PARASETAMOL VE MEFENOKSALON'UN ÜÇÜNÇÜ TÜREV UV SPEKTROFOTOMETRİSİ İLE YANYANA MIKTAR TAYINI

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

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SUMMARY

In this paper, the simultaneous determination of paracetamol and mephenoxaline 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 mephenoxaline, 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 mephenoxaline (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 mephenoxaline, respectively.

ÖZET

Bu çalışmada, üçüncü tür rev spektrofotometrisi ile, paracetamol için 239.4 nm de, mfenoksalon için 249.8 nm de "zero-crossing" ölçüm tekniğinden yararlanarak iki madde birarada iken miktar tayinleri gerçekleştirdi. Paracetamol için 5-20 μg.mL⁻¹ (r = 0.9999) ve mfenoksalon için 5-13 μg.mL⁻¹ (r = 0.9994) konsantrasyon aralığında, doğrulan ölçüler grafikleri elde edildi. Yöntem, ilaç piyasasındaki bir tablete uygulandı. Sırası ile paracetamol ve mfenoksalon 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 mephenoxaline 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 (9), fluorimetric (10, 11), TLC-densitometric (12), GC (13-15), HPLC(16, 17), GC-MS (18), TD$_x$ (19) methods have been published for the determination of paracetamol in both biological fluids and pharmaceutical preparations. Florimetric (20), radiometric (20), HPLC (21), calorimetric and 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, this 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$^{-1}$ 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 solutions against ethanol were recorded at a slit width of 3 nm, a scanning speed of 40 nm/sec., a $\Delta \lambda$ of 6.3 nm. The absolute values of the derivative were measured at 239.4 nm and 249.5 nm for the determination of paracetamol and mephenoxaline, respectively. The calibration graphs were prepared by plotting the derivative absorbances of standard solutions 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 mephenoxal-
one) 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 spec-
trum 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 mephe-
noxalone 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 mephe-
noxalone (M) (20 µg. mL⁻¹) in ethanol.](image)
Figure - 2: The zero-order spectrum of the mixture of paracetamol (10 μg. mL⁻¹) and mephenoxaline (10 μg. mL⁻¹) in ethanol.

The corresponding third-derivative spectra of paracetamol and mephenoxaline 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 mephenoxaline (M) (20 μg. mL⁻¹) in ethanol.
Figure - 4: The third-derivative spectrum of the mixture of paracetamol (10 µg. mL\(^{-1}\)) and mephenoxalnone (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 mephenoxalnone 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 mephenoxalnone, 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 mephenoxalnone (\(r = 0.9994\)) were obtained. Calibration graphs for paracetamol and mephenoxalnone resulted in the following regression equations:

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

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 mephenoxalnone. 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 mephenoxalnone, respectively.
Table - 1: Results of the simultaneous determination of paracetamol and mephenoxalolone in commercial tablets.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Label claim (mg)</th>
<th>n</th>
<th>(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>Mephenoxalolone</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 mephenoxalolone 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 mephenoxalolone (200-275 mg) and, 200 mg of mephenoxalolone 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>450</th>
<th>450</th>
<th>450*</th>
<th>500</th>
<th>550</th>
<th>600</th>
<th>675</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>275</td>
<td>250</td>
<td>200*</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Mephenoxalolone</td>
<td>275.4</td>
<td>249.2</td>
<td>200.6</td>
<td>198.8</td>
<td>202.4</td>
<td>195.2</td>
<td>196.8</td>
</tr>
<tr>
<td>Found (mg)</td>
<td>455.6</td>
<td>450.8</td>
<td>449.6</td>
<td>493.2</td>
<td>551.2</td>
<td>600</td>
<td>673.2</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>101.2</td>
<td>100.1</td>
<td>99.9</td>
<td>98.6</td>
<td>100.2</td>
<td>100.0</td>
<td>99.7</td>
</tr>
<tr>
<td>Mephenoxalolone</td>
<td>99.7</td>
<td>99.6</td>
<td>100.3</td>
<td>99.4</td>
<td>101.2</td>
<td>97.6</td>
<td>98.4</td>
</tr>
<tr>
<td>Recovery %</td>
<td>99.7</td>
<td>99.6</td>
<td>100.3</td>
<td>99.4</td>
<td>101.2</td>
<td>97.6</td>
<td>98.4</td>
</tr>
</tbody>
</table>

* 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 mephenoxalolone in tablets for routine analysis.
ACKNOWLEDGEMENTS

I wish to thank The Head of Council of Forensic Medicine Prof. Dr. Şemsı Gök, The Head of Dept. Chemistry of Council of Forensic Medicine and The Director of Institute of Forensic Medicine Prof. Dr. Sevil Atasoy for their help in letting me to use all the facilities of the Forensic Medicine Council.

REFERENCES


(Received October 8, 1990)