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PARASETAMOL VE MEFENOKSALON'UN ÜÇÜNCÜ TÜREV UV SPEKTROFOMETRİSİ İLE YANYANA MİKTAR TAYİNİ

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

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SUMMARY

In this paper, the simultaneous determination of paracetamol and mephenoxalone 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 mephenoxalone, respectively. Linear correlations over the concentration ranges of 5-20 $\mu g.mL^{-1}$ for paracetamol (r = 0. 9999) and 5-13 $\mu g.mL^{-1}$ for mephenoxalone (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 mephenoxalone, respectively.

ÖZET

Bu çalışmada, üçüncü türev spektrofotometrisi ile, parasetamol için 239.4 nm de, mefenoksalon için 249.8 nm de "zero-crossing" ölçüm tekniğinden yararlanılarak iki madde birarada iken miktar tayinleri gerçekleştirildi. Parasetamol için 5-20 $\mu g.mL^{-1}$ (r = 0. 9999) ve mefenoksalon için 5-13 $\mu g.mL^{-1}$ (r = 0.9994) konsantrasyon aralığında, doğrusal ölçü grafikleri elde edildi. Yöntem, ilaç piyasasındaki bir tablete uygulandı. Sırası ile parasetamol ve mefenoksalon için standart sapma değerleri 0.33 % ve 1.17 %, ortalama geri kazanma değerleri ise 99.96 % ve 99.46 % dır.

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 mephenoxalone 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-spectroph metric (2, 3), derivative UV-spectrophotometric (4-8), colorimetric fluorimetric (10, 11), TLC-densitometric (12), GC (13-15), HPLC(16, GC-MS (18), TD_x (19) methods have been published for the determ tion of paracetamol in both biological fluids and pharmaceutical pre ations. Fluorimetric (20), radiometric (20), HPLC (21), calorimetric potentiometric (22) methods have been reported for the determinatio mephenoxalone. No method has been published for the simultaneous termination of paracetamol and mephenoxalone. For this purpose, paper describes a method based on third-derivative U spectrophotometry.

EXPERIMENTAL PART

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

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

Stock solutions of paracetamol and mephenoxalone : 1 mg.m each in ethanol were freshly prepared.

Standard solutions : Suitable aliquots of the paracetamol stock lution (0.5 – 2.5 mL) were transferred into 100 mL calibrated flas and 0.6 mL of mephenoxalone stock solution was added to each fla and diluted to volume with ethanol. Suitable aliquots of the mephenox lone stock solution (0.5-2 mL) were transferred into 100 ml calibrat flasks, 2 mL of paracetamol stock solution was added to each flask a diluted to volume with ethanol.

Procedure : The third-derivative spectra of the standard solutio against ethanol were recorded at a slit width of 3 nm, a scanning spe of 40 nm/sec., a $\Delta\lambda$ of 6.3 nm. The absolute values of the derivative we measured at 239.4 nm and 249.8 nm for the determination of paracet mol and mephenoxalone, respectively. The calibration graphs were pr pared by plotting the derivative absorbances of standard solutio against their concentrations ($\mu g.mL^{-1}$).

Assay procedure for tablets : Twenty tablets were weighed an powdered. An accurately weighed amount of the powder, equivalent t

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.

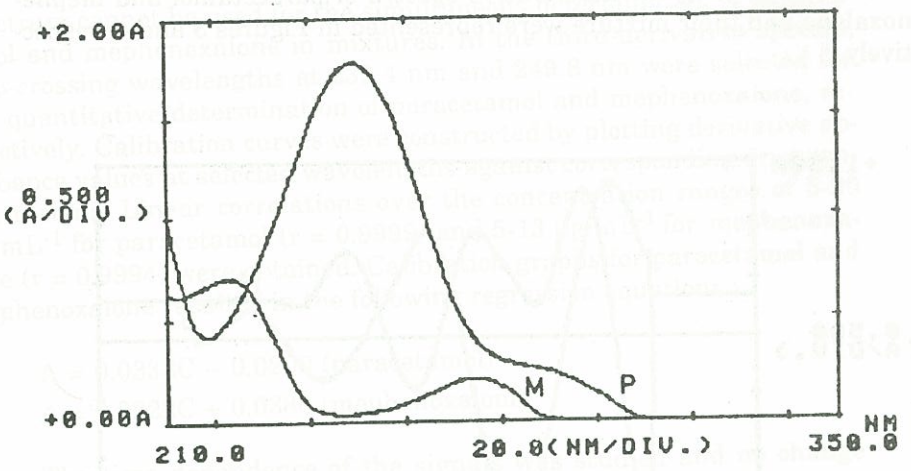

Figure - 1: The zero-order absorption spectra of paracetamol (P) (20 μg. mL^{-1}) and mephenoxalone (M) (20 μg. mL^{-1}) in ethanol.

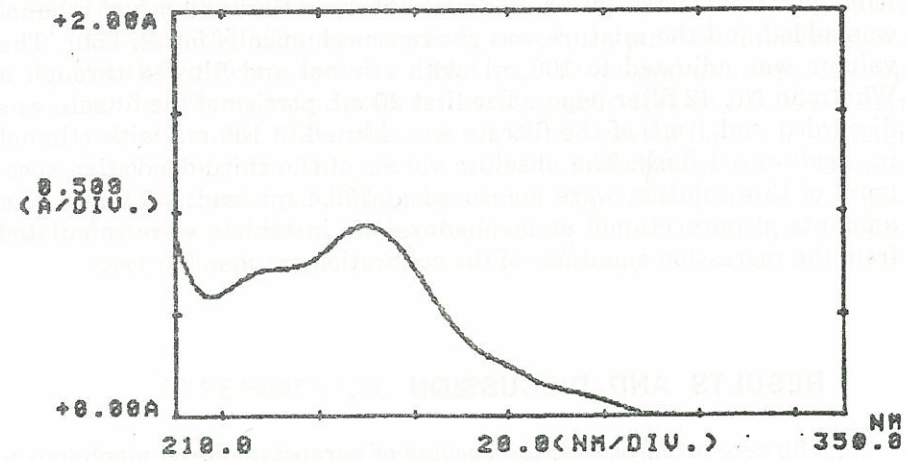

Figure - 2: The zero-order spectrum of the mixture of paracetamol (10 µg. mL^{-1}) and mephenoxalone (10 µg. mL^{-1})in ethanol.

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

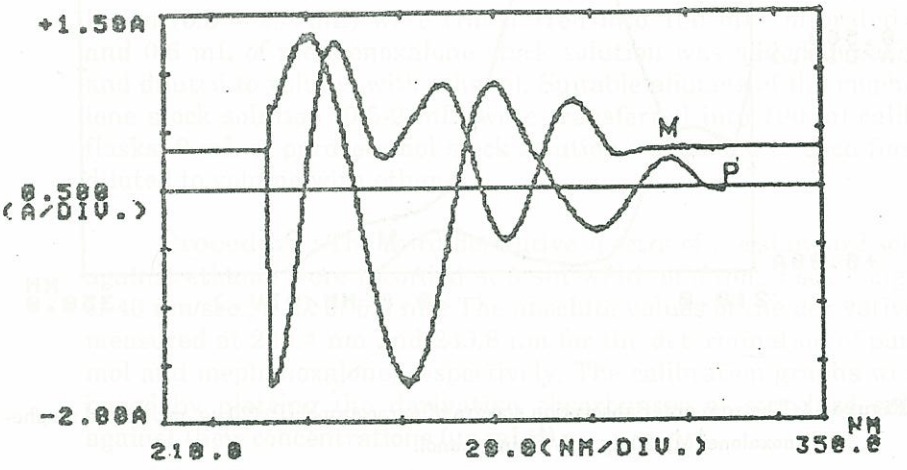

Figure - 3: The third-derivative spectra of paracetamol (P) (20 µg. mL^{-1}) and mephenoxalone (M) (20 µg. mL^{-1})in ethanol.

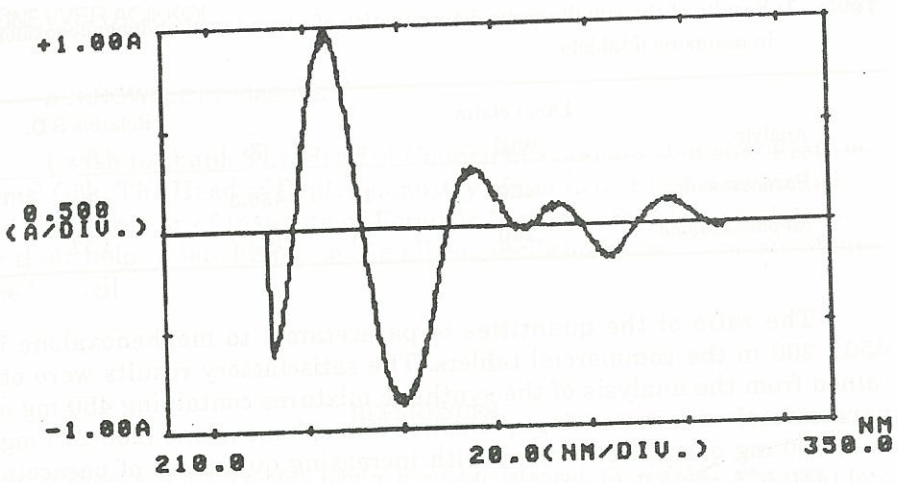

Figure - 4: The third-derivative spectrum of the mixture of paracetamol (10 μg. mL^{-1}) and mephenoxalone (10 μg. mL^{-1})in ethanol.

Due to the overlapping of the spectral bands, the total zero-order spectrum cannot be used for the simultaneous determination of paracetamol and mephenoxalone 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 mephenoxalone, 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 mephenoxalone (r = 0.9994) were obtained. Calibration graphs for paracetamol and mephenoxalone resulted in the following regression equations :

$$A = 0.0338C - 0.0200 \text{ (paracetamol)}$$

$$A = 0.0222C + 0.0386 \text{ (mephenoxalone)}$$

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 mephenoxalone. 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 mephenoxalone, respectively.

Table - 1: Results of the simultaneous determination of paracetamol and mephenoxalone in commercial tablets.

Analyte	Label claim (mg)	n	$\bar{X}$	Relative S.D. %
Paracetamol	450	10	450.3	0.33
Mephenoxalone	200	10	199.7	1.17

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

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

Amount added (mg)		Found (mg)		Recovery %	
Paracetamol	Mephenoxalone	Paracetamol	Mephenoxalone	Paracetamol	Mephenoxalone
450	275	455.6	274.4	101.2	99.7
450	250	450.8	249.2	100.1	99.6
450*	200*	449.6	200.6	99.9	100.3
500	200	493.2	198.8	98.6	99.4
550	200	551.2	202.4	100.2	101.2
600	200	600	195.2	100.0	97.6
675	200	673.2	196.8	99.7	98.4
		Average		99.96	99.46
		Average deviation		± 0.76	± 1.19

* 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 mephenoxalone in tablets for routine analysis.

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REFERENCES

1. *Türk Farmakopesi 1974,* Milli Eğitim Basımevi, İstanbul, 1974, p. 487.
2. *British Pharmacopoeia 1980,* **2,** The University Press, Cambridge, p. 800.
3. Elsayed, M.A.H., Belal, S.F., Elwalily, A.F.M., Abdine, H. : *Analyst (London),* **104,** 620 (1979).
4. Onur, F., Acar, N. : *FABAD J. Pharm. Sci.,* **14,** 1(1989).
5. Yücesoy, C. : *ibid.,* **15,** 175 (1990).
6. Onur, F., Acar, N. : *J. Fac. Pharm. Gazi,* **6** (1), 23 (1989).
7. Dingeon, B., Charvin, M.A., Quenard, M.T., Thome, H. : *Clin. Chem.,* **34** (6), 1119 (1988).
8. Korany, M.A., Bedair, M., Mahgoub, H., Elsayed, M.A. : *J. Assoc. Off. Anal. Chem.,* **69,** 608 (1986); Ref., *C.A.,* **105,** 102712n (1986).
9. Chafetz, L., Daly, R.E., Schriftman, H., Lomner, J.J.: *J. Pharm. Sci.,* **60,** 463 (1971).
10. Öztunç, A. : *Sci. Pharm.,* **54** (2), 111 (1986).
11. Nakamura, H., Tamura, Z. : *Anal. Chem.,* **52,** 2087 (1980).
12. Wintersteiger, R., Gübitz, G. : *Sci. Pharm.,* **45,** 18 (1977).
13. Prescott, L.F. : *J. Pharm. Pharmacol.,* **23,** 807 (1971).
14. Grove, J. : *J. Chromatogr.,* **59,** 289 (1971).
15. Kaa, E. : *ibid.,* **221,** 414 (1980).
16. Ascione, P.P., Chrekian, G.P. : *J. Pharm. Sci.,* **64,** 1029 (1975).
17. Sisco, W.R., Rittenhouse, C.T., Everhart, L.A. : *J. Chromatogr.,* **348,** 253 (1985).
18. Brooks, K.E., Smith, N.B. : *Clin. Chem.,* **35** (10), 2100 (1989).
19. Koizumi, F., Kawamura, T., Ishimori, A., Ebina, H., Satoh, M. : *Tohoku J. Exp. Med.,* **155** (2), 159 (1988); Ref., *C.A.,* **109,** 125362v (1988).
20. Morrison, J.A. : *Arch. int. Pharmacodyn,* **157,** 385 (1965).
21. Rollas, S., Sert, F. : *J. Pharm. Univ. Mar.,* **3** (2), 85 (1987).
22. Donhal, J., Volkova, Z., Vytras, K. : *J. Pharm. Biomed. Anal.,* 7 (6), 755 (1989); Ref., *C.A.,* **111,** 180868f (1989).

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