PARASETAMOL VE MEFENOKSALON'UN ÜÇÜNÇÜ TÜREV UV SPEKTROFOMETRİSİ İLE YANYANA MİKTAR TAYINI

SIMULTANEOUS DETERMINATION OF PARACETAMOL AND MEPHENOXALONE BY THIRD-DERIVATIVE UV SPECTROPHOTOMETRY

Münevver AÇIKKOL

SUMMARY

In this paper, the simultaneous determination of paracetamol and mephenoaxalone in admixture was realised by third-derivative UV spectrophotometry using a "zero-crossing" technique of measurement at 239.4 nm and 249.8 nm for paracetamol and mephenoaxalone, respectively. Linear correlations over the concentration ranges of 5-20 µg.mL⁻¹ for paracetamol (r = 0.9999) and 5-13 µg.mL⁻¹ for mephenoaxalone (r = 0.9994) were obtained. The proposed method was applied to a commercially available tablet. The relative standard deviations obtained are 0.33 % and 1.17 % and, the average percentage recoveries are 99.96 % and 99.46 % for paracetamol and mephenoaxalone, respectively.

ÖZET

Bu çalışmada, üçüncü tür ev spektrofotometrisi ile, parasetamol için 239.4 nm de, mefenoksalon için 249.8 nm de "zero-crossing" yönteminden yararlanılanlar iki madde birarada iken miktar tahminleri gerçekleştirilirdi. Parasetamol için 5-20 µg.mL⁻¹ (r = 0.9999) ve mafenoksalon için 5-13 µg.mL⁻¹ (r = 0.9994) konsantrasyon aralığındada, doğruluk Ölçü grafikleri elde edildi. Yöntem, ilaç piyasasındaki bir tablet uygulandı. Sıralı ile para setamol ve mafenoksalon için standart sapma değerleri 0.33 % ve 1.17 %, ortalama geri kazanma değerleri ise 99.96 % ve 99.46 % dir.

INTRODUCTION

Paracetamol is an analgesic and antipyretic drug widely used alone or in combinations with several other drugs for a number of years. The combination of paracetamol with mephenoaxalone is a muscle relaxant and used for the aches of skeleton muscles and spasms caused by

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anxiety. Several techniques, including titrimetric (1), UV-spectrophotometric (2, 3), derivative UV-spectrophotometric (4-8), colorimetric fluorimetric (10, 11), TLC-densitometric (12), GC (13-15), HPLC(16), GC-MS (18), TDx (19) methods have been published for the determination of paracetamol in both biological fluids and pharmaceutical preparations. Fluorimetric (20), radiometric (20), HPLC (21), calorimetric potentiometric (22) methods have been reported for the determination of mephenoxaline. No method has been published for the simultaneous determination of paracetamol and mephenoxaline. For this purpose, the paper describes a method based on third-derivative UV spectrophotometry.

EXPERIMENTAL PART

Apparatus: A Shimadzu UV-160 double-beam UV-visible spectrophotometer with 1 cm quartz cells was used.

Chemicals: Mephenoxaline and paracetamol were kindly supplied by İlsan İlaç Hammaddeleri ve Sanayii LTD, İstanbul, Turkey. Ethanol was obtained from E.Merck, Dramstadt, FRG.

Stock solutions of paracetamol and mephenoxaline: 1 mg/mL each in ethanol were freshly prepared.

Standard solutions: Suitable aliquots of the paracetamol stock solution (0.5 - 2.5 mL) were transferred into 100 mL calibrated flasks and 0.6 mL of mephenoxaline stock solution was added to each flask and diluted to volume with ethanol. Suitable aliquots of the mephenoxaline stock solution (0.5-2 mL) were transferred into 100 mL calibrated flasks, 2 mL of paracetamol stock solution was added to each flask and diluted to volume with ethanol.

Procedure: The third-derivative spectra of the standard solution against ethanol were recorded at a slit width of 3 nm, a scanning speed of 40 nm/sec., a Δλ of 6.3 nm. The absolute values of the derivative were measured at 239.4 nm and 249.8 nm for the determination of paracetamol and mephenoxaline, respectively. The calibration graphs were prepared by plotting the derivative absorbances of standard solution against their concentrations (μg·mL⁻¹).

Assay procedure for tablets: Twenty tablets were weighed and powdered. An accurately weighed amount of the powder, equivalent to
about 150 mg of paracetamol (it includes about 66.6 mg mephenoxalone) was transferred into a 100 mL calibrated flask. 60 mL of ethanol was added and the mixture was shaken mechanically for an hour. The volume was adjusted to 100 mL with ethanol and filtered through a Whatman No. 42 filter paper. The first 20 mL portion of the filtrate was discarded and 1 mL of the filtrate was diluted to 100 mL with ethanol in a calibrated flask. The absolute values of the third-derivative spectrum of this solution were measured at 239.4 nm and 249.8 nm. The amounts of paracetamol at mephenoxalone in tablets were calculated from the regression equations of the calibration graphs.

RESULTS AND DISCUSSION

The zero-order absorption spectra of paracetamol and mephenoxalone in ethanol were given in Figure-1. Figure-2 shows the zero-order spectrum of the mixture of paracetamol and mephenoxalone.

![Figure 1: The zero-order absorption spectra of paracetamol (P) (20 μg. mL⁻¹) and mephenoxalone (M) (20 μg. mL⁻¹) in ethanol.](image-url)
Figure - 2: The zero-order spectrum of the mixture of paracetamol (10 µg. mL⁻¹) and mepheno- 
oxaline (10 µg. mL⁻¹) in ethanol.

The corresponding third-derivative spectra of paracetamol and mephenoaxalone and their mixture were represented in Figures 3 and 4, respectively.

Figure - 3: The third-derivative spectra of paracetamol (P) (20 µg. mL⁻¹) and mephenoax-
alone (M) (20 µg. mL⁻¹) in ethanol.
Figure - 4: The third-derivative spectrum of the mixture of paracetamol (10 μg/mL\(^{-1}\)) and mephenoxaline (10 μg/mL\(^{-1}\)) in ethanol.

Due to the overlapping of the spectral bands, the total zero-order spectrum cannot be used for the simultaneous determination of paracetamol and mephenoxaline in mixtures. In the third-derivative spectra, zero-crossing wavelengths at 239.4 nm and 249.8 nm were selected for the quantitative determination of paracetamol and mephenoxaline, respectively. Calibration curves were constructed by plotting derivative absorbance values at selected wavelengths against corresponding drug concentrations. Linear correlations over the concentration ranges of 5-20 μg/mL\(^{-1}\) for paracetamol \((r = 0.9999)\) and 5-13 μg/mL\(^{-1}\) for mephenoxaline \((r = 0.9994)\) were obtained. Calibration graphs for paracetamol and mephenoxaline resulted in the following regression equations:

\[
A = 0.0338C - 0.0200 \text{ (paracetamol)}
\]
\[
A = 0.0222C + 0.0386 \text{ (mephenoxaline)}
\]

The time dependence of the signals was studied and no change was observed after 24 hours.

The proposed method was applied to the commercial tablets including paracetamol and mephenoxaline. The assay results were given in Table 1. Relative standard deviation of the method was 0.33 % \((n = 10)\) and 1.17 % \((n = 10)\) for paracetamol and mephenoxaline, respectively.
Table - 1: Results of the simultaneous determination of paracetamol and mephenoxaline in commercial tablets.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Label claim (mg)</th>
<th>n</th>
<th>$\bar{X}$</th>
<th>Relative S.D. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>450</td>
<td>10</td>
<td>450.3</td>
<td>0.33</td>
</tr>
<tr>
<td>Mephenoxaline</td>
<td>200</td>
<td>10</td>
<td>199.7</td>
<td>1.17</td>
</tr>
</tbody>
</table>

The ratio of the quantities of paracetamol to mephenoxaline is 450 : 200 in the commercial tablets. The satisfactory results were obtained from the analysis of the synthetic mixtures containing 450 mg of paracetamol with increasing quantities of mephenoxaline (200-275 mg) and, 200 mg of mephenoxaline with increasing quantities of paracetamol (450-675 mg) (Table-2).

Table - 2: The results of the analysis of the synthetic mixtures.

<table>
<thead>
<tr>
<th>Amount added (mg)</th>
<th>Found (mg)</th>
<th>Recovery %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paracetamol</td>
<td>Mephenoxaline</td>
</tr>
<tr>
<td>450 275</td>
<td>455.6</td>
<td>274.4</td>
</tr>
<tr>
<td>450 250</td>
<td>450.8</td>
<td>249.2</td>
</tr>
<tr>
<td>450* 200*</td>
<td>449.6</td>
<td>200.6</td>
</tr>
<tr>
<td>500 200</td>
<td>493.2</td>
<td>198.8</td>
</tr>
<tr>
<td>550 200</td>
<td>551.2</td>
<td>202.4</td>
</tr>
<tr>
<td>600 200</td>
<td>600</td>
<td>196.2</td>
</tr>
<tr>
<td>675 200</td>
<td>673.2</td>
<td>196.8</td>
</tr>
</tbody>
</table>

Average: 99.96, 99.46
Average deviation: $\pm0.76$, $\pm1.19$

* The amount of the drugs in the commercial tablets.

The proposed method is simple, rapid, sensitive and reproducible. Therefore it can easily be applied to the simultaneous determination of paracetamol and mephenoxaline in tablets for routine analysis.
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REFERENCES


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