance versus concentration were prepared. The calibration curves were found to be linear in the concentration range under study **(Fig. 4 & 5)**. For ESO and DIC, analytical wavelengths of 301.00 nm and 280.00 nm were selected respectively.

Absorptivity of ESO and DIC were calculated at both the wavelengths. The concentrations of ESO and DIC can be calculated from following equations [13]:

Cx (DIC) = (A2 ay1 – A1 ay2) / (ax2 ay1 – ax1 ay2)

Cy (ESO) = (A1 ax2 – A2 ax1) / (ax2 ay1 – ax1 ay2)

Where; Cx & Cy are concentrations of DIC and ESO respectively in gm/100 ml in the sample solution. A1 & A2 are the absorbances of the mixture at 301.00 nm & 280.00 nm respectively; aX1 and aX2 = Absorptivity of DIC at 301.00 nm and 280.00 nm; aY1 and aY2 = Absorptivity of ESO at 301.00 nm and 280.00 nm respectively.

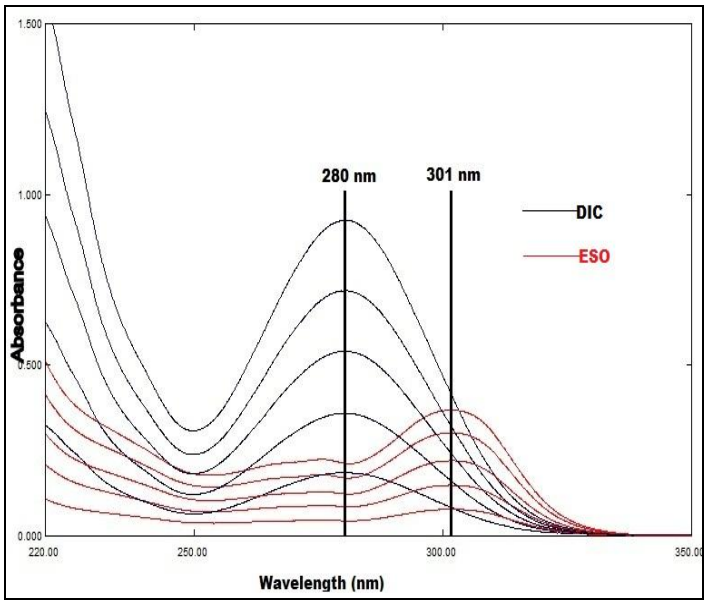


FIG. 3: ZERO ORDER OVERLAIN SPECTRA OF DIC (5, 10, 15, 20, 25 µg/ml) and ESO (2, 4, 6, 8, 10 µg/ml).

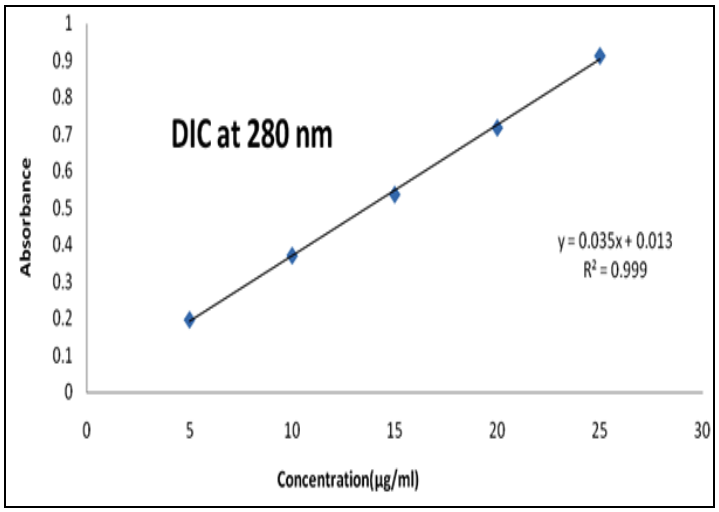


FIG. 4: CALIBRATION GRAPH OF DIC

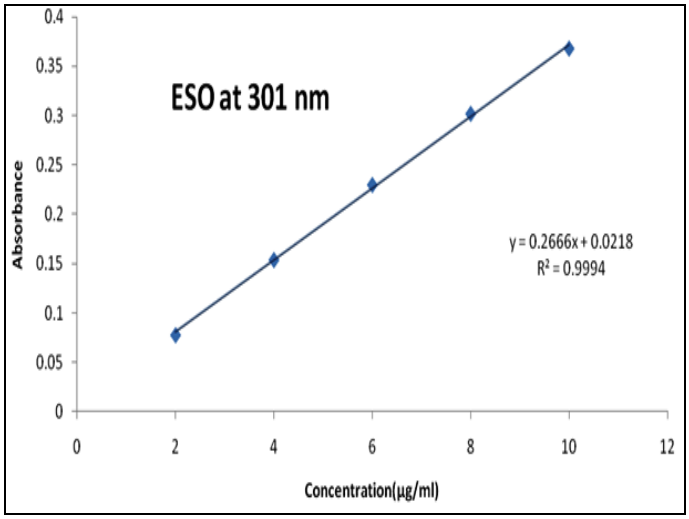


FIG. 5: CALIBRATION GRAPH OF ESO

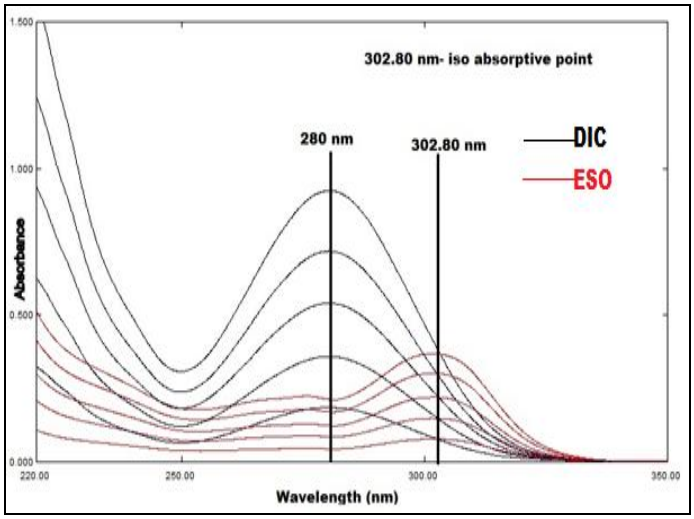


FIG. 6: ZERO ORDER OVERLAIN SPECTRA OF DIC (5, 10, 15, 20, 25 µg/ml, black) and ESO (2, 4, 6, 8, 10 µg/ml, red).

Method B-

Absorbance ratio method (Q method) : Q method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and other being the λ_{max} of one of the two compounds. From the stock solutions, working standard solutions of ESO (50 µg/ml) and DIC (50µg/ml) were prepared. By appropriate dilutions, the solutions with concentrations 2.0-10 µg/ml (for ESO) and 5.0-25.0 µg/ml (for DIC) were prepared and scanned between 200 to 400 nm **(Fig. 6).**

Series of standard solutions ranging from 5.0-25.0 µg/ml for DIC and 2.0-10.0 µg/ml for ESO were prepared and the absorbance of solutions was recorded at 302.80 nm (isoabsorptive point) and 280.00 nm (λ_{max} of DIC) to plot a calibration curve of absorbance versus concentration **(Fig. 7 & 8)**. Calibration curves were found to be linear in the concentration range under study. Absorptivity values of DIC and ESO were determined at selected wavelengths and are presented in Table 2. The concentration of two drugs in mixture was calculated by using following equations [13]:

$$CX = [(QM - QY) / (QX - QY)] \times A1/aX1$$

$$CY = [(QM - Qx) / (Qy - Qx)] \times A1/ay1$$

Where; Qm = A2/A1, Qx = ax2/ax1, Qy = ay2/ay1; **1** designates isoabsorptive point and **2** designates λ_{max} of ESO; ax1 and ax2 is Absorptivity of DIC at 1 and 2 wavelength respectively; ay1and ay2 is Absorptivity of ESO at 1 and 2 wavelength respectively; A1 and A2 are absorbances of the mixture at 1 and 2 wavelength respectively.

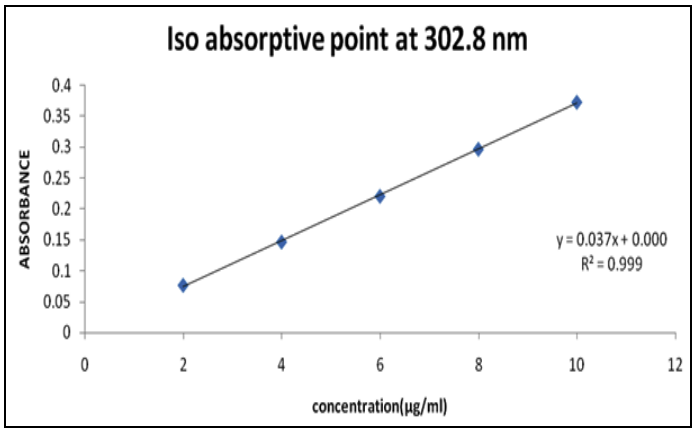


FIG. 7: CALIBRATION GRAPH AT ISOABSORBTIVE POINT

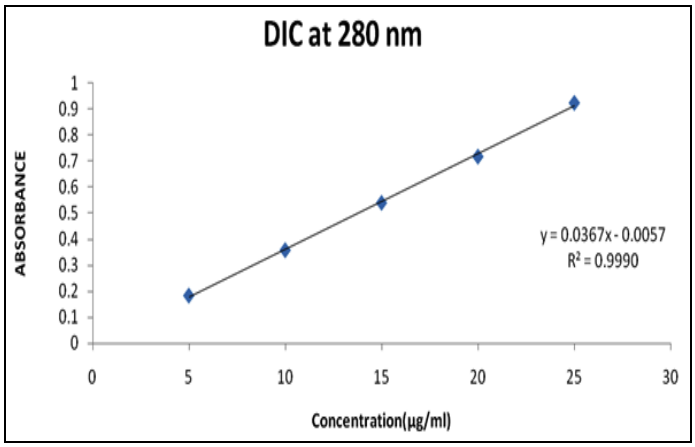


FIG. 8: CALIBRATION GRAPH OF DIC

Assay of Synthetic mixtures by Method A and B: Synthetic mixture was weighed and dissolved in methanol: water (50: 50) to make up the volume 100 ml, the solutions were further diluted with methanol: water (50: 50) to obtain the final solutions in the concentration range of 2 to 10 µg/ml for ESO and 5 to 25 µg/ml for DIC for recovery study **(Table 2).**

TABLE 2: RESULTS OF SIMULTANEOUS ESTIMATION OF DIC AND ESO IN SYNTHETIC MIXTURE FOR METHOD A AND B:

Synthetic Mixture		
Labelled Claim :- DIC : ESO (100mg :40mg)		
Method	**DIC*±SD**	**ESO*±SD**
A	98.71±1.34	99.58±0.82
B	99.97±0.97	98.67±1.65

*****Mean value of three determinations

RESULTS AND DISCUSSION: Developed spectrophotometric methods for the simultaneous estimation of DIC and ESO were validated according to ICH guidelines and data complying with the standards were obtained [11]. The results of validation parameters for all the three developed methods are reported **(Table 3 and 4).**

TABLE 3: SUMMARY OF VALIDATION PARAMETERS BY DEVELOPED METHODS:

Parameters	Method – A		Method - B	
	DIC	**ESO**	**DIC**	**ESO**
Analytical wavelength (nm)	280.00 & 301.00		280.00 & 302.80	
Beer's range (µg/ml)	5.0 -25.0	2.0 -10.0	5.0 - 25.0	2.0 - 10.0
Slope	0.0356	0.2666	0.0367	0.0371
Intercept	0.0135	0.0218	0.0057	0.0004
Correlation coefficient	0.9991	0.9994	0.9990	0.9997
Intraday precision (%RSD)	0.5130	0.9760	0.5123	0.9725
Interday precision (%RSD)	1.3750	1.5790	1.5634	1.5874
LOD (µg/ml)	0.1537	0.1762	0.1491	0.6230
LOQ (µg/ml)	0.4658	0.5181	0.4518	1.8871

TABLE 4: RESULTS OF RECOVERY STUDY OF DIC AND ESO BY DEVELOPED METHODS

METHOD	%SPIKING	C_{ACTUAL} (µg/ml)		C_{ADDED} (µg/ml)		C_{FOUND}* (µg/ml)		%RECOVERY ± S.D.	
		DIC	**ESO**	**DIC**	**ESO**	**DIC**	**ESO**	**DIC**	**ESO**
A	**80**	10	4	8	3.2	8.03	3.17	100.44±0.178	99.17±0.625
	100	10	4	10	4	9.97	4.02	99.75±0.106	100.67±0.667
	120	10	4	12	4.8	12.14	4.73	101.20±0.204	98.70±0.424
B	**80**	10	4	8	3.2	8.06	3.08	100.87±0.123	98.76±0.234
	100	10	4	10	4	9.85	4.03	98.51±0.309	100.87±0.158
	120	10	4	12	4.8	12.12	4.78	101.08±0.110	99.76±0.210

* Mean of three determinations

CONCLUSION: Two Spectrophotometric methods (Absorbance ratio method and Simultaneous equation method) were developed for simultaneous estimation of DIC and ESO in bulk drugs and synthetic mixture without prior separation. Methods were found to be precise and accurate as can be reflected from validation data. Developed methods were successfully applied for estimation of DIC and ESO in Synthetic mixture.

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