Simultaneous Estimation of Mefenamic Acid and Ethamsylate in Tablets

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The simple spectrophotometric methods for the determination of mefenamic acid and ethamsylate in pharmaceutical formulations have been developed. The methods are based on the additivity of absorbances and the determination of graphical absorbance ratio at two selected wavelengths, one being the isoabsorptive point for the two drugs (301 nm) and the other being the absorption maximum of mefenamic acid (336 nm) and ethamsylate (305 nm). The Beer Lambert's law is obeyed for mefenamic acid in the concentration range 4-28 µg/ml and for ethamsylate is 10-60 µg/ml. Both the methods were found to be simple, rapid, and accurate and can be adopted in routine analysis of drugs in formulations. The accuracy and reproducibility of the proposed method was statistically validated by recovery studies.

Mefenamic acid, N-(2,3-Xylyl)-2-aminobenzoic acid is an analgesic and non-steroidal antiinflammatory drug with haemostatic drug ethamsylate, 2, 5-dihydrobenzene sulfonic acid used as combination drug therapy for treatment of painful menstruation. Mefenamic acid is official in BP¹ USP² and IP³, while Ethamsylate is official in BP⁴. The BP suggest a spectrophotometric and IP suggest a potentiometric method for the assay of mefenamic acid in bulk drugs. BP suggests potentiometric method for the estimation of ethamsylate in bulk drugs. Literature survey revealed that HPLC⁵ and spectrophotometric⁶ methods have been reported for the estimation of mefenamic acid and spectrophotometric⁷ and chemiluminescence⁸ methods for the ethamsylate in pharmaceutical dosage forms. The review of literature revealed that there is no simultaneous method for the estimation of the above drugs in combined dosage forms, which strongly advocates the need of simple, rapid and accurate simultaneous method for the routine analysis of the combined dosage forms.

The Shimadzu Pharmaspec 1700 UV/Vis spectrophotometer with 10 mm matched quartz cells was used for experiments. The chemicals used were of analytical grade. The commercially available marketed tablet brands Sylate-M (Emcure pharma, Pune) and E-sylate M (Saf Fermion Ltd., Kolkata) containing 500 mg of mefenamic acid and 500 mg of ethamsylate has been used for estimation.

Standard stock solution of mefenamic acid and ethamsylate were prepared separately by dissolving 100 mg each (accurately weighed) of standard mefenamic acid and ethamsylate in 10 ml 0.1 N NaOH and 90 ml of methanol. Working standard solutions (A) and (B) were further prepared by taking 1ml of stock solution of mefenamic acid and ethamsylate in 10 ml volumetric flasks and made up the volume with methanol.

Simultaneous equations method or Vierodt’s method⁹ was employed as the method I. Overlaid spectra of standard solutions of mefenamic acid and ethamsylate were scanned (fig. 1). Mefenamic acid shows absorption maxima at 336 nm and ethamsylate shows at 305 nm. The calibration curves for mefenamic acid and ethamsylate were prepared in the concentration range of 4-28 µg/ml and 10-60 µg/ml at both the wavelengths respectively i.e. 336 nm and 305 nm. The absorptivities/specific absorbance were determined for both the drugs at both the wavelengths and following equations were used, \( A_1 = 231.14C_x + 29.33C_y \) (1) and \( A_2 = 331C_x + 102.50C_y \) (2), where \( A_1 \) and \( A_2 \) are absorbances at 336 nm and 305 nm, respectively, \( C_x \) and \( C_y \) are concentrations of mefenamic acid and ethamsylate, respectively, 231.14 and 331 are absorptivities of mefenamic acid at 336 nm and 305 nm, respectively, 29.33 and 102.5 are absorptivities of ethamsylate at 336 nm and 305 nm, respectively. The

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mixture concentration was determined by using the Eqns. (1) and (2).

In the second method (Method II), graphical absorbance ratio was used, which is based on the method used by Ghanem et al.\textsuperscript{10} and takes advantage of iso-absorptive point\textsuperscript{11}, of the two drugs i.e. the wavelength of equal absorptivity of the two components of the mixture. The iso-absorptive point was 301 nm (fig. 1). The other wavelength selected is the absorption maximum of one of the components. In this case it was 336 nm, the absorption maximum of mefenamic acid. The concentrations of the two components are related to the ratio of the absorbances at these two wavelengths. The absorbance of the mixture was noted at 336 nm and 301 nm. Calibration curves of mefenamic acid and ethamsylate were plotted in the concentration range 4-28 µg/ml and 10-60 µg/ml respectively (range for which Beer Lambert’s law followed). The absorptivity coefficients were determined, and the values were substituted in the Eqns. 3 and 4 to give the results.

The methods developed were found to be accurate, simple and rapid, for routine simultaneous analysis of the formulations. The first method is based on the determination of content of the mefenamic acid and ethamsylate directly from the Eqns. 1 and 2. The second method is based on the absorbance ratio and the absorptivity coefficients were determined, and the values were substituted in the Eqns. 3 and 4 to give the results. The reproducibility, repeatability and accuracy of these

![Fig. 1: Overlain spectra of mefenamic acid and ethamsylate. The (-) Line indicates mefenamic acid and (-----) indicates ethamsylate.](image)

<table>
<thead>
<tr>
<th>Method</th>
<th>Tablet brand</th>
<th>Tablet component</th>
<th>Label claim* (mg/tab)</th>
<th>Amount found* (mg/tab)</th>
<th>SD*</th>
<th>%RSD*</th>
<th>SE*</th>
<th>‘t’ Calc.*</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>Mefenamic acid</td>
<td>500</td>
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<td>0.3184</td>
<td>0.0159</td>
<td>0.1299</td>
<td>0.2547</td>
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<td></td>
<td>B</td>
<td>Ethamsylate</td>
<td>500</td>
<td>496.47</td>
<td>1.6315</td>
<td>0.0843</td>
<td>0.6659</td>
<td>0.3052</td>
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<td></td>
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<td>498.25</td>
<td>0.2916</td>
<td>0.0146</td>
<td>0.1190</td>
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<td></td>
<td></td>
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<td>500</td>
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<td>0.4264</td>
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<td></td>
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<td>0.0048</td>
<td>0.0394</td>
<td>0.0772</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethamsylate</td>
<td>500</td>
<td>497.50</td>
<td>0.0964</td>
<td>0.0048</td>
<td>0.0393</td>
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<td>A</td>
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<td>0.0665</td>
<td>0.0033</td>
<td>0.0271</td>
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<tr>
<td></td>
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<td>0.0670</td>
<td>0.0034</td>
<td>0.0273</td>
<td>0.0536</td>
</tr>
</tbody>
</table>

*Average of six determinations, Theoretical ‘t’ values are at 95% confidence level for (n-1) degrees of freedom. ‘t’ (0.05,5) = 2.571, SD is standard deviation; % RSD is percent relative standard deviation, SE is standard error, Method I; Simultaneous equations and Method II; Graphical absorbance ratio method.

### Table 2: Compilation of Results of Drug Recovery Study

<table>
<thead>
<tr>
<th>Method</th>
<th>Tablet brand</th>
<th>Percent recovery ± SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mefenamic acid</td>
<td>Ethamsylate</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
<td>102.5±0.39</td>
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<tr>
<td></td>
<td>B</td>
<td>101.25±0.18</td>
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<tr>
<td>II</td>
<td>A</td>
<td>100.10±0.11</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>100.25±0.08</td>
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</tbody>
</table>

*Average of six determinations, SD is standard deviation, Method I; Simultaneous equations, Method II; Graphical absorbance ratio method.
A simple, specific, accurate and precise reverse phase high pressure liquid chromatographic method has been developed for the simultaneous determination of nimesulide and tizanidine from tablets. The sample was analyzed using methanol: water in the ratio of 65:35, pH adjusted to 4.15 with orthophosphoric acid on an octadecylsilane C18 column. The effluent was monitored at 1.4 ml/min flow rate using 307 nm as detecting wavelength. The linear dynamic ranges for nimesulide and tizanidine were 0.2-1.0 µg/ml and 10-50 µg/ml respectively. Coefficients of correlation obtained for nimesulide and tizanidine were 0.998 and 0.996 respectively.

Simultaneous RPHPLC Determination of Nimesulide and Tizanidine in Tablets

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Nimesulide is an antiinflammatory drug. Chemically, nimesulide is N-(4-nitro-2-phenoxyphenyl)methane sulphonamide. It is approved for used in treatment of musculoskeletal disorder, dysmenorrhoea, thrombophlebitis and dental pain, inflammation. Some HPLC and spectrophotometric methods have been reported in the literature for its estimation. Tizanidine is a pharmaceutical agent used for the treatment of vasomotor symptoms of multiple sclerosis, including hot flashes, flushing, and sweating. Some of these methods were found to be good which is evidenced by low values of standard deviation, percent relative standard deviation and standard error (Table 1). The percent range of error (at 95% confidence level) shows the precision of the methods. The accuracy and reproducibility of the proposed methods was confirmed by recovery experiments by adding known amount of the drugs to the preanalyzed formulations and reanalyzing the mixture by proposed methods (Table 2). The percent recovery obtained indicates non-interference from the excipients used in the formulations. Hence, these can be successfully applied for simultaneous estimation of mefenamic acid and ethamsylate in pharmaceutical formulations, as both the methods are simple, sensitive, precise and economical as well.

ACKNOWLEDGEMENTS

The authors wish to thank the Director, Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur for providing necessary facilities and AICTE New Delhi for financial assistance under the scheme RPS, also thanks to Mercury Health Care Pvt. Ltd. Mumbai and Blue Cross Labs. Ltd. Mumbai for providing the authentic sample of drugs.

REFERENCES


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Accepted 6 April 2007
Revised 3 July 2006
Received 23 November 2005