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SPECTROPHOTOMETRIC DETERMINATION OF MEXILETINE HYDROCHLORIDE BY CHARGE-TRANSFER FORMATION WITH 2,3-DICHLORO-5, 6-DICYANOBENZO-QUINONE (DDQ)

MEKSİLETİN HİDROKLORÜRÜN 2,3-DİKLORO-5, 6-DİSİYANOBENZOKİNON İLE YÜK-TRANSFER KOMPLEKSİ OLUŞUMUNA DAYANAN SPETROFOTOMETRİK MİKTAR TAYİNİ

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A new, sensitive and rapid spectrophotometric method has been developed for the determination of mexiletine and its capsules. This method was based on the interaction between the primer amine of mexiletine (n-donor) and 2,3-dichloro 5,6-dicyanobenzoquinnone (DDQ) (π-acceptor) in chloroform to form a stable charge-transfer complex. Calibration curve was linear within the concentration range of 2-13 μg/ML at λ_{max} 480 nm (r= 0.9999). Results optained from the developed method were compared statiscally with the results obtained by UV-spectrophotometric method.

Meksiletin ve kapsüllerindeki miktar tayini için yeni, hassas ve hızlı bir spektrofotometrik miktar tayini yöntemi geliştirilmiştir. Bu method, 2,3-dikloro-5,6-disiyanobenzokinon (DDQ) (π-akseptör) ile meksiletenin (n-donör) primer amin grubu arasında kloroform çözeltisinde stabil bir yük-transfer kompleksi oluşumuna dayanmaktadır. Kalibrasyon eğrisi maksimum 480 nm dalga boyunda, 2-13 μg/mL konsatrasyon aralığında doğrusaldır (r=0.9999).Geliştirilen yöntemden elde edilen sonuçlar UV-spektrofotometrik yöntemle elde edilen sonuçlarla istatistiksel olarak kıyaslanmıştır.

Keywords: *Spectrophotometry; Mexiletine hydrochloride; DDQ; Charge-transfer complex*

Anahtar Kelimeler: *Spektrofotometri; Meksiletin hidroklorür; DDQ; Yük-transfer kompleksi*

Introduction

Mexiletine hydrocloride, [1-(2,6-(dimethylphenoxy)-2-aminopropane] [**1**] is an antiarrhythmic drug used for the treatment of ventricular arrhythmias (1-3) Although a variety of UV-spectrophotometric (4), fluorimetry (5), gas (6,7) and column liquid chromatographic (8,9) techniques have been described for assaying mexiletine in both capsules and biological materials, only one derivative spectrophotometric method (10) has been reported.

A new, sensitive and rapid spectrophotometric method is described for the analysis of mexiletine and its capsules in the present study .The method was based on the interaction between the primer amine of mexiletine (n-donor) and 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ) (π-acceptor) in chloroform to form a stable charge-transfer complex(11).

Metarials and Methods

Apparatus: A Shimadzu UV-160 A UV-visible spectrophotometer with 1 cm path length glass and quartz cells and a WTW Ph 526 pH meter with combined electrode were used.

Chemicals: Mexiletine and its capsules (Mexitil®) were kindly supplied from Eczacıbaşı Pharmaceuticals (İstanbul, Turkey). Other chemicals and solvents used were of analytical reagent grade.

Stock solution of 1: An amount equivalent to 6.3 mg of mexiletine base was dissolved in 25 mL distilled water.

Reagent solution: 66.3 mg of DDQ was dissolved in 50ml chloroform.

Calibration graph plotting: 5 mL stock solution of **1** was transferred into stoppered glass tubes. This solution was adjusted to alkalene medium with 0.25 mL of 1N ammonia. Each mixture was extracted three times with 5 mL chloroform by vortex mixer for 5 min. The combined organic phases were shaken with anhydrous sodium sulphate, filtered and the volume was adjusted to 25 mL with the same solvent in a calibrated fask (stock solution **3**). Suitable aliquots of **3** (0.4-2.6 mL) were transferred into 10mL calibrated flasks and 2.6 mL of reagent solution was added to each.

This mixture was allowed to stand for 5 min and then the volume was diluted to 10 mL with chloroform. Absorbance values were measured against a reagent blank at 480 nm.

The calibration graph of mexiletine hydrochloride was plotted and the regression equation was calculated therefrom.

Assay procedure for capsules: Capsule powder equivalent to one capsule was accurately weighed and transferred into a 250 mL calibrated flask.100 mL distilled water was added, then the mixture was shaken mechanically for 30 min, diluted with water to volume ,mixed thoroughly and filtered. 5 mL of the filtrate was withdrawn form this solution and after treatment with ammonia, extracted with chloroform as described above. 0.6 mL was drawn from this final solution into a 10 mL calibrated flask. 0.6 mL of the reagent solution was added and mixed. The mixture was diluted to volume with chloroform. The amount of **1** in capsules was calculated from the regression equation of the calibration graph.

Results and Discussion

Optimum conditions of this reaction with respect to solvent, reaction time, amount of the reagent, λ_{max} and stability of the radical anion were investigated. Among the solvents used (Fig.1), acetonitril, methanol, acetone and chloroform reaction was proceeded quantitatively in chloroform within 5 min when the molar ratio of DDQ/mexiletine was 5 (Fig. 2).

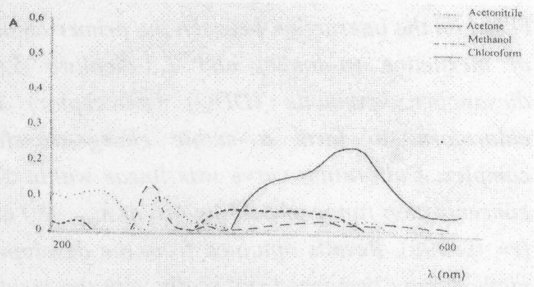

Fig. 1. Absorption spectra in various solvents

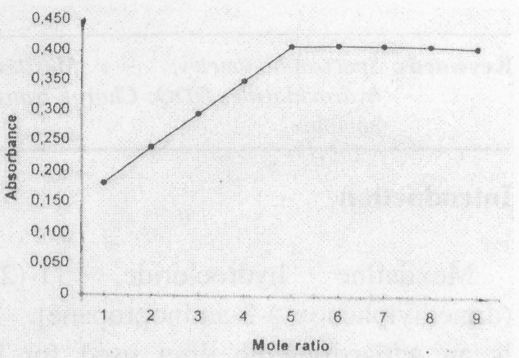

Fig. 2. Effect of reagent concentration on the reaction of mexiletine HCL with DDQ

The absorption spectrum in chloroform showed a maximum at 480 nm. The color developed was stable for at least 30 min at room temperature. The stoichiometric ratio of DDQ/mexiletine was determined by Job's Curve method and was found to be 1:1. At these conditions, a linear correlation was

observed between absorbance and final concentration of mexiletine base over the range of 2-13 µg/mL with corresponding molar absorptivity of $1.2x10^4$ L/mol.cm.

The regression equation was A=0.0708 C-0.0147 (r = 0.9999) (Fig.3).

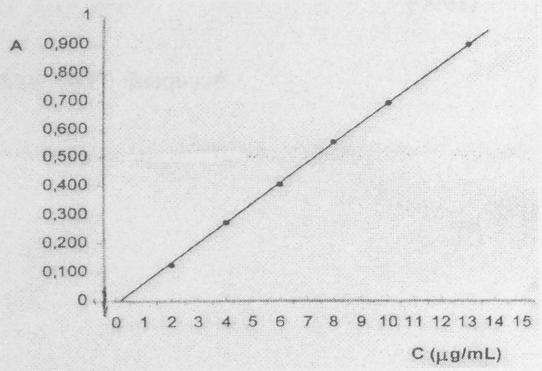

Fig. 3. Calibration curve of mexiletine HCL

Amounts of mexiletine hydrochloride in capsules were calculated by the following equation: C x A/B.

A and B are the formula weight of mexiletine HCl and its base respectively. C is the concentration in $mg.ml^{-1}$ of mexiletine base in capsules. Different capsule additives such as lactose, starch, magnesium stearate, carboxymethylcellulose did not interfere. The results were compared with those of the UV-spectrophotometric method (4). Statistical comparisons in terms of t-and F-tests for these methods are given in the Table. There was no significant difference between the two methods at 95% confidence level.

Table. Comparison of the results obtained by spectrophotometric and UV-spectrophotometric methods for the assay of mexiletine in capsules (each capsule contains 200 mg of **1**)

Statistical values	Proposed method	UV-spectrophotometric method (BP 1993)
Mean (mg)	200.13	200.19
Recovery ± standart deviation (%)	100.07 ± 0.85	100.09 ± 0.76
Confidence limit	199.35 – 200.90	199.49 – 200.89
t-test of significance*	0.13	
F-test of significance*	1.24	

*n = 6 p = 0.05 t = 2.23 F = 5.05

In conclusion, the proposed method provided a more sensitive, rapid, specific and inexpensive analytical procedure and can be recommended for routine pharmaceutical analysis of **1.**

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