

## Determination of Maprotiline Hydrochloride by Ion- Pair Extraction Using Bromophenol Blue and Bromocresol Purple

### Maprotilin Hidroklorürün Bromfenol Mavisi ve Bromkrezol Yeşili Kullanarak İyon Çifti Ekstraksiyonu ile Tayini

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#### Abstract

Two simple, rapid, sensitive and accurate spectrophotometric methods are described for the determination of maprotiline hydrochloride in tablets. The methods are based on the reactions of the drug with bromophenol blue (BPB) and bromocresol purple (BCP) in buffered aqueous solutions at pH 3 and 4, respectively to give coloured ion-pair complexes extractable with chloroform. The coloured products are quantitated spectrophotometrically at 411 nm with BPB and 409 nm with BCP. Beer's law is obeyed in the concentration range 2-12 µg ml<sup>-1</sup> with both reagents. The proposed methods are applied successfully to the analysis of the drug in its tablet form.

**Key Words:** Maprotiline Hydrochloride, Ion-pair Complex, Spectrophotometry, Bromophenol Blue, Bromocresol Purple.

#### Introduction

Maprotiline hydrochloride (MA), 1-(3-methyl amino propyl)-dibenzo [b,e] bicyclo [2,2,2] octadien hydrochloride, is a tetracyclic antidepressant although its chemical structure looks like tricyclic antidepressants. It strongly inhibits the uptake of noradrenalin in the brain and peripheral tissues (Martindale, The Extra Pharmacopoeia, 1982). A variety of analytical techniques such as HPLC (Aymard and Livi, 1997; Bakkali *et al.*, 1999), GC (Keller and Zollinger, 1997; Ulrich and Martens, 1997; Hallbach *et al.*, 1999), CE (Buzinkova and Korinkova, 1995; Carkt *et al.*, 2000; Vujic *et al.*, 1999) have been reported for its determination in biological fluids. To determine the drug in tablets, UV- (The United States Pharmacopodia XXII, 1990), visible (Soonhee *et al.*, 1986; Ersoy and Alpertunga, 1998; Öztunç, 1989; Özkul and Öztunç, 2000) spectrophotometric and a high performance liquid chromatographic (The United States Pharmacopodia XXIII, 1995) methods have been published.

The present study describes two visible extractive spectrophotometric methods for the determination of MA through ion pair complex formation using bromophenol blue (BPB) and bromocresol purple (BCP) as the dye reagents. The developed methods have been applied to determine the drug in tablets.

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## Materials and Methods

**Apparatus:** A Shimadzu UV-160 A UV-visible spectrophotometer with 1 cm matched glass cells were used for absorbance measurements. pH Measurements were made with a WTW pH 526 digital pH Meter.

**Reagents:** All chemicals and reagents were of analytical grade. MA was obtained from Sigma (St.Louis, MO, USA) and Ludiomil tablets were products of Novartis (Turkey). The reagents BPB and BCP were purchased from Merck (Darmstadt, Germany). Distilled water was used to prepare all solutions.

**Solutions:** The standard solution of MA ( $100 \mu\text{g ml}^{-1}$ ) was prepared in water. BPB ( $2 \times 10^{-3} \text{ M}$ ) and BCP solutions ( $1.85 \times 10^{-3} \text{ M}$ ) were prepared in water and ethanol: water (1:10) mixture, respectively.

Phthalate buffer solutions in the pH range 2-4.4 were prepared as follows: To a solution of 1.28 g potassium hydrogen phthalate in water, calculated volume of 0.2 N HCl was added. Required pH was adjusted using a pH meter and then the volume was brought to 250 ml with water.

**Procedure For Calibration Curves:** For both methods, accurate aliquots containing 10-60  $\mu\text{g}$  of MA were transferred into separate stoppered glass tubes and total volume was brought to 1 ml with water. Then 1 ml of buffer (pH 3 for BPB and pH 4 for BCP method) and 1 ml of dye solutions were added and mixed. Each mixture was extracted with 5 ml of chloroform by shaking with vortex for 2 min. Absorbances of the yellow-coloured organic layers were measured at 411 nm and 409 nm for BPB and BCP methods, respectively against a reagent blank prepared similarly. Calibration curves were constructed using the measured absorbances.

**Assay Procedure For Tablets:** 10 tablets were weighed and powdered. An accurate amount of the powder equivalent to 25 mg of MA was transferred into a 500 ml calibrated flask and 300 ml of water was added. The mixture was sonicated in an ultrasonic bath for 60 min, then was adjusted to volume with water, mixed and filtered. 2 ml of the filtrate was diluted to 10 ml and a suitable aliquot was subjected to the analysis following the procedure described above. The concentration of MA was calculated from the corresponding regression equation.

## Results and Discussion

MA is a tetracyclic antidepressant bearing a secondary aliphatic amino group protonated with hydrochloric acid (Figure 1).

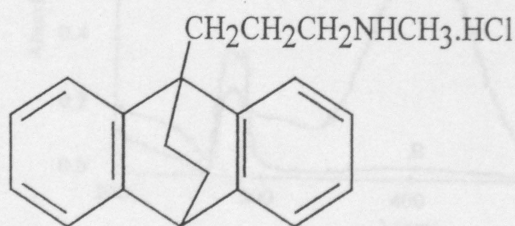


Fig.1. Structure of MA.

Few visible spectrophotometric methods reported for its assay are based on dithiocarbamic acid copper complex formation (Soonhee *et al.*, 1986) and reactions of maprotiline base with  $\pi$ -acceptors, p-chloranile (Ersoy and Alpertunga, 1998) and TCNQ (Öztunç, 1989). The last two



methods require extraction of the base and heating for the reaction. An extractive spectrophotometric method has also been developed in our laboratory using bromothymol blue (BTB) as the ion-pair forming reagent. Ion-pair extractive spectrophotometry has gained great attention for the determination of many pharmaceutically important compounds (Sane *et al.*, 2000; Gowda *et al.*, 2001; Somashekara *et al.*, 2001; Mostafa *et al.*, 2002; Reddy *et al.*, 2002). The present study describes two alternative methods for the assay of MA in tablets using BPB and BCP as the dye reagents.

MA as a positively charged amino compound in acidic medium, formed yellow coloured ion-pair complexes with negatively charged counter ions of BPB and BCP. The absorption curves of the complexes extracted into chloroform showed maxima at 411 and 409 nm, respectively (Figures 2 and 3).

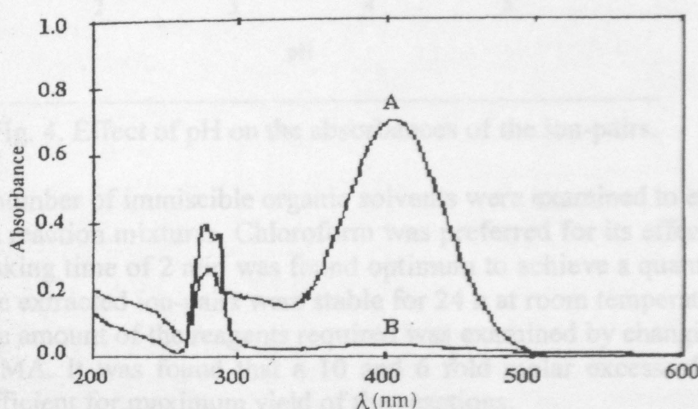


Fig.2. A : Absorption spectrum of the ion-pair complex with BPB in chloroform against the reagent blank.

B: Absorption spectrum of the reagent blank against chloroform.

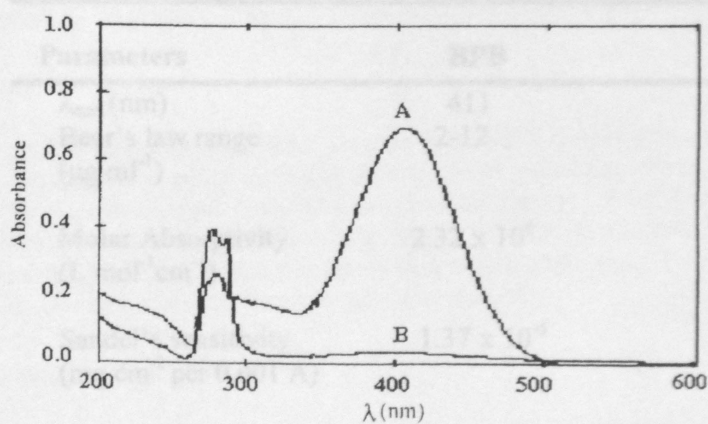


Fig.3. A: Absorption spectrum of the ion-pair complex with BCP in chloroform against the reagent blank.

B: Absorption spectrum of the reagent blank against chloroform.

In the study, optimum experimental conditions were first determined. Since the pH is important for the reactions, different buffer solutions in the pH range 2-4.4 were tested and pH 3 and 4 were found to be the optimum values for BPB and BCP methods, respectively (Figure 4).

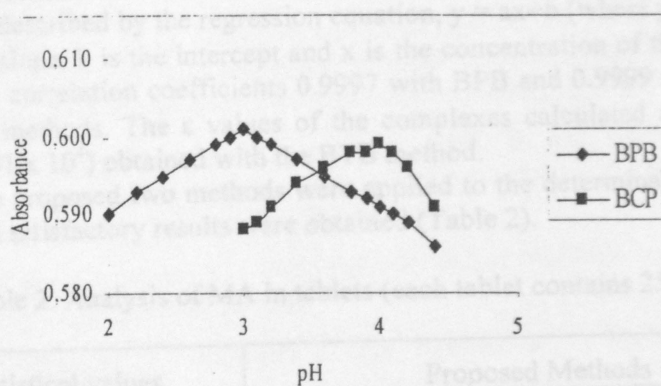


Fig. 4. Effect of pH on the absorbances of the ion-pairs.

A number of immiscible organic solvents were examined to extract the ion-pair complexes from the reaction mixtures. Chloroform was preferred for its effective and selective extraction and a shaking time of 2 min was found optimum to achieve a quantitative recovery of the complexes. The extracted ion-pairs were stable for 24 h at room temperature in the dark.

The amount of the reagents required was examined by changing the mole ratio of BPB and BCP to MA. It was found that a 10 and 6 fold molar excess of BPB and BCP, respectively was sufficient for maximum yield of the reactions.

Under the described experimental conditions, calibration curves for two methods were constructed and Table 1 summarizes the values for Beer's law limits, molar absorptivity, regression equation, correlation coefficients and Sandel's sensitivity for each method.

Table 1. Optical characteristics and statistical data.

Parameters	BPB	BCP
$\lambda_{\max}$ (nm)	411	409
Beer's law range ( $\mu\text{g ml}^{-1}$ )	2-12	2-12
Molar Absorptivity ( $\text{L mol}^{-1}\text{cm}^{-1}$ )	$2.32 \times 10^4$	$2.41 \times 10^4$
Sandel's sensitivity ( $\text{mg cm}^{-2}$ per 0.001 A)	$1.37 \times 10^{-5}$	$1.27 \times 10^{-5}$
Regression equation*Y		
Slope (a)	0.0728	0.0756
Intercept (b)	-0.0070	0.0090
Correlation coefficient (r)	0.9997	0.9999



As seen from Table 1, with both reagents linear relationship was found between the absorbances at  $\lambda$  max and the concentrations of the drug in the range 2-12  $\mu\text{g ml}^{-1}$ . The graphs are described by the regression equation,  $y = ax+b$  (where y is the absorbance of 1 cm layer, a is the slope, b is the intercept and x is the concentration of the measured solution in the  $\mu\text{g ml}^{-1}$ ). The correlation coefficients 0.9997 with BPB and 0.9999 with BCP indicate good linearity for the methods. The  $\epsilon$  values of the complexes calculated are somewhat higher than the value ( $1.91 \times 10^4$ ) obtained with the BTB method.

The proposed two methods were applied to the determination of MA in its commercial tablets and satisfactory results were obtained (Table 2).

Table 2. Analysis of MA in tablets (each tablet contains 25 mg of MA).

Statistical values	Proposed Methods		Reference method
	BPB	BCP	
Recovery (%) $\pm$ SD	99.45 $\pm$ 0.19	99.32 $\pm$ 0.21	99.55 $\pm$ 0.10
RSD	0.75	0.85	0.11
t-test of significance*	0.22	0.38	
F-test of significance*	2.31	3.92	

\*  $p = 0.05$ ,  $t = 2.23$  and  $F = 6.39$

The standard deviations are found 0.193 and 0.212 for BPB and BCP methods, respectively. The results were compared with those of obtained with the official HPLC method (The United States Pharmacopodia XXIII, 1995). No significant difference has been found in terms of the means and standard deviations using Student's t-test and F-ratio at 95% confidence level.

## Conclusion

The proposed extractive spectrophotometric methods are rapid, sensitive, accurate and economic. Therefore they can be recommended in routine analysis of MA in tablets.

## Özet

Maprotilin hidroklorürün (MA) tabletlerde analizi için iyon çifti ekstraksiyonuna dayanan basit, hızlı ve duyarlı iki metot geliştirildi. Kloroforma ekstre edilebilen iyon çifti kompleksleri, bromfenol mavisi (BFM) ve bromkrezol moru (BKM) ile sırasıyla pH 3 ve 4 tampon çözeltilerde elde edildi. İyon çiftlerinin maksimum absorpsiyonları BFM ile 411 nm, BKM ile 409 nm de ölçüldü. Her iki metot için de MA konsantrasyonunun doğrusal olduğu aralık 2-12  $\mu\text{g ml}^{-1}$  olarak saptandı. Geliştirilen yöntemler MA içeren tabletlere başarıyla uygulandı.

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