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SPECTROPHOTOMETRIC DETERMINATION OF MEPHENOXALONE AND PARACETAMOL IN TABLETS USING VIERORDT METHOD

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Summary: *The objective of this study was to perform quantitative analysis of mephenoxalone-paracetamol containing tablets utilized for myorelaxan and analgesic purposes by using Vierordt method. In this study, A_1^1 values at 291.3 and 243 nm for mephenoxalone and paracetamol have been determined and the values of $a = \alpha_2/\alpha_1$ and $b = \beta_2/\beta_1$ were calculated by using A_1^1 values. From total absorption value ratios at the defined wavelengths of synthetic mixtures prepared at different concentrations, sensitive and reproducible results for mephenoxalone and paracetamol have been obtained at the concentrations of 1.25-6.60 and 2.5-15.0 mcg/ml respectively. The relative standart deviations of the method was found to be 1.6 % for mephenoxalone and 1.1 % for paracetamol.*

The quantitative analysis and the determination of the dissolution rate of tablets containing these active substances were realized by using the proposed method on routine basis.

Keywords : *Mephenoxalone, Paracetamol, Vierordt method.*

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MEFENOKSALON - PARASEMATOL İÇEREN TABLETLERDE VİERORDT YÖNTEMİ İLE SPEKTROFOTOMETRİK MİKTAR TAYİNİ ÇALIŞMALARI

Özet: *Bu çalışmada adale gevşetici - ağrı kesici amaçla kullanılan mefenoksalon - parasetamol içerikli tabletlerde Vierordt yöntemi ile miktar tayini çalışmaları yapılmıştır. Uygulanan bu yöntemde mefenoksalon ve parasetamolün 219.3 ve 243 nm'deki (A_1') değerleri saptanmış ve bulunan değerlerden yararlanılarak $a = \alpha_2/\alpha_1$, $b = \beta_2/\beta_1$ değerleri bulunmuştur. Farklı konsantrasyonlarda tarafımızdan hazırlanan sentetik karışımlara anılan dalga boylarında saptanan toplam absorbans oranları kullanılarak mefenoksalon ve parasetamol için 1.25-6.60 mcg/ml ve 2.5-15.0 mcg/ml aralığında doğrusal, duyarlı ve tekrarlanabilir sonuçlar elde edilmiştir. Önerilen yöntemlerin bağıl standart sapması mefenoksalon ve paresetamol için sıra ile % 1.6 ve % 1.1. bulunmuştur.*

Yöntemin, mefenoksalon - parasetamol içeren tabletlerin rutin kantitatif miktar ve dissolusyon hızı tayininde kullanılabilecek duyarlıkta, hızlı, kolay uygulanabilir bir yöntem olduğu gösterilmiştir.

Anahtar Kelimeler : *Mefenoksalon, Parasetamol, Vierordt Yöntemi*

INTRODUCTION

Mephenoxalone is classicaly used for tranquillizing aims. It is used alone or in combination with paracetamol for myorelaxananalgesic purpose in Turkey.

According to the previous studies, the quantitative determination of mephenoxalone and paracetamol one at a time in pharmaceutical dosage form and body fluids has been assayed by using TLC (1), spectrophotometry (2, 3, 4), derivative spectrophotometry, (5, 6, 7) HPLC (8, 9, 10) and fluorometry (11). In literature screening, no analytical method for combination of mephenoxalone and paracetamol was met. This paper presents a procedure for the quantitative determination of mephenoxalone and paracetamol in tablets simultaneously by using Vierordt method.

EXPERIMENTAL

MATERIAL and METHOD

Mephenoxalone and paracetamol were obtained from İltaş Co. The Commercial samples with different series numbers were purchased from the local pharmacies in Ankara. All solvent and chemicals were reagent grade.

A spectrophotometer model UV-160A (Shimadzu) was used in this study.

METHOD

Determination of (A_1^1) values of mephenoxalone and paracetamol.

Stock Solutions:

Stock solution P_1 : 200 mcg/ml paracetamol in methanol

Stock solution M_1 : 500 mcg/ml mephenoxalone in methanol

Stock solution M_2 : 10 mg/ml mephenoxalone in methanol

Absorbance values have been determined at 219,3 and 243 nm for mephenoxalone and paracetamol Figure 1.

1.2.3.4 and 5 ml of Stock P_1, put into a 100 ml of volumetric flask and diluted with 0.1 N HCl. The absorption of P_1 series were measured at 219.3 and 243 nm using 0.1 N HCl as a reference separately.

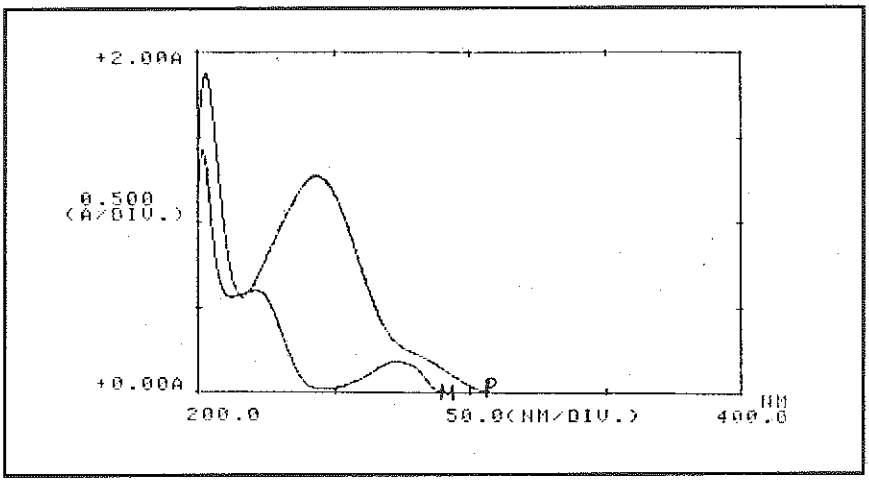
1, 2, 3, 4 and 5 ml of Stock M_1, put into a 100 ml of volumetric flaks and diluted with 0.1 N HCl. The absorption of M_1 series were measured at 219.3 nm using 0.1 N HCl as a reference.

1, 2, 3, 4 and 5 ml were taken Stock M_2, and put into a 100 ml of volumetric flask and diluted with 0.1 N HCl. The absorption of M_2 series were measured at 243 nm using 0.1 N HCl as a reference.

The (A_1^1) values of the substances were calculated from the measured absorbance values. These values are shown in Table-1.

Preparation of Standart Mixtures:

Different volumes were taken from the stock solution containing 100 mcg/ml



p - Paracetamol 20 mcg/ml in 0.1N HCl
M - Mephenoxalone 20 mcg/ml in 0.1N HCl

Figure 1 - Spectrum of Paracetamol and Mephenoxalone in 0.1 N HCl

Table 1 - A_1 values for mephenoxalone - paracetamol

α_1	α_2	$ß_1$	$ß_2$	$a = \alpha_2/\alpha_1$	$b = ß_2/ß_1$	m
630	317	13.2	316	0.5032	24	A_2/A_1

α_1 = Paracetamol 243 nm A_1^1 value in 0.1 N HCl

α_2 = Paracetamol 219.3 nm A_1^1 value in 0.1 N HCl

$ß_1$ = Mephenoxalone 243 nm A_1^1 value in 0.1 N HCl

$ß_2$ = Mephenoxalone 219.3 nm A_1^1 value in 0.1 N HCl

A_1 = Total absorbance at 243 nm

A_2 = Total absorbance at 219,3 nm

mephenoxalone and paracetamol diluted 100 ml with 0.1 N HCl (e.g. 7 ml mephenoxalone and 5 ml of paracetamol were taken from the stock solutions into a 100 ml of volumetric flask and diluted to 100 ml with 0.1 N HCl). The total absorbances of this solution were measured at 291,3 and 243 nm. The recovery found in the mixtures which were prepared by us are shown in Table 2 and 3.

Table 2 - Results obtained by using Vierordt method for the analysis of mephenoxalone and paracetamol in synthetic mixtures

Synthetic mixtures mcg/ml		Found mcg/ml	
Mephenoxalone	Paracetamol	Mephenoxalone	Paracetamol
5	2	4.87	1.98
5	4	5.01	4.04
5	6	4.94	5.94
5	8	4.97	7.94
5	10	5.10	10.1
2	5	1.95	5.11
4	5	3.96	5.14
6	5	6.16	5.09
8	5	7.88	5.08
10	5	10.1	5.08

	$\overline{X}$	St. Dev.	Rel. St. Dev. %	95 % Confidence limits
Mephenoxalone	4.97	0.08	1.6	4.97 ± 0.07
Paracetamol	5.10	0.06	1.1	5.10 ± 0.05

Table 3 - Results obtained by using Vierordt method for the analysis of mephenoxalone and paracetamol in synthetic mixtures

Synthetic mixtures mcg/ml		Found mcg/ml			
Mephenoxalone	Paracetamol	Mephenoxalone		Paracetamol	
		mcg/ml	%	mcg/ml	%
3	7	3.06	102	6.95	99.3
4	6	3.95	98.7	6.11	101
5	5	4.87	97.4	5.02	100
6	4	5.95	99.2	3.92	98.0
7	3	6.84	97.2	2.95	98.3

Preparation of the Sample

Twenty tablets were weighted, powdered and mixed homogenously. Approximately 100 mg of this powder was accurately weighed and extracted with 60 ml methanol for fifteen minutes. Then it was filtred and the filtrate were diluted to 100 ml with methanol. Various dilutions were prepared from this solution with 0.1 N HCl.

These dilutions had to be in the limits of 1.25-6.60 mcg/ml for mephenoxalone and 2.5 - 15.0 mcg/ml for paracetamol. The results of commerical samples are shown in Table 4.

Table 4 - Results obtained by using Vierordt method for the analysis of active substances in commerical tablets

Commercial tablet Mephenoxalone : 200 mg Paracetamol : 450 mg	Mephenoxalone		Paracetamol	
	mg*	%	mg*	%
	201	101	447	99.3
	198	98.9	457	101.
	198	99.2	451	100.
	195	97.7	445	98.8
	197	98.5	445	99.0

	$\overline{X}$	St. Dev.	Rel. St. Dev. %	95 % Confidence limits
Mephenoxalone	198	2	1.11	1.98 ± 2
Paracetamol	449	5	1.12	449 ± 5

* Average of three determinations

Calculations

The amounst of mephanoxalone and paracetamol were calculated according to the following equations using the values given in Table - 1.

$$\text{Paracetamol (c)} = \frac{A_1}{\alpha_1 . 10^{-3}} \cdot \frac{b - m}{b - a}$$

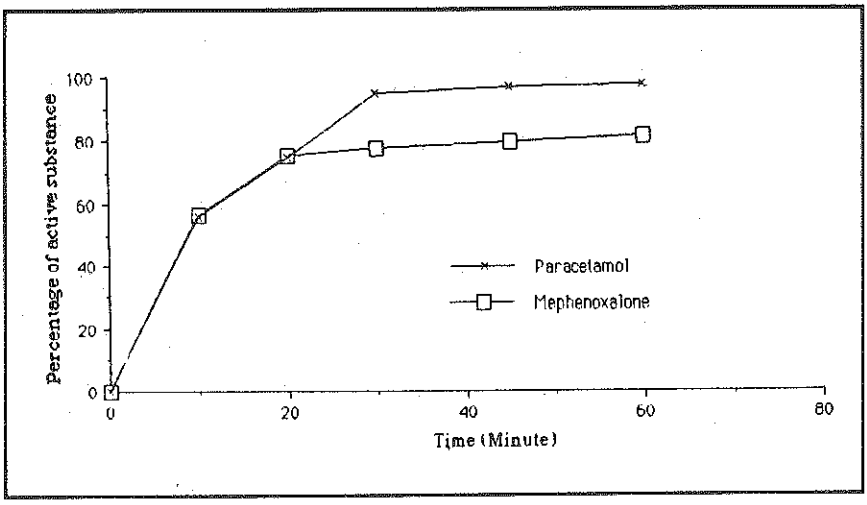
$$\text{Mephenoxalone (c)} = \frac{A_2}{\beta_2 . 10^{-3}} \cdot \frac{b\,(m - a)}{m\,(b - a)}$$

(c is calculated as mg/100 ml).

Determination of Dissolution Rate

Tablets were put into the dissolution apparatus. 10 ml samples were taken within 10, 20, 30, 45, 60 minute intervals and filtered 2 ml filtrates were diluted to 100 ml with 0.1 N HCl.

Their total absorbance at 219.3 and 243 nm were measured. The percentages of active substance versus time were mentioned. These results and operating conditions are presented in Figure - 2.



Operating Conditions :
Medium : 0.1 N HCl (900 ml) Speed 50 rpm
Apparatus 2 : USP XXI

Figure 2 - Profile of Dissolution rate Mephenoxalone - Paracetamol Commerical Tablet

RESULTS and DISCUSSION

The procedure described in this paper is provided for the quantitative determination of mephenoxalone and paracetamol in commerical tablets without seperation process. The proposed method is convenient, sensitive, accurate and reproducible. The relative standart deviations are 1.6 % and 1.1 % for mephenoxalone and paracetamol, respectively. This method was not also effected from the inert excipients present in the tablets. The limits of concentrations have been established as 1.25 - 6.60 mcg/ml for mephenoxalone and 2.5 - 15 mcg/ml for paracetamol.

On the other hand the proposed method have also been used for the determination of the dissolution rate of the commercial pharmaceuticals. According to the results, the total amount of paracetamol were dissolved in sixty minutes where as 83.4% of the amount of mephenoxalone has been dissolved in an hour.

In conclusion, the described method was found to be useful for the determination of amounts of active ingradients and dissolution rates of tablets containing mephenoxalone and paracetamol. Additionally this method is simple, fast, sensitive and reproducible as well.

REFERENCES

1. Eckhart. G. et al.. "Isolation and Identification of some Metabolites of Mephenoxalone", *Clin. Chem. Clin. Biochem.*, 15 (3), 15-20, 1977.
2. El Kheir, A.A., Belal, S., El Sadek, M., El Shanwami, A., "Spectrophotometric Determination of Acetaminophen. Oxyphenbutazone and Salicylamide by Nitration and Subsequent Complexation Reactions", *Analyst.*, 111 (3). 319-21, 1986.
3. Yücesoy, C., "Parasetamol ve Klorzoksazonun Absorbans Oranları Yöntemi ile Spektrofotometrik Miktar Tayini", *Pharmacia*, 30 (1), 13-18, 1990.
4. Atay, O., Orbey, T. M., "Metokarbamol ve Parasetamol İçeren Tabletlerde Spektrofotometrik Miktar Tayini Çalışmaları", *FABAD, Farm. Bil. Der.*, 15, 223-30, 1990.
5. Korany, M. A., Badeir, M., Mahgoub H., El Sayed, M.A., "Second Derivative Spectrophotometric Determination of Paracetamol and Phenacetine in Presence of Their Degradation Products", *J. Assoc. Off. Anal. Chem.*, 69, 608-11, 1986.
6. Yücesoy, C., "Parasetamol ve Klorzoksazonun İkinci Türev UV - Spektrofotometrisi ile Miktar Tayini", *FABAD, Farm. Bil. Der.*, 15, 175-82, 1990.
7. Tabias, D.Y., "First-Derivative Spectrophotometric Determination of Acetaminophen and Sodium Salicylate in Tablets", *J. Assoc. Off. Anal. Chem.*, 66, 1450-54, 1983.
8. Sisco, W.R., et al., "Simultaneous HPLC Stability-indicating Analysis of Acetaminophen and Codein Phosphate in Tablets and Capsules", *J. Chromatogr.*, 348 (1), 253-63, 1985.
9. Gilpin, R.K., Guadet, M.H., Rapid, H.P.L.C "Determination of Acetaminophen in Dosage Form Using a Totally Aqueous Mobil Phase", *J. Chromatogr.*, 248, 160-64, 1982.
10. Rollas, S., Sert, F., "Mefenoksalon'un Yüksek Basınçlı Sıvı Kromatografik Miktar Tayini", *Mar. Üniv. Ecz. Der.*, 3 (2), 85-89, 1987.
11. Öztunç, A., "Fluoremetric Determination of Acetaminophen in Pharmaceuticals", *Sci. Pharm.*, 54 (2), 111-13, 1986.