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# Simultaneous Estimation of Drotaverine HCl and Mefenamic Acid in Tablet Dosage Form Using Spectrophotometric Method

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A simple, fast an precise simultaneous estimation method using Vierodt's method has been developed for the simultaneous determination of drotaverine HCl and mefenamic acid in pure and combined tablet dosage forms. Shimadzu UV-1700 instrument was used and the $\lambda_{max}$ of drotaverine HCl and mefenamic acid was found to be 228 and 288 nm, respectively using methanol and 0.01 M sodium hydroxide in the ratio of 9:1. Drotaverine HCl and mefenamic acid were found to be linear in the concentration range of 2-12 µg/mL and 4-24 µg/mL, respectively at their respective wavelengths. Amount found for drotaverine HCl and mefenamic acid was found to be 80.08 and 250.79 mg/tablet, respectively. Percentage recovery range was found to be within 99.9-100.3 % for drotaverine HCl and 99.80-100.08 % for mefenamic acid. The percentage RSD was found to be lower than 2 % proves that the method is precise. The application of simultaneous equation method by UV spectroscopy can be employed for the estimation of drotaverine HCl and mefenamic acid for routine analysis for a combination containing these two components in pure and tablet dosage forms.

**Key Words: Drotaverine HCl, Mefenamic acid, Simultaneous equation method.**

## INTRODUCTION

Drotaverine HCl is an isoquinoline derivative. Chemically, it is 1-[3,4-diethoxyphenyl)methylene]-6,7-diethoxy-1,2,3,4-tetrahydro isoquinoline HCl. Its empirical formula is $C_{24}H_{31}NO_4$.HCl and molecular weight is 433.97 g/mol. Its antispasmodic effect is mediated *via* inhibition of phosphodiesterase-IV specific for smooth muscle. It acts to correct cyclic AMP and calcium imbalance at the spastic site and thereby relieves smooth muscle spasm and pain.

Mefenamic acid[1-4] is an orally administered amino benzoic acid derivative on a variety. It forms the class of non-steroidal antiinflammatory drug (NSAID). Chemically, it is 2-(2,3-dimethylphenyl)amino benzoic acid. Its empirical formula is $C_{15}H_{15}NO_2$ and molecular weight is 241.28 g/mol. The mode of action of mefenamic acid is largely based on the inhibition of prostaglandin synthesis. It also inhibits the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

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The earlier literature survey[5-15] reveals the analytical methods like UV, HPLC and HPTLC and available for determination of these drugs individually and other combinations in pharmaceuticals and biological preparations. There is no method has been reported for the estimation of drotaverine HCl and mefenamic acid simultaneously. In the present investigation an attempt was made to develop a simple and economical spectrophotometric method[16,17] with greater precision, accuracy and sensitivity for the simultaneous estimation of drotaverine HCl and mefenamic acid in pure and tablet dosage forms.

## EXPERIMENTAL

Methanol and sodium hydroxide pellets were of analytical grade. Spectral absorbance measurements were made on Shimadzu UV-1700 with 10 mm matched quartz cell. The commercially available tablets were procured from the local market.

**Solvent solution:** The solvent solution used for this study was methanol:0.1 M sodium hydroxide which was prepared in the ratio of 9:1.

**Preparation of standard stock:** Standard stock solutions of drotaverine HCl and mefenamic acid were prepared separately by dissolving about 40 mg of drotaverine HCl standard individually in solvent solution and made up to 100 mL volume with solvent solution dissolving about 125 mg of mefenamic acid standard individually in solvent solution and made up to 100 mL volume with solvent solution.

**Working standard solution:** From the above stock solution 1, 2 and 3 mL of drotaverine HCl and mefenamic acid were transferred to 100 mL volumetric flasks which were then made up to volume with mobile phase to give final concentrations of 4, 8 and 12 µg/mL of drotaverine HCl and 12.5, 25 and 37.5 µg/mL of mefenamic acid. The optical characteristics of drotaverine HCl and mefenamic acid were shown in Table-1.

TABLE-1
OPTICAL CHARACTERISTICS AND STATISTICAL DATA OF THE REGRESSION EQUATION

| Parameters | Drotavarine HCl | Mefenamic acid |
|---|---|---|
| Absorption maximum (nm) | 228 | 288 |
| Beer's law limit (µg/mL) | 2-12 | 4-24 |
| Correlation coefficient | 1.0 | 0.9997 |
| Regression equation | 0.0929x - 0.001 | 0.0477x + 0.0016 |
| Intercept (a) | -0.001 | 0.0016 |
| Slope (b) | 0.0929 | 0.0477 |

**Linearity and calibration:** The stock solution of drotaverine HCl was suitably diluted with solvent solution to provide varying concentrations of 2,4,6,8,10 and 12 µg/mL which were scanned at its respective absorption maxima and the absorbances were plotted against concentration.

The stock solution of mefenamic acid was suitably diluted with solvent solution to provide varying concentrations of 4,8,12,16,20 and 24 µg/mL, which were scanned at its respective absorption maxima and the absorbances were plotted against concentration. From the graph it was found that the Beer's law limit lies between 2-12 µg/mL for drotaverine HCl and 4-24 µg/mL for mefenamic acid. The regression analysis was carried out for calibration graph to find out correlation coefficient (r), intercept and slope of the regresssion line which were estimates the degree of linearity. Correlation coefficient was found out to be 1.0 for drotaverine HCl and 0.9997 for mefenamic acid, respectively The overlain spectra of drotaverine HCl and mefenamic acid were depicted in Figs. 1 and 2.

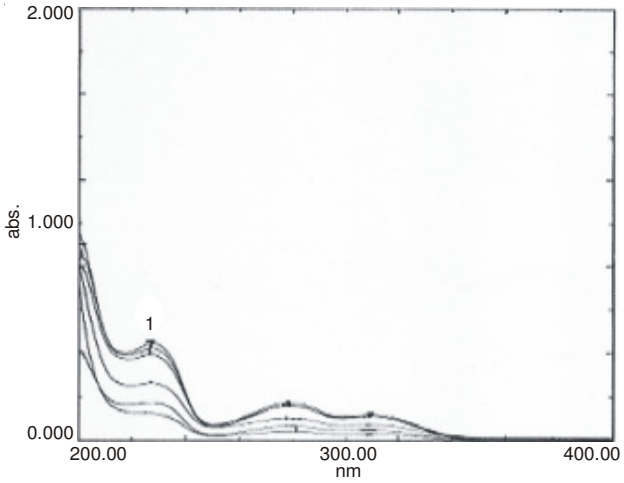


Fig. 1. Overlay spectra of drotaverine HCl standard by UV method

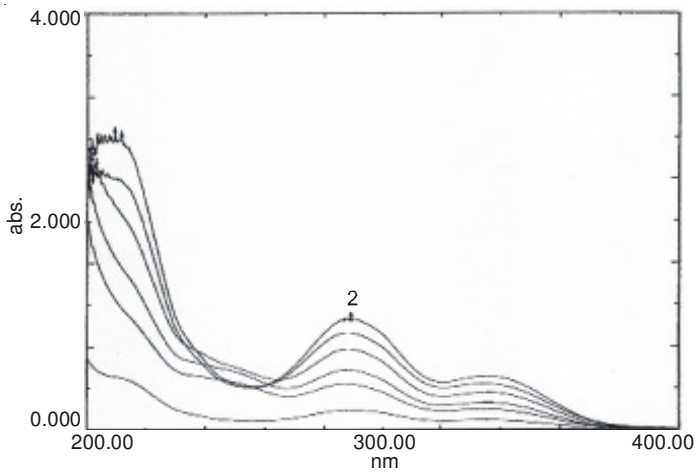


Fig. 2. Overlay spectra of mefenamic acid standard by UV method

**Simultaneous equation method**

**Preparation of sample solution:** Twenty tablets were weighed accurately and grounded to fine powder. An accurately weighed quantity of powder equivalent to 40 mg of drotaverine HCl and transferred to 100 mL volumetric flask. The contents in the flask was dissolved with minimum amount of solvent solution, sonicated for 0.5 h and then diluted to 100 mL with solvent solution. The resultant was filtered with Whatmann filter No. 4. The filtrate was further diluted to made concentrations of 4, 8, 12 µg/mL of drotaverine HCl and 12.5, 25, 37.5 µg/mL of mefenamic acid, respectively. These dilutions were scanned over the range 200-400 nm.

**Assay:** Mixed standards and sample solutions were scanned over the range of 200-400 nm in the spectral mode. The concentration of each component was obtained by analysis of the spectral data of sample solution with reference to that of three mixed standard dilutions in the spectral mode of analysis.

The concentration of each component was obtained by analysis of the spectral data of sample solution using the Cramer's rule. Amount of drug present in sample was calculated and given in Table-2. Statistical analysis data's were presented in Table-3 and the overlain spectra of sample formulation was shown in Fig. 3.

$$\text{Amount of drug present} = \frac{\text{Concentration} \times \text{Dilution factor} \times \text{Average weight}}{\text{Weight taken}}$$

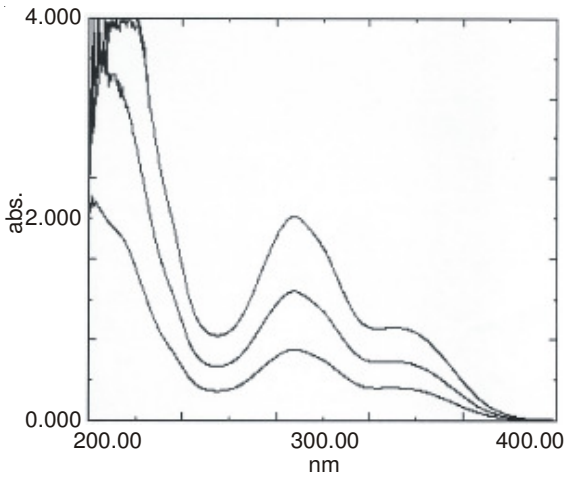


Fig. 3. Overlay spectra of sample formulation by UV method

TABLE-2
ASSAY OF SAMPLE FORMULATION BY SIMULTANEOUS EQUATION METHOD

| Sample | Label claim (mg/tab) | Amount found (mg) | Label claim (%) |
|---|---|---|---|
| Drotaverine HCl | 80 | 80.08 | 100.14 |
| Mefenamic acid | 250 | 250.79 | 100.32 |

*Mean of five determinations.

TABLE-3
STATISTICAL VALIDATION

| Drug | Label claim (mg/Tablet) | % Amount estimated* | S.D | % RSD | SE |
|---|---|---|---|---|---|
| Drotaverine HCl | 80 | 100.14 | 1.1987 | 1.4968 | 0.5360 |
| Mefenamic acid | 250 | 100.32 | 1.4969 | 0.5969 | 0.6694 |

**Method validation:** As per ICH guidelines the method is validated and following parameters were evaluated. Accuracy of the method was checked by recovery studies. Precision of the method was studied by inter-day and intra-day analysis of multiple samplings of homogenous sample and expressed as % RSD.

**Recovery studies:** Accuracy, specificity of the proposed method was satisfied by conducting recovery studies. Recovery studied were carried out by mixing a known quantity of standard drug in three levels to preanalyzed sample solution and the contents were reanalyzed by the proposed method. The data were given in Table-4.

TABLE-4
RECOVERY DATA

| Drug | Amount added (µg) | Amount recovered* (µg) | % Recovery* | Average recovery (%) | % RSD |
|---|---|---|---|---|---|
| Droverine HCl 80 mg | 4.0 | 4.012 | 100.30 | 100.14 | 0.214 |
| | 8.0 | 7.992 | 99.90 | | |
| | 12.0 | 12.028 | 100.23 | | |
| Mefenamic acid 250 mg | 12.5 | 12.483 | 99.86 | 99.92 | 0.148 |
| | 25.0 | 25.023 | 100.08 | | |
| | 37.5 | 37.429 | 99.80 | | |

*Mean of three determinations at each level.

**Repeatability Studies:** Repeatability is given by inter-day and intra-day precision. Intra-day precision was determined by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was determined by analyzing the three different concentration of the drug for three days in a week and the results were presented in Table-5.

TABLE 5
REPEATABILITY STUDIES

| Drug | Amount taken (µg/mL) | Inter day | | Intra day | |
|---|---|---|---|---|---|
| | | Amount found (µg/mL) | % RDS | Amount found (µg/mL) | % RSD |
| Drotaverin HCl | 4.0 | 4.0555 | 1.67 | 4.0311 | 0.50 |
| | 8.0 | 6.0014 | 0.34 | 6.0095 | 0.21 |
| | 6.0 | 7.8902 | 0.36 | 7.9129 | 0.66 |
| Mefenamic acid | 12.50 | 12.0223 | 0.17 | 12.0414 | 0.05 |
| | 18.75 | 18.7355 | 0.13 | 18.7598 | 0.02 |
| | 25.00 | 24.9552 | 0.46 | 25.0399 | 0.28 |

*Mean of three determination; RSD-relative standard deviation.

## RESULTS AND DISCUSSION

Simultaneous estimation of drotaverine HCl and mefenamic acid was carried out by simultaneous equation method.

**Absorption maxima:** The absorption maxima of the proposed drug were determined scanning in the entire UV region between 200-400 nm. Absorption maxima were found to be 228 and 288 nm, respectively.

**Beer's law concentration range linearity:** The method was validated by linearity studies which were performed by plotting five different concentrations of standard solution against their respective absorbances. Drotaverine HCl and mefenamic acid were found to be linear in the concentration range of 2-12, 4-24 µg/mL, respectively. Linearity was expressed in terms of linear regression equation $Y_{\text{drotaverine HCl}}$ : 0.0929x - 0.001; $Y_{\text{mefenamic acid}}$ : 0.0477x + 0.0016 and correlation co-coefficient values were found to be 1.0 and 0.9997 for drotaverine HCl and mefenamic acid, respectively.

**Assay:** The quantitative estimation was carried out on marketed tablets (Drotin M) and the amount was found to be 80.08 and 250.79 mg/tablet, respectively. The results obtained from the quantitative work were subjected to statistical analysis. The percentage purity values near to 100 % w/w and percentage RSD values less than 2 % and low standard error values shows that the method is accurate.

**Accuracy:** The proposed method was further validated by recovery analysis performed by adding known concentrations of standard drugs to preanalyzed sample solution at three different levels. Percentage recovery range was found to be within 99.9-100.3 % for drotaverine HCl and 99.80-100.08 % for mefenamic acid.

**Repeatability studies:** Repeatability is given by inter-day and intra-day precision. Intra-day precision was determined by analyzing, the three different concentration of drug for three times in the same day. Inter-day precision was determined by analyzing the three different concentration of the drug for three days in a week were determined. The percentage RSD was found to be lower than 2 % proves that the method is precise.

### Conclusion

The application of simultaneous equation method by UV spectroscopy can be employed for the estimation of drotaverine HCl and mefenamic acid for routine analysis for a combination containing these two components in tablet dosage forms.

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