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SPECTROPHOTOMETRIC DETERMINATION OF MEXILETINE IN CAPSULES USING METHYLORANGE

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SUMMARY

Mexiletine is an antiarrhytmic drug used in the treatment of acute and chronic ventricular arrhythmias. We described a new spectrophotometric method for the determination of mexiletine in capsules through the formation of an ion–pair with methylorange. The absorption spectrum in chloroform showed a maximum at 423 nm. The calibration graph was linear in the concentration range of 1.1 to 7.6 $\mu g.ml^{-1}$ for mexiletine.

The proposed method was applied to the determination of mexiletine in the pharmaceuticals dosage form (capsule). The results were compared statistically with those obtained by the UV-spectrophotometric method using t- and F-tests. There was no significant difference between the two methods in the respect of mean values and standard deviations at 95% confidence level.

ÖZET

Meksiletin Hidroklorür akut ve kronik ventriküler aritmilerde kullanılan antiaritmik etkili bir ilaçtır. Bu çalışmada, meksiletinin kapsüllerde metiloranj ile iyon çifti olu-

şumuna dayanan yeni bir spektrofotometrik yöntem geliştirilmesi esas alınmıştır. Oluşan iyon çiftinin kloroformdaki maksimum absorpsiyonu 423 nm de gözlenmiştir. Ölçü eğrisi 1.1- 7.6 μg.ml^{-} arasında doğrusaldır.

Geliştirilen yöntem kapsüllerde meksiletin hidroklorür miktar tayinine uygulanmıştır. Sonuçlar UV-spektrofotometrik yöntem ile elde edilen sonuçlarla t- ve F- testleri kullanılarak istatistiksel olarak kıyaslanmış ve iki yöntem arasında ortalamalar ve standart sapmalar yönünden % 95 olasılık düzeyinde anlamlı bir fark bulunmamıştır.

Key words: Mexiletine, Spectrophotometric determination, Methylorange, Ion-pair extraction

INTRODUCTION

Mexiletine (**1**), chemically [1-(2,6-dimethylphenoxy)-2-aminopropane], is used as an antiarrhytmic drug.

Various methods have been reported for the assay of **1** in both capsules and biological materials, UV-spectrophotometry (1), fluorimetry (2), gas chromatography (GC) (3,4), high-performance liquid chromatography (HPLC) (5-7) and capillary electrophoresis (CE) (8,9).

In this study, a new spectrophotometric method is described for the analysis of **1** and its capsules. The method was based on the formation of an ion-pair with methylorange (2). To our best knowledge this is the first report for colorimetric determination of **1**

RESULTS AND DISCUSSION

In order to determine optimum condititions for the reaction and the extraction , the effect of pH, amount of the reagent and different solvents were investigated. The absorption spectrum in chloroform showed a maximum at 423 nm. Maximum absorbance was obtained at pH 4.0 using phtalate buffer (Fig.1)

The reagent amount required was examined by changing the mole ratio of methylorange to mexiletine. A 6 fold molar excess of the reagent was found to be sufficient to complete the reaction (Fig. 2).

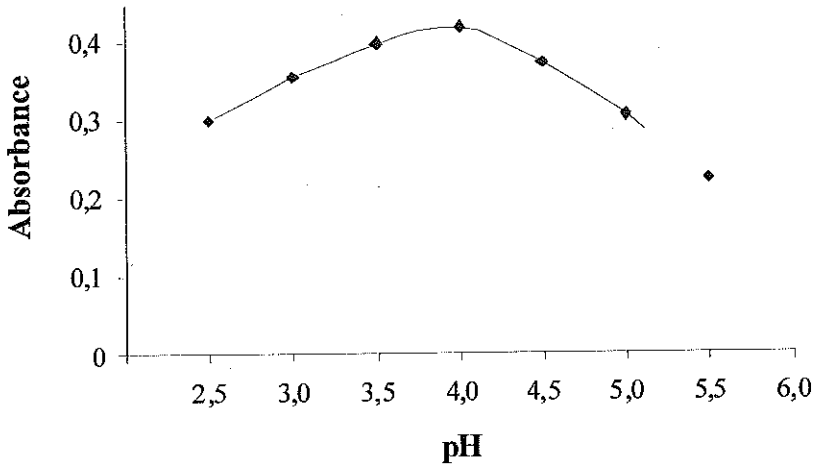

Figure 1 : Effect of pH on the reaction of mexiletine with methylorange

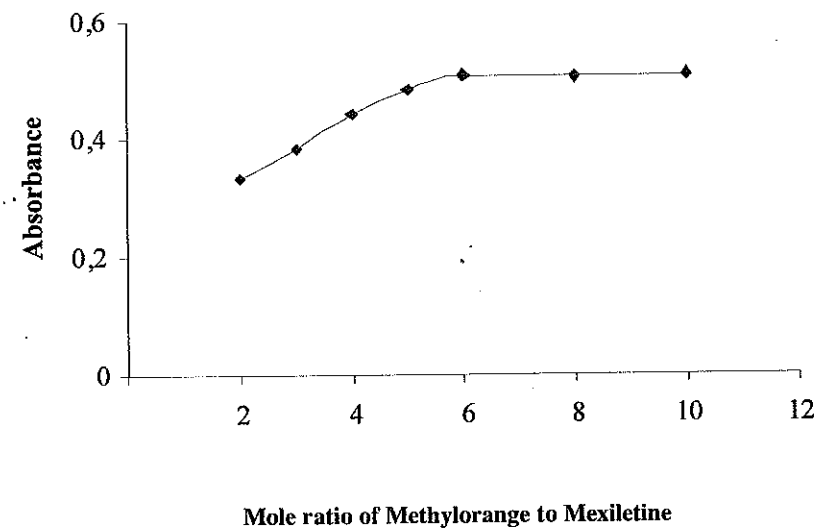

Figure 2 : Effect of reagent concentration on the reaction of methylorange with mexiletine

Stoichiometric balance between **1** and **2** was determined as 1:1 using Job's continuous variation method. The calibration graph was linear in the concentration range of 1.1 to 7.6 $\mu g.ml^{-1}$ for **1** (A= 0.1235 C- 0.013, r = 0.9997).

The developed method was applied to the commercially avalaible capsules and the results were compared statistically with those obtained by the UV- spectrophotometric method reported in BP 1993 (1), using t- and F- tests. At 95% confidence level there is no significant difference between the two methods (Table).

In conclusion, the proposed method are the first colorimetric method developed for the determination of **1** and it is simple, sensitive, and rapid analytical procedure that can be easily used for routine analysis of **1**.

Table 1 : Comparison of the results obtained by the proposed and UV-spectrophotometric methods for the assay of **1** in capsules (each capsule equivalent to 200 mg of **1**)

Statistical value	Proposed method	UV-Spectrophotometric Methods
Mean	201.62	199.56
Recovery (%)	100.81	99.78
s	1.7899	1.1961
RSD (%)	0.89	0.60
Confidence limits	199.90-203.25	198.47-200.65
t-test of significance *	0.73	
F-test of significance *	2.19	
* n =6	p=0.05 t=2.23	F=5.05

EXPERIMENTAL

Apparatus and chemicals

Mexiletine and its capsules (Mexitil®,) were kindly supplied from Eczacıbası Pharmaceuticals (Istanbul, Turkey). The other chemicals and solvents used were analytical grade. Absorbance measurements were made with a Shimadzu UV- 160 A UV visible spectrophotometer.

Solutions

Stock solutions: Amount equivalent to 10.79 mg of **1** was dissolved in 50 ml distilled water.

Reagent solutions: 98.20 mg of **2** was dissolved in 50 ml in pH 4.0 phtalate buffer.

Assay Procedure

Preparation of calibration graphs

Suitable aliquots of the stock solution of **1** (0.25-1.75 ml) were transferred to stoppered glass tubes and after the volume was brought to 2 ml with distilled water. It was treated with 2 ml of the reagent solution. The mixture was extracted with 5 ml of chloroform for 2 min with vortex mixer and centrifuged. 1 ml of this organic phase pipetted into 10 ml calibrated flask and diluted to volume with chloroform. The absorbance of the chloroform layer was measured at 423 nm against a blank solution prepared similarly.

Assay procedure for tablets

Capsule powder equivalent to one capsule (each capsule equivalent 200 mg of **1**) was accurately weighed and transferred into a 250 ml calibrated flask. 100 ml of water was added, then the mixture was shaken mechanically for 30 min and diluted with water to the volume, mixed and filtered. 0.25 ml of the filtrate was analysed smilarly as described at the section "Preparation of calibration graphs". The amount of **1** in capsules was calculated from the regression equation obtained from the calibration graph.

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