Assay of Memantine Hydrochloride by UV Spectrophotometer

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ABSTRACT - Memantine hydrochloride is a class of N-Methyl-D-Aspartase receptor antagonist used in the treatment of Alzheimer's disease. The main aim of the present study was to develop a method to determine Memantine hydrochloride in tablet formulation which is simple, sensitive, precise and economical as per ICH guidelines. The method was validated at λ_{max} of 254nm. Beer-Lambert's was obeyed between the concentration ranges of 0.2-0.6µg/ml. A good linear relationship with correlation co-efficient of 0.998 was obtained and the LOD and LOQ values were 0.48µg/ml and 1.48µg/ml respectively. The method was also employed on the tablet formulation (Namenda) and the recovery was found to be 99.8%.

Keywords: Memantine hydrochloride, Alzheimer's disease, ICH guidelines, Validation,

INTRODUCTION

Memantine hydrochloride, chemically known as 3,5-dimethyadamantan-1-amine;hydrochloride, with the molecular formula of $C_{12}H_{21}N.HCl$ and molecular weight 215.765g/mol, is the first drug to be approved by US FDA, manufactured as Namenda by Forest Pharmaceuticals.[1-2] It has been widely used to treat cognitive symptoms of Alzheimer's disease such as memory loss, confusion, problems with thinking and reasoning.[3-7] It acts as antagonist to Glutamatergic NMDA receptor [8-9] which is responsible for cognitive symptoms and also at $5\text{-}HT_3$ [10] where it acts as anti-emetic. Literature study reveals several assay methods for determining the drug by HPLC [11], and spectrofluorimetry [12] techniques. Its determination in the rat and human plasma were also noted by derivatized flourimetric [13] and mass spectroscopic [14] methods respectively. In the present study, the developed method was validated as per ICH guidelines [15] to determine the presence Memantine hydrochloride in bulk and tablet formulation (Namenda) using methanol as a solvent. The method was found to be economical, simple and precise. The detection by UV spectroscopy was done at the absorption maxima (λ_{max}) of 254nm.

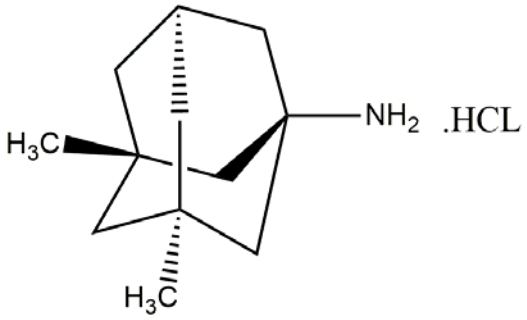

Figure 1: Structure of Memantine Hydrochloride

MATERIALS AND METHODOLOGY

Instrumentation and reagents

Memantine hydrochloride was obtained as a gift sample from Chandra labs, Hyderabad, Telangana, India. Nicolet Evolution 100 UV-Visible spectrophotometer empowered with Vision Pro software was used to determine the absorption maxima. Methanol of HPLC grade was used as solvent. 0.45µ filter paper, used for filtering the solutions prepared, was purchased from Millipore. Tablet formulation of Memantine hydrochloride (Namenda) was purchased from nearby local pharmacy.

Preparation of Standard Stock Solution for Memantine hydrochloride

Weighed amount of 100mg of the Memantine drug was mixed in methanol and sonicated for 5 minutes to dissolve the drug completely and filtered through 0.45µ filter paper. It was then diluted up to the mark in a 100ml volumetric flask of which 10ml was pipette out and diluted to 100ml with methanol. 1ml of this solution was then pipette and dissolved in 10ml volumetric flask and made up the volume with the solvent to obtain 10µg/ml. From this, required dilutions were made to get the concentration of 0.2, 0.3, 0.4, 0.5, 0.6 µg/ml.

Preparation of Sample Solution for Memantine

Twenty tablets were taken and crushed into fine powder. An accurately weighed amount of powder equivalent to 5mg of Memantine drug was taken and dissolved in methanol and made up to the mark of a 50ml volumetric flask. From this solution, required dilutions were done to get the final concentration of 10µg/ml.

The concentration of Memantine was determined by measuring absorbance of the sample at 254nm and values were substituted in the following formula to obtain concentrations.

$$\%Assay = \frac{Mean\ Test\ absorbance}{Mean\ standard\ absorbance} x \frac{Dilution\ of\ standard}{Dilution\ of\ sample} x \frac{Mean\ Test\ weight}{Label\ claim} xPotency\ of\ standard$$

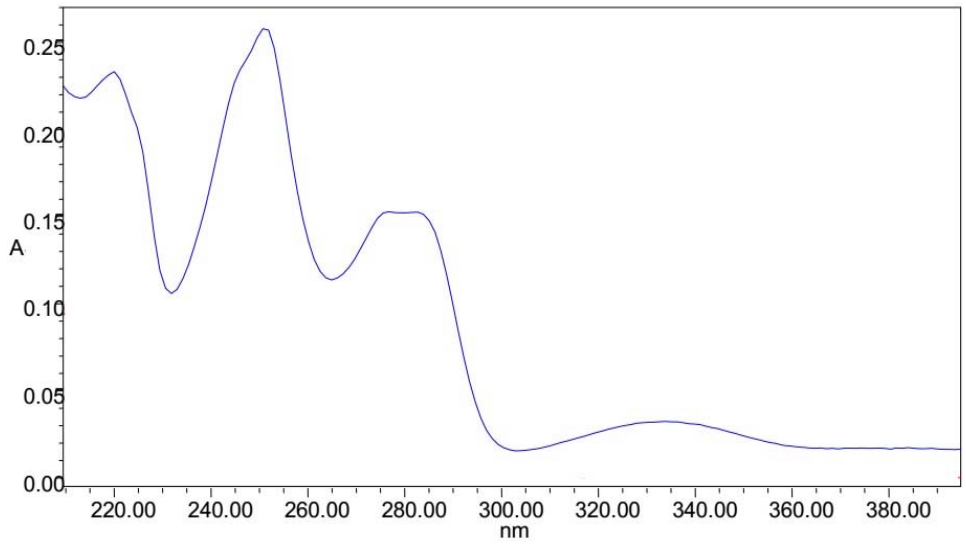

Figure 2: UV spectra of Memantine hydrochloride

RESULTS AND DISCUSSION

Linearity

Linearity was checked by preparing standard solutions at five different concentrations, ranging from 0.2-0.6µg/ ml of Memantine at 254nm, Calibration curves (n=5) were plotted in the range 0.2-0.6µg/ ml between absorbance taken on y-axis and concentration of drug on y-axis. The results of linearity study of Memantine measured in Methanol are shown in Table 1 and calibration curve is shown in figure 3.

TABLE 1: ABSORBANCE OF DIFFERENT CONC OF MEMANTINE

S .no	Concentrations(µg/ml)	Absorbance
1	0.2	0.208
2	0.3	0.310
3	0.4	0.419
4	0.5	0.502
5	0.6	0.614

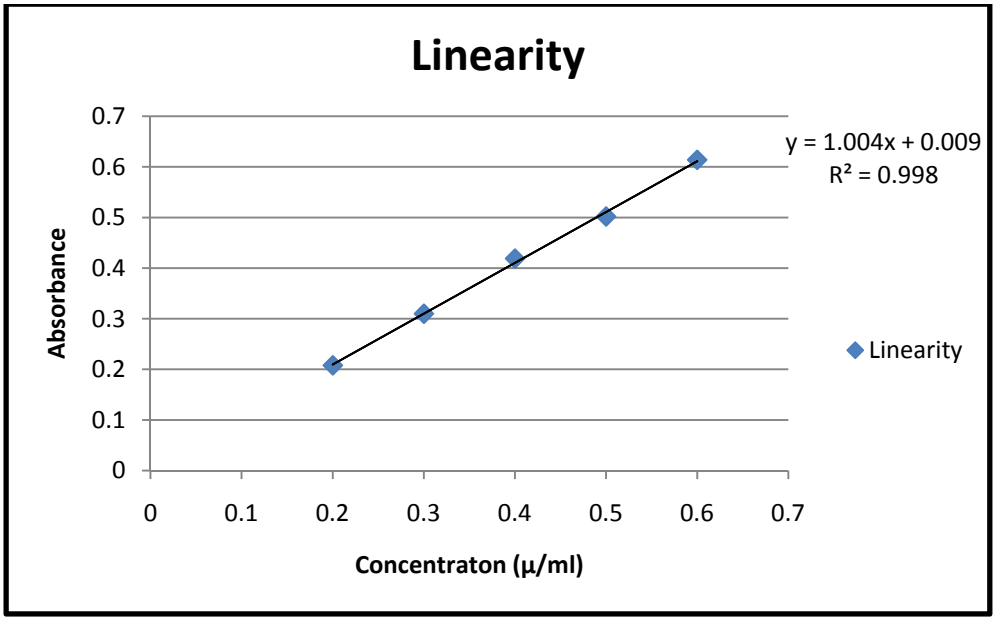

Figure 3: Linearity of Memantine hydrochloride

Accuracy

To check the accuracy of the developed method and to study the interference of formulation excipients, analytical recovery experiments were carried out by using standard addition method, at 100% levels. Percentage recovery of the drug was calculated from the total amount of drug found. The results reveal no interference of excipients.

Recovery & Precision

The method to be precise was determined by analyzing variation of results within the same day (intraday) and between the days (interday). The samples were checked for absorbance for 5 times at 254nm on the same day as well as on different days and RSD was found to be less than 1%. Table 2 shows the result of the precision and recovery studies.

TABLE 2: RESULTS OF RECOVERY STUDIES OF MEMANTINE BY Q-ANALYSIS METHOD (INTRADAY & INTERDAY)

Drug	**Amount added**	**% Recovery**	**SD (n=3)**
Memantine (Intraday)	2mcg	101.25	0.77
Memantine (Interday)	1mcg	100.99	0.73
Drug	**Labelled Amount (mg)**	**Amount Found in Mg**	**% Recovery**
Memantine	5mg	4.96mg	99.8

Sensitivity

Limit of detection (LOD) and limit of quantitation (LOQ) of the developed method were calculated using the following equations;

LOD=3.3σ/s and LOQ=10σ/s

Where,

σ = Standard deviation from calibration curve

S = slope of regression equation.

Results are shown in Table 3.

TABLE 3: VALIDATION RESULTS OBTAINED BY THE ADOPTED METHOD

PARAMETER	254nm
Beer's law limits (mcg)	0.2-0.6 µg
Molar absorptivity (1/mol/cm)	19071.19046
Correlation coefficient (R^2)	0.998
Regression Equation (Y)	y = 1.004x + 0.009
Slope, b	1.004
Intercept, c	0.009
Standard deviation	0.149
Limit Of Detection (LOD)	0.48 µg/ml
Limit Of Quantification (LOQ)	1.48 µg/ml

CONCLUSION

The proposed method was found to be simple, sensitive, and precise. A good linear relationship with correlation co-efficient of 0.9984 was obtained. The developed method was found to be accurate as the recovery of the sample was more than 99%. Therefore, validated the method can be successfully employed for the routine analysis of Memantine hydrochloride in tablet as well as bulk formulation as the method is economical and avoids expensive equipments.

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