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# ESTIMATION OF MEMANTINE HYDROCHLORIDE USING ULTRAVIOLET-VISIBLE SPECTROPHOTOMETRY IN BULK DRUG AND FORMULATION

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**ABSTRACT**

Memantine HCl (ME-HCl) is a novel class of Alzheimer's disease medication acting on glutamatergic system by blocking NMDA glutamate receptors. ME-HCl is lacking of chromophores or auxochromes, thus it shows no distinct absorption in UV-VIS region. Therefore, no direct UV spectrophotometry method is available for its analysis. Thus, main aim of present study was to develop and validate simple and sensitive UV spectrophotometric method for estimation of ME-HCl and application of validated method for routine analysis of ME-HCl. Me-HCl was converted to free base with ammonia and allowed to react with iodine. The complex formed, shows UV absorptions bands at two wavelengths, 291 nm and 365 nm, but method was validated using 291 nm as $\lambda_{max}$. The Lambert-Beer's law is obeyed in range of (10-30 μg/ml). Developed method was found to be linear ($r^2$ = 0.9999), accurate (102.2 %), precise (% RSD <1 %) and sensitive (LOD = 2.51 μg/ml, LOQ = 7.62 μg/ml). The method was successfully applied to marketed formulation and % purity was found to be 97.17 % w/w.

**Keywords:** *Memantine HCl (ME-HCl*); *Iodine; Spectrophotometery; Charge transfer complex*.

## INTRODUCTION

Memantine HCl (ME-HCl) [Fig. 1], is 3,5-dimethyl-1-adamantanamine hydrochloride or 1-amino-3,5-dimethyladamatine hydrochloride with molecular formula $C_{12}H_{21}N.HCl$, molecular mass 215.7 g/mol and melting point 258 ºC (HCl salt)[1]. It is first in a novel class of Alzheimer's disease medications acting on glutamatergic system by blocking NMDA glutamate receptors[2,3]. Analytical methods for ME-HCl include HPLC with RI detector[4], Mass spectrophotometery[5], LC/MS/MS[6] and GC[7]. ME-HCl is lacking of chromophores and/or auxochromes, thus it shows no distinct absorption in UV-VIS region. Therefore, no direct UV-VIS spectroscopy method is available for its analysis. All above mentioned methods are time consuming, costly, and requires specific instrument. Even no spectrophotometric method has been reported for its determination. The present study describes development of simple, sensitive and cost effective spectrophotometric method for ME-HCl. This method is based on charge-transfer complexation reaction between ME-HCl base as an electron donor and iodine as σ-receptor. The reaction product was determined at its maximum absorption wavelength.

## EXPERIMENTAL

### Instrument

Spectrophotometric measurements were made on a PerkinElmer Lambda 35 double beam UV Visible spectrophotometer with a fix slit width of 1 cm, coupled with computer, loaded with PerkinElmer Winlab Pro Software.

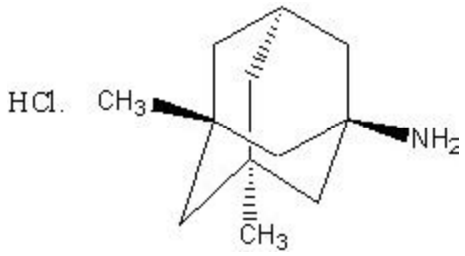


***Fig. 1 :*** *Structure of ME-HCl.*

### Reagents

Pure ME-HCl and ME-HCl Tablets (ALZITIN-10, Batch Number : A10AZNO2) were procured as a gift samples from Concern Pharma. Pvt. Ltd., India. Other reagents such as iodine, dichloromethane, ammonia solution and chloroform were obtained from CDH Labs, New Delhi. All other reagents and chemicals were of analytical grade. Iodine solution with concentration 0.05 % w/v (in dichloromethane) was used for reaction procedure.

## PROCEDURE

### Stock solution of pure ME-HCl

Pure ME-HCl (1 mg/ml in water) was basified with ammonia to liberate free base which was further extracted with chloroform (25×3). Combined chloroform extracts were passed through anhydrous sodium sulphate bed to remove moisture. Excess of chloroform was evaporated to get a solution of required volume i.e. 10 ml. 1 ml of above solution was added to 1 ml of 0.05 % iodine solution. The reaction was allowed to proceed for 20 min at room temperature (30 ºC). After

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20 min solution was made up to 10 ml with dichloromethane to prepare 100 μg/ml. All further dilutions were made from above solution. Absorbance of final dilutions was recorded at 291 nm against dichloromethane.

**Solution of tablet formulation**

20 tablets of ME-HCl were weighed and powdered. Amount equivalent to 10 mg of ME-HCl was dissolved in 10 ml of water. Solution was filtered and same procedure was followed for the filtrate as described for pure ME-HCl. Absorbance was measured at 291 nm against dichloromethane.

## RESULT AND DISCUSSION

It was observed from absorption spectra of ME-HCl that it has a good linearity in the range of 10-30 μg/ml. [Fig. 2] describes zero order spectra of ME-HCl (10-30 μg/ml). Method was validated and all validation parameters were in limit as per ICH guidelines[8]. Detailed validation parameters of developed method are given in Table 1.

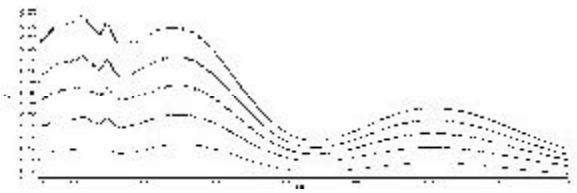
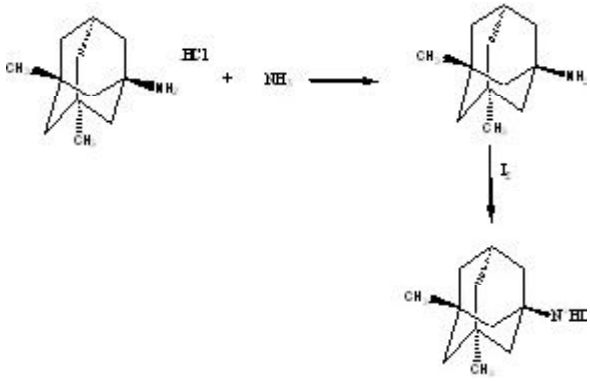


***Fig. 2 :*** *Overlay spectra of ME-HCl of 10-30 μg/ml*

***Table 1:*** *Validation parameters results obtained by the method*

| S. No. | Validation Parameters | Result |
|---|---|---|
| 1 | Absorption maxima, $\lambda_{max}$ (nm) | 291 |
| 2 | Linearity range (μg/ml) | 10-30 |
| 3 | Coefficient of determination ($r^2$) | 0.9999 |
| 4 | Regression equation ($Y^a$) | Y=0.0258X -0.0877 |
| 5 | Slope (b) | 0.0258 |
| 6 | Intercept (a) | 0.0877 |
| 7 | Limit of detection LOD, (μg/ml) | 2.516 |
| 8 | Limit of quantitation LOQ (μg ml) | 7.624 |
| 9 | Accuracy (% w/w) | 102.2 |
| 10 | Precision (% R. S. D) | 0.6272 |
| 11 | Robustness (% R. S. D) | <1 % |
| 12 | % Purity (w/w) | 97.17 |

In the present work, charge transfer complexation reaction of ME-HCl base with σ-acceptor iodine was investigated and used as basis for development of simple and convenient spectrophotometric method. ME-HCl being amine and containing a lone pair of electrons on the nitrogen atom can potentially act as an excellent electron donor. Since, free amines have good electron donating ability than their corresponding salts[9]. Thus, first ME-HCl was allowed to react with ammonia to get free base of ME-HCl. Reaction between liberated ME-HCl and iodine caused formation of charge transfer complex which is sensitive in UV region. [Fig. 3] explains reaction mechanism which results in formation of complex measurable at 291 and 365 nm[10].



*Charge transfer complex* of Memantine

***Fig. 3:*** *Reaction Mechanism*

## CONCLUSION

Thus, proposed method is useful to convert less UV sensitive ME-HCl to UV sensitive moiety by charge transfer complexation. This complex is easily quantified in UV-VIS spectrophotometer. The newly developed and validated spectrophotometeric method for determination of ME-HCl is sensitive, specific, accurate, precise and rapid. The proposed validated method is simple and economical than other reported analytical methods. Proposed developed method is first UV-VIS spectrophotometric method and no attempt has been made to investigate UV determination of ME-HCl. Thus, in conclusion proposed method can be successfully utilized for routine analysis of ME-HCl without need of highly sophisticated instrumentation.

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