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# Spectrophotometric Methods for Simultaneous Estimation of Diclofenac Sodium and Rabeprazole in Combined Dosage Form

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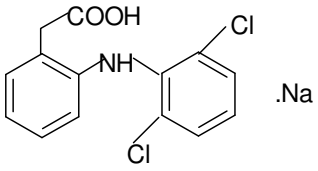
Two fast, precise and economical spectrophotometric methods have been developed for the simultaneous estimation of diclofenac sodium and rabeprazole in a combined dosage form. Simultaneous determination of the marketed brands was carried out using simultaneous equation method and two wavelength calculation methods. An attempt was made to estimate both the drugs in a combined dosage form. Methanol was used as a common solvent for both the drugs. Linearity was observed at both wavelengths in the concentration range of 10-50 µg/mL for each drug. The result of analysis have been validated statistically and also by recovery studies.

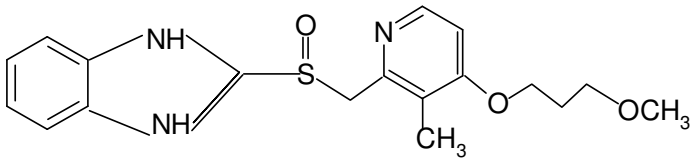
**Key Words: Rabeprazole, Diclofenac sodium, Spectrohotometry.**

## INTRODUCTION

Diclofenac sodium is chemically sodium salt of 2-[{2,6-dichloro phenyl}amino]-benzene acetic acid[1]. It is having antiinflammatory and analgesic properties[2].




Rabeprazole is chemically 2-[{{4-{3-methoxypropoxy}-3-methyl-2-pyridinyl}-methyl}sulfinyl}-1*H*-benzimidazole and used as antiulcer agent[3].




Estimation of these drugs was carried out individually and with other drugs by HPLC[4,5], spectrophotometrically[6-9], HPTLC[10,11], supercritical fluid chromatography[12,13] but no HPLC and spectrophotometric method have been developed. In the present study two new spectrophotometric methods were developed.

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## EXPERIMENTAL

**Simultaneous equation method:** For simultaneous analysis of diclofenac sodium and rabeprazole using simultaneous equation method, methanol was used as a solvent. From the overlain spectra of two drugs presented in Fig. 1, it was observed that diclofenac sodium shows zero absorbance at 327 nm, whereas rabeprazole have substantial absorbance. So rabeprazole was estimated directly by measuring absorbance at 327 nm. For diclofenac sodium estimation in the presence of rabeprazole, an absorptivity equation was framed on the basis of absorptivity of two drugs at 274 nm. Linearity was observed at both wavelengths in the concentration range of 10-50 µg/mL of each drug.

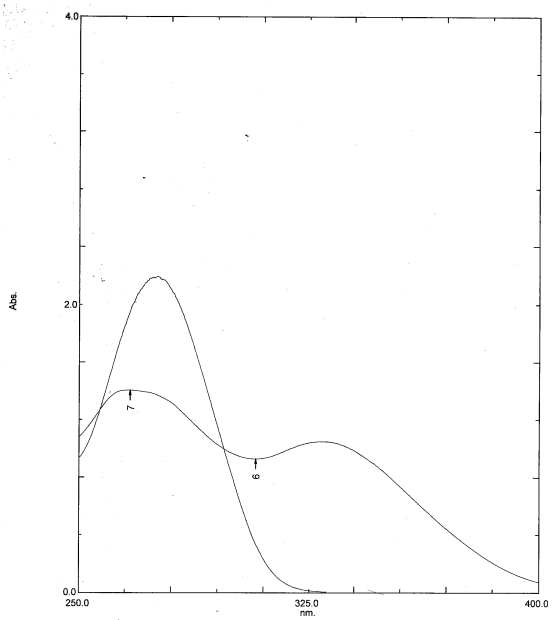


Fig. 1. Overlain spectra of diclofenac sodium and rabeprazole

**Calibration curve for estimation of rabeprazole:** Pure drug sample of rabeprazole was dissolved in methanol and diluted with the same so as to get several dilutions in concentration ranging from 10-50 µg/mL. Absorbance of all the dilutions was measured against blank and calibration curve was plotted between measured absorbance and concentration of rabeprazole (Fig. 2).

**Determination of the absorptivity of drugs and framing absorptivity equation:** The absorptivities of diclofenac sodium and rabeprazole were determined at two selected wavelengths. The absorptivities of two drugs used for framing the simultaneous equation are respective means of four independent estimated values and are as follows:

Absorptivity of diclofenac sodium at 274 nm $ax_1 = 393\ cm^{-1}\ g/L$

Absorptivity of rabeprazole at 274 nm $ay_1 = 287.33\ cm^{-1}\ g/L$

Absorptivity equation can be presented as:

$$A = Ax_1Cx + Ay_1C_y$$

where A = absorbance of sample solution at 274 nm, $C_x$ = concentration of diclofenac sodium in g/L in sample solution, $C_y$ = concentration of rabeprazole in g/L in sample solution.

After obtaining the recorded absorbance A and substituting the value of Cy (determined from direct estimation method) Cx was calculated.

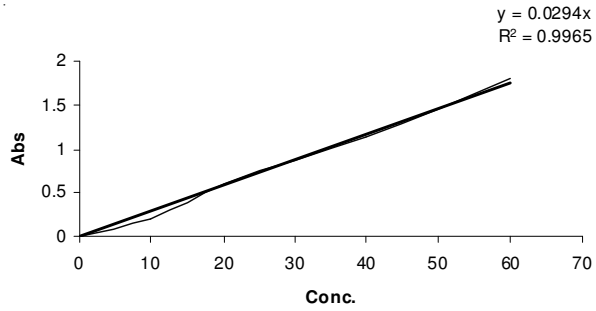


Fig. 2. Calibration for determination of rabeprazole

Where as Cy (concentration of rabeprazole) can be calculated by using direct estimation method by using the equation y = 0.0294x where $R^2 = 0.9965$ as shown in Fig. 2.

**Standardization of method:** To cheek the validity of above framed equation five mixed standard solutions were prepared from the standard stock solution of the drugs. The absorbance of mixed standards (Fig. 3) were measured at respective wavelengths and compared with the absorbance calculated using above framed equation. The concentration of two component of mixed standard was calculated using above framed equation. Results of validation study are reported in Table-1.

TABLE-1
VALIDATION STUDIES OF MIXED STANDARDS OF
DICLOFENAC SODIUM AND RABEPRAZOLE

| Concentration (μg/mL) | | Absorbance | | | | Concentration (%) | |
|---|---|---|---|---|---|---|---|
| | | Calculated | | Observed | | Observed | Observed |
| Diclo | Rabe | 274 nm | 327 mn | 274 nm | 327 nm | Diclo | Rabe |
| 10 | 35 | 0.390 | 0.370 | 0.389 | 0.369 | 98.76 | 99.70 |
| 15 | 30 | 0.785 | 0.625 | 0.784 | 0.629 | 99.70 | 100.11 |
| 20 | 25 | 1.185 | 1.020 | 1.187 | 1.023 | 98.99 | 99.80 |
| 25 | 20 | 1.570 | 1.335 | 1.596 | 1.331 | 100.78 | 100.43 |
| 30 | 15 | 2.030 | 1.620 | 2.032 | 1.617 | 100.98 | 100.98 |

Diclo = Diclofenac sodium, Rabe = Rabeprazole.

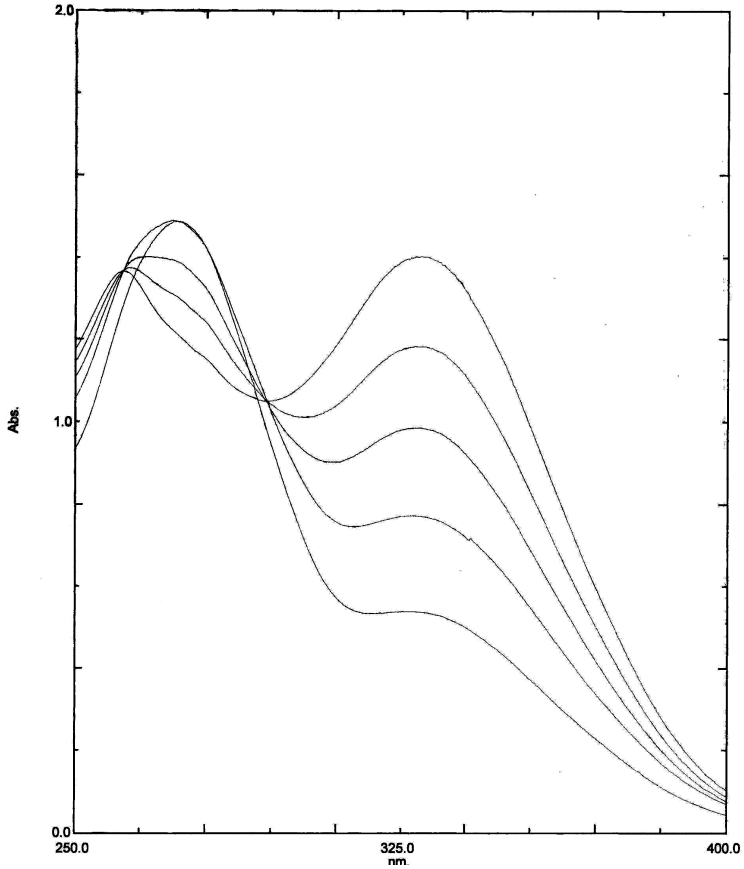


Fig. 3. Mixed spectra of diclofenac sodium and rabeprazole in methanol

**Two wavelength calculation method:** Estimation of rabeprazole by two wavelength calculation method was carried out in the similar manner as simultaneous equation method. While diclofenac sodium was estimated by using two wavelength calculation method. For simultaneous estimation of diclofenac sodium and rabeprazole, methanol was used as the solvent. The set of two wavelengths 246 and 266 nm were selected for estimation of diclofenac sodium from combined dosage form, on the basis of principle that, absorbance difference between two points on mixture spectra is directly proportional to concentration of component of interest and independent of interfering component.

**Standardization of the method:** To check the validity of the selected wavelengths, several dilutions of pure drug samples of diclofenac sodium and rabeprazole were prepared separately. These dilutions were subjected to determination of absorbance values at 327 nm and the absorbance difference values at respective set of two wavelengths for estimation of rabeprazole and diclofenac sodium respectively.

It was observed that in case of rabeprazole standard drug solution, the absorbance differences value were zero at 246 and 266 nm for all dilutions. Thus it was assured that the set of two wavelengths selected were proper.

**Preparation of calibration curve:** For preparation of calibration curve in estimation of diclofenac sodium, five mixed standard of pure drug containing different concentration of 10-60 µg/mL of both the drugs were prepared in methanol. All standards were subjected to determine absorbance at selected wavelengths using methanol as blank. Absorbance difference values were measured at 246 and 266 nm and calibration curve was plotted shown in Fig. 4 between concentration of diclofenac sodium and absorbance difference value at selected wavelengths.

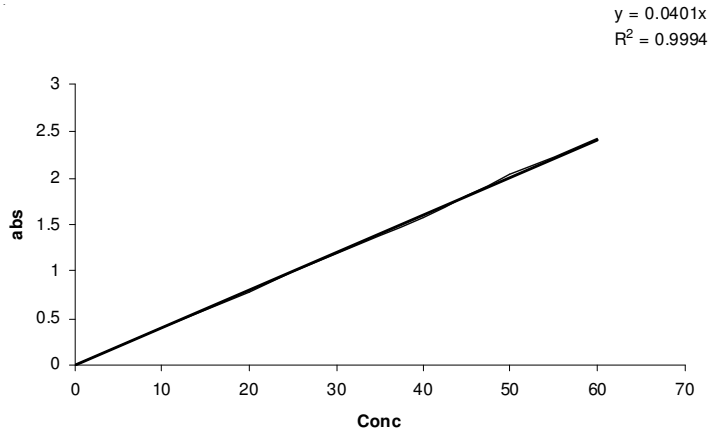


Fig. 4. Calibration for direct determination of diclofenac sodium

**Analysis of commercial formulations:** In case of simultaneous equation method, 20 tablets were accurately weighed and average weight per tablet was determined. Tablets were crushed to fine powder and tablet powder equivalent to rabeprazole 10 mg was accurately weighed and extracted four times with 20 mL portion of methanol and filtered through Whatman filter paper no. 41 into 100 mL volumetric flask. Filter paper was washed with methanol, added washing to the filtrate. From this solution 1 mL transferred to another 10 mL volumetric flask so as to get concentration of 10 µg/mL. The absorbance of dilution was measured at 274 and 327 nm, respectively. Concentration of rabeprazole was determined directly from the respective calibration curve and concentration of diclofenac sodium was calculated using above absorptivity equation. Analysis of commercial formulations by two wavelength method was carried out in the same way except that, in the estimation of diclofenac sodium, absorbance difference value of sample solution was recorded at 246 and 266 nm and determined the concentration of diclofenac sodium using respective calibration curve. The analysis procedure was repeated five times for both the marketed formulation and result of analysis of tablet formulation are reported in Table-2.

TABLE-2
ANALYSIS OF MARKETED FORMULATION OF
DICLOFENAC SODIUM AND RABEPRAZOLE

| Formulations | Label claim | | % Label claim estimated* | | SD | | RSD | | Coefficient of variance | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Diclo | Rabe | Diclo | Rabe | Diclo | Rabe | Diclo | Rabe | Diclo | Rabe |
| Simultaneous equation method | | | | | | | | | | |
| A | 100 | 20 | 99.8 | 100.54 | 0.8973 | 0.7645 | 0.00892 | 0.00766 | 0.8921 | 0.7656 |
| B | 100 | 20 | 100.12 | 100.13 | 0.7314 | 0.8549 | 0.00795 | 0.00831 | 0.7954 | 0.8313 |
| Two wavelength calculation method | | | | | | | | | | |
| A | 100 | 20 | 100.58 | 99.32 | 0.7404 | 0.3098 | 0.00749 | 0.00312 | 0.7489 | 0.3125 |
| B | 100 | 20 | 99.32 | 99.89 | 0.9606 | 0.2986 | 0.00965 | 0.00294 | 0.9651 | 0.2949 |

*Each value is an average of five determinations.

**Recovery studies:** Recovery studies were carried out for both the marketed formulations by addition of known quantity of standard drug solution to pre analyzed tablet sample solution at three different concentration levels. The concentration of drug in final dilution was determined after addition of known concentration of pure drug and determined the percentage recovery after deduction of concentration of drug in original tablet sample. Results of recovery studies are reported in Table-3.

TABLE-3
RECOVERY STUDIES OF DICLOFENAC SODIUM AND RABEPRAZOLE

| Method | Formulations | Amount added to final dilution (µg/mL) | | Amount Recovered (µg/mL) | | Recovery (%) | |
|---|---|---|---|---|---|---|---|
| | | Diclo | Rabe | Diclo | Rabe | Diclo | Rabe |
| Simultaneous equation method | A | 2 | 2 | 1.96 | 2.01 | 98.01 | 100.55 |
| | | 4 | 4 | 4.05 | 4.08 | 101.25 | 102.00 |
| | | 6 | 6 | 5.96 | 6.08 | 99.34 | 101.33 |
| | B | 2 | 2 | 1.98 | 2.01 | 99.00 | 100.50 |
| | | 4 | 4 | 3.95 | 4.05 | 98.75 | 101.25 |
| | | 6 | 6 | 5.97 | 6.03 | 99.50 | 100.53 |
| Two wavelength calculation method | A | 2 | 2 | 1.97 | 2.04 | 98.50 | 102.00 |
| | | 4 | 4 | 4.03 | 3.94 | 100.75 | 98.52 |
| | | 6 | 6 | 6.05 | 6.08 | 100.83 | 101.33 |
| | B | 2 | 2 | 2.01 | 1.96 | 100.53 | 98.00 |
| | | 4 | 4 | 4.04 | 3.99 | 101.00 | 99.75 |
| | | 6 | 6 | 5.97 | 5.94 | 99.50 | 99.00 |

## RESULTS AND DISCUSSION

The first technique used for estimation of diclofenac sodium in presence of rabeprazole involves formation and solving of absorptivity equation, methanol used as the solvent. It requires only accurately determined absorptivity of the two drugs at 274 nm. Percentage label claim estimated for two drugs were found to be in the

range of 99-101 % for diclofenac sodium and 100-101 % for rabeprazole. The respective values of standard deviation were in the range of 0.7314-0.8973 for diclofenac sodium and 0.7645-0.8549 for rabeprazole. Percentage recovery was found in the range of 98-102 % for diclofenac sodium and 100-102 % for rabeprazole for two different batches of tablet formulations of diclofenac sodium and rabeprazole.

The second technique used for estimation of diclofenac sodium in presence of rabeprazole makes use of two wavelength calculation so as to remove interference between two components. Set of two wavelengths selected for estimation of diclofenac sodium were 246 and 266 nm. Percentage label claim estimated for drugs from two different batches of tablet formulation were found to be in the range of 99-101 % for diclofenac sodium and 99-100 % for rabeprazole. The respective values of standard deviation were in the range of 0.7404-0.9606 and 0.2986-0.3098. Percentage recovery was found in the range of 98-101 % for diclofenac sodium and 98-102 % for rabeprazole.

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