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DETERMINATION OF MEXILETINE BY ION-PAIR EXTRACTION WITH BROMPHENOL BLUE

MEKSİLETİNİN BROMFENOL MAVİSİ KULLANILARAK İYON ÇİFTİ EKSTRAKSİYONU İLE MİKTAR TAYİNİ

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A rapid and sensitive spectrophotometric method has been developed for the assay of mexiletine in capsules. The method is based on measuring the absorption maximum at 411 nm of the reaction between mexiletine and bromphenol blue (BPB). A linear calibration graph was obtain-ed for mexiletine concentration range of 1.1-8.6 μg.mL^{-1} with a correlation coefficient of 0.9997. The method was applied to commercially available capsules and the results obtained were compared statistically with those obtained by UV-spectrophotometric method.

Meksiletinin kapsüllerdeki miktar tayini için hassas ve hızlı bir spektrofotometrik yöntem geliştirilmiştir. Bu metod meksiletinin bromfenol mavisi ile oluşturduğu iyon çifti kompleksinin 411 nm de gösterdiği maksimum absorpsiyonunun ölçülmesi esasına dayanmaktadır. Yapılan ölçümlerde, kalibrasyon eğrisinin 1.1-8.6μg.mL^{-1} konsantrasyon aralığında doğrusal olduğu saptanmıştır (r=0.9997). Geliştirilen yöntem meksiletin içeren kapsüllerde miktar tayini için uygulanmış ve bulunan sonuçlar UV-spektrofotometrik yöntem sonuçlarıyla istatistiksel olarak kıyaslanmıştır.

Key words: *Spectrophotometry; Mexiletine; Bromphenol blue; Ion-pair extraction*

Anahtar kelimeler: *Spektrofotometri; Meksiletin; Bromfenol mavisi; İyon-çifti ekstraksiyonu*

Introduction

Mexiletine (**I**), chemically [1-(2,6-dimethylphenoxy)-2-aminopropane], is used as an antiarrhytmic drug. Various methods as spectrophotometry (1), fluorimetry (2), gas chromatography (GC) (3,4), high-performance liquid chtomatography (HPLC) (5-7) and capillary electrophoresis (CE) (8,9) have been reported for the assay of **I** in capsules and biological materials.

A simple, rapid and sensitive spectrophotometric method for the determination of mexiletine in capsules is reported herein. This method involves the formation of an ion-pair between the drug and bromphenol blue (BPB) (**II**) and measuring its absorbance after extraction with chloroform.

Materials and methods

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

Chemicals: Mexiletine and its capsules (Mexitil®) were kindly supplied from Eczacıbası Pharmaceuticals (Istanbul, Turkey).The other chemicals and solvents used were of analytical reagent grade. The water was deionized and bidistilled.

Standard solutions: An amount equivalent to 10.79 mg of **I** was dissolved in 50 ml distilled water.

Sample solution: Capsule powder, equivalent to one capsule (200 mg of **I**) was accurately weighed and transferred into a 250 ml calibrated flask. 100 ml of water was added and the mixture was shaken mechanically for 30 min and diluted with water to volume, mixed and filtered.

Reagent solution: 167.50 mg of **II** was dissolved in 50 ml pH 4.0 phthalate buffer. (Stock sol. **II**). For the determination of the reagent amount and Job's Continuos Variation, 1x10^{-3} M and 2x10^{-3} M BPB solutions were used respectively.

Buffer solution was prepared by mixing 50 ml of 0.2M potassium hydrogen phthalate with an appropriate amount of 0.2M hydrochloric acid and the pH was adjusted to 4 with 0.2 M HCl and then diluted with water to 200 ml.

Method : Suitable aliquots of 0.25-2.00 ml of standard or sample solutions were transferred into glass tubes and the volume was made up to 2 ml with distilled water and treated with 2 ml of the reagent solution (Stock sol. **II**). The mixture was then extracted with 5 ml chloroform for 2 min with a vortex mixer and centrifuged. 1 ml of the organic phase was pipetted into a 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.

Results and discussion

The optimum conditions for ion-pair formation with respect to the pH of aqueous phase, extraction solvent and amount of the reagent were investigated. The pH was changed from 2.5 to 5.5 and the absorbances were measured at maximum wavelengths after extraction of the ion-pair with different solvents. Maximum absorbance was obtained with chloroform at 411 nm. The results of the pH study indicated that maximum absorbance was obtained at pH 4 using phthalate buffer. (Fig.1)

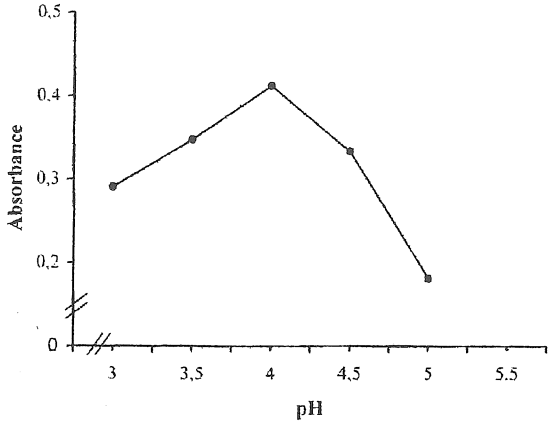

Fig. 1. Effect of pH on the ion-pair extraction with bromphenol blue.

The stoichiometric balance of the reaction was established by Job's Continuous Variation method. The molar fraction of mexiletine and dye varied within a constant total molarity. The results showed that 1:1 complex was formed between mexiletine and the dye. This was also confirmed by molar ratios method and the optimum molar ratio of reagent to mexiletine was found to be 5 according to this method (Fig. 2). The ion-pair complex was stable in chloroform for at least 24 h at room temperature.

Under the optimum conditions described above, a linear correlation was obtained for 1.1-8.6 $\mu g.ml^{-1}$ concentrations of mexiletine. The regression equation was A=0.0965 C-0.001 (r=0.9997) (Fig. 3).

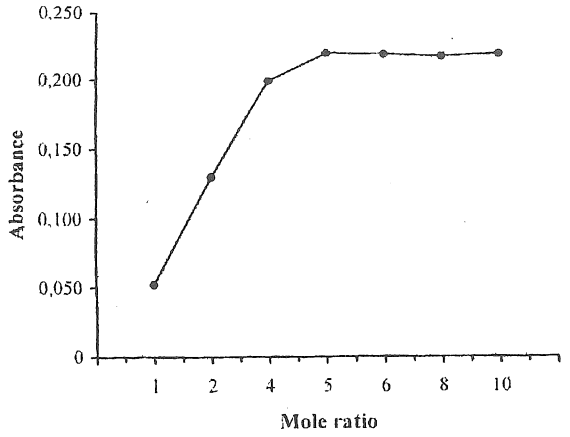

Fig. 2. Effect of reagent concentration on the reaction of mexiletine with bromphenol blue.

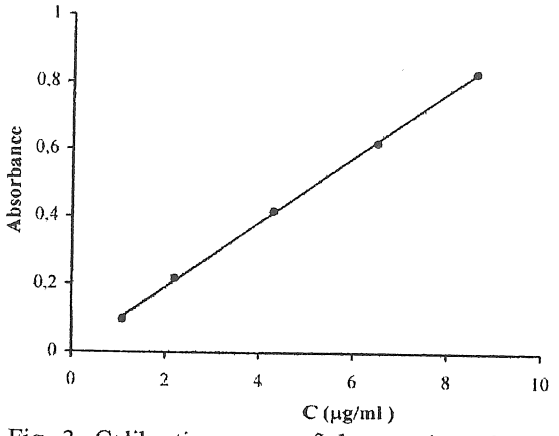

Fig. 3. Calibration curve of the reaction of mexiletine with bromphenol blue.

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 (10),

Table. Determination of mexiletine in capsules (200 mg mexiletine/capsule).

Statistical value	Proposed method	UV-Spectrophotometric method
Mean	199.90	199.43
Recovery(%)	99.95	99.72
S	1.5633	1.1057
RSD (%)	0.78	0.55
Confidence limits	198.48-201.32	198.42-200.44
t-test of significance*= 0.60		F-test of significance*= 1.99
*n=6	p=0.05	t=2.23	F=5.05

using t- and F- tests. At 95% confidence level there was no significant difference between the two methods (Table). Different tablet additives such as lactose, starch, magnesium stearate, and carboxymethylcellulose did not interfere.

In conclusion, the proposed method is a simple, sensitive, and rapid (a single determination time was 5 min) analytical procedure that can easily be used for routine analysis of I.

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