

## COLORIMETRIC DETERMINATION OF MEBEVERINE HYDROCHLORIDE IN TABLETS BY CHARGE TRANSFER COMPLEXATION

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### ABSTRACT

Three simple, rapid and sensitive colorimetric methods for the assay of mebeverine hydrochloride are described. The first method is based on the reaction of mebeverine with iodine to give a yellow molecular charge transfer complex in chloroform with a maximum absorbance at 292nm. The other two methods depend on the formation of radical anions between mebeverine hydrochloride and tetracyanoethylene (TCNE) or 7,7,8,8-tetracyanoquinodimethane (TCNQ) in acetonitrile with absorbance maxima at 416, 840 nm, respectively. Beer's law was obeyed for the proposed methods, the apparent molar absorptivities were calculated to be  $1.42 \times 10^5$ ,  $1.46 \times 10^4$  and  $1.59 \times 10^4$  respectively. The proposed methods have been applied for the assay of mebeverine hydrochloride in commercial tablets.

### INTRODUCTION

Mebeverine hydrochloride is a musculotropic spasmolytic agent frequently used in the treatment of gastrointestinal disorders. As it is relatively a new drug, few procedures have been described for its assay. Derivative spectrophotometry has been used for determining mebeverine hydrochloride in presence of its degradation products<sup>(1)</sup>, while their separation was described using HPLC<sup>(2)</sup>.

Iodine has been used as  $\sigma$ -acceptor for many pharmaceutical compounds such as pethidine, antazoline and naphazoline, piperazine, thioxanthenes, retinol, guanidino compounds and captopril<sup>(3)</sup>.

$\pi$ -Acceptors such as tetracyanoethylene (TCNE) and 7,7,8,8-tetracyanoquinodimethane (TCNQ) are known to yield charge transfer complexes and radical anions with a variety of electron donors. TCNE has been used for the determination of several compounds including amines<sup>(4)</sup>, phenols and aromatic

hydrocarbons, indoles and alkaloids<sup>(5)</sup>. While TCNQ has been utilized for determination of pentazocine, antihistamines, retinol, pethidine, terfenadine and MAO - inhibitors<sup>(6)</sup>.

The need for a simple, rapid and sensitive method for the quantitative assay of mebeverine hydrochloride directed us to develop three simple spectrophotometric methods using iodine, TCNE and TCNQ reagents.

## **EXPERIMENTAL**

### **APPARATUS :**

A Perkin - Elmer Model 550S UV-VIS double beam spectrophotometer with 1-cm quartz cuvettes and a Hitachi Model 561 recorder were used.

### **Materials and Reagents :**

All reagents and solvents were of analytical grade. A pharmaceutical grade of mebeverine hydrochloride was kindly provided by (pharco Pharmaceuticals, Egypt) and its purity was certified and analyzed to be 100%. The commercial tablets, duspataline is labelled to contain 100mg of mebeverine hydrochloride per tablet, obtained from Duphar Weesp, Holland .

Iodine : 0.05% solution in dry chloroform.

Tetracyanoethylene (TCNE) obtained from Aldrich Chem. Co.

0.1% solution in acetonitrile.

7,7,8,8- Tetracyanoquinodimethane (TCNQ) obtained from Aldrich Chem. Co.

0.2% solution in acetonitrile.

### **Procedures :**

#### **Preparation of standard solution :**

Transfer accurately 25mg mebeverine hydrochloride into 100-ml separatory funnel. Dissolve in about 20ml water. Render the solution alkaline with few drops of 10% sodium hydroxide . Extract with three 25ml successive portions of chloroform. Filter the chloroform extracts through a filter paper containing anhydrous sodium sulphate. Wash the filter paper with about 10ml of chloroform and collect the combined filtrate and washing in 100ml volumetric flask . Complete to the mark with chloroform. The drug base solution is further diluted with chloroform to contain 0.01mg/ml (standard solution A) or to contain 0.1mg/ml (standard solution B) .

#### **Preparation of calibration graphs :**

##### Iodine - method.

Transfer 0.5-3.0ml of standard solution A into separate 10-ml volumetric flasks. Add 3.0ml iodine solution to each flask, mix and dilute to volume with chloroform. Keep the solutions in the dark for 30 minutes. Measure the absorbances at 292 nm against simultaneously prepared blank.

##### TCNE and TCNQ- methods:

Transfer accurate volumes of standard solution B within the concentration range stated in Table 1 into separate 10-ml volumetric flasks. Remove the

**Table 1**

Analytical Data for Mebeverine Hydrochloride with Iodine, Tetracyanoethylene (TCNE) and 7,7,8,8- Tetracyanoquinodimethane (TCNQ).

Mehtod	Concentration range (ug/ml)	Linear regression*			Absorptivity $\epsilon$
		(a)	(b)	(r)	
I <sub>2</sub>	0.5 - 3.0	0.0104	0.331	0.9986	$1.42 \times 10^5$
TCNE	5.0 - 15.0	-0.01	0.034	0.9967	$1.46 \times 10^4$
TCNQ	5.0 - 25.0	0.204	0.037	0.9988	$1.59 \times 10^4$

\* (a), (b) and (r) are the values of the intercept, slope and correlation coefficient respectively

solvent by immersing the flasks in a water bath at 70°C. Cool, add 1.0ml TCNE (or 1.5ml TCNQ) solution to each flask and complete to volume with acetonitrile.

For TCNE -method: Measure the absorbances at 416 nm against similarly prepared blank.

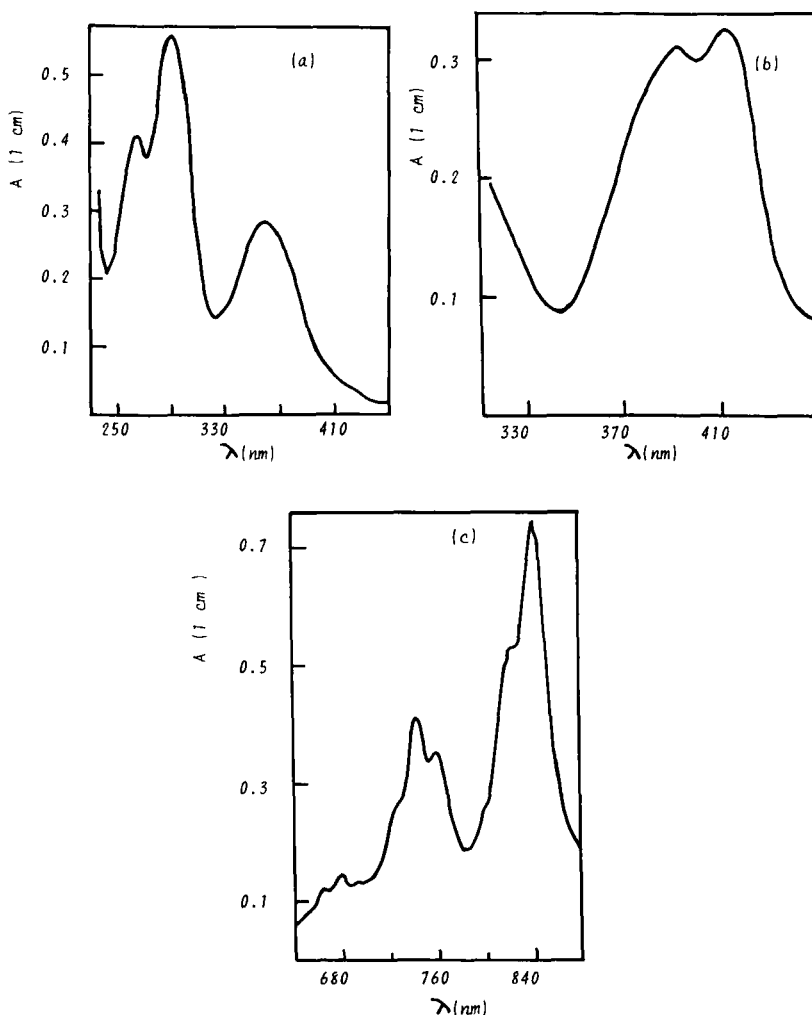
For TCNQ - method: Leave the solutions at room temperature for 45 minutes and measure the absorbances at 840 nm against simultaneously prepared blank.

#### Tablet assay :

Weigh and powder twenty tablets. Extract accurate weight (equivalent to 100mg drug) with three 25ml portions of water and filter the combined extract into a 100-ml volumetric flask. Complete to volume with water. Transfer 25-ml portion of this solution into 100-ml separatory funnel. Extract the drug base as under preparation of standard solution starting from "Render the solution alkaline.....". The drug base is further diluted with chloroform to contain 0.01mg/ml (tablet solution A) or to contain 0.1mg/ml (tablet solution B). Then proceed as under preparation of calibration graphs replacing standard solution A by tablet solution A (iodine - method) and standard solution B by tablet solution B (TCNE and TCNQ- methods).

### RESULTS AND DISCUSSION

The developed spectrophotometric methods are based on charge transfer reactions where the drug base (electron-donnor) reacts with iodine ( $\sigma$ -acceptor) in chloroform, TCNE and TCNQ ( $\pi$ -acceptors) in acetonitrile to give charge transfer complexes and radical anions<sup>(7,8)</sup>. The maximum absorbance bands are at 292nm (yellowish - purple color), 416nm (yellow color) and at 840nm (green color) for iodine, TCNE and TCNQ reactions, respectively (Fig. 1).



**Figure 1:** a) Absorption spectrum of Mebeverine-iodine complex in chloroform (Mebeverine 1.5 ug/ml). b) Absorption spectrum of Mebeverine-TCNE complex in acetonitrile (Mebeverine 10 ug/ml). c) Absorption spectrum of Mebeverine-TCNQ complex in acetonitrile (Mebeverine 15 ug/ml).

The reaction conditions for the three methods have been optimized with respect of reagent concentration, reaction time and stability of the chromogen.

The mole-ratio for the reaction of iodine with mebeverine hydrochloride was found to be 1:1. This agrees with the presence of a single tertiary nitrogen in the drug molecule.

Under the above described experimental conditions, Beer's law was obeyed over the concentration ranges stated in Table 1. Regression analysis was also

**Table 2**

Precision Study of the Iodine, TCNE and TCNQ Methods.

	Iodine-method 2.0 ug/ml at 292 nm	TCNE-method 15 ug/ml at 416 nm	TCNQ-method 15ug/ml at 840 nm
	0.667	0.491	0.789
	0.653	0.481	0.784
	0.673	0.486	0.782
	0.649	0.484	0.775
	0.650	0.478	0.798
Mean	0.658	0.484	0.786
S.D.	0.010	0.005	0.0086
CV%	1.52	1.03	1.09

**Table 3**

Results of Mebeverine Hydrochloride in Commercial Tablets\* Using the Proposed Charge Transfer Methods and the Official Method.

Method							
Iodine		TCNE		TCNQ		Reference	
Conc. ug/ml	% Recovery	Conc. ug/ml	% Recovery	Conc. ug/ml	% Recovery	Conc. ug/ml	% Recovery
0.5	98.0	5.0	98.86	5.0	98.1	8	98.9
1.0	98.5	7.5	98.7	10.0	99.3	10	99.4
1.5	99.3	10.0	99.1	15.0	99.4	14	99.9
2.5	98.9	12.5	99.6	20.0	99.6	18	99.4
3.0	99.5	15.0	98.3	25.0	98.6	20	98.7
Mean	98.84		98.91		99.0		99.26
CV%	0.61		0.49		0.63		0.47
t-** (2.31)	1.23		1.15		0.75		
F- (6.39)	1.63		1.04		1.74		

\* Each tablet is labelled to contain 100mg mebeverine hydrochloride.

\*\* Between brackets are the theoretical t- and F-values at 95% level.

made for the intercept (a), slope (b) and correlation coefficient (r) (Table1). Replicate determination at different concentration levels of mebeverine hydrochloride using the three described methods gave a coefficient of variation less than 2% (Table 2).

The apparent molar absorptivity,  $\epsilon$ , using the different reagents showed that the iodine method was the most sensitive one (Table 1). The proposed methods have been applied to the determination of mebeverine hydrochloride in tablets and the results obtained were compared with the official method 9 (Table 3). The  $t$ - and  $F$ - values did not exceed the theoretical values indicating the good accuracy and precision.

In conclusion, the suggested charge-transfer methods are simple, rapid and precise. They may be applied for routine analysis of mebeverine hydrochloride tablets in drug quality control laboratories.

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