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Research Article

SPECTROPHOTOMETRIC DETERMINATION OF MEMANTINE IN BULK AND IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Two simple, sensitive and reproducible colorimetric methods have been developed for the estimation of Memantine (MEM) in bulk and in pharmaceutical formulations. Method A is based on the reduction of Folin-Ciocalteau (F.C) reagent by the drug and the reduced species posses a characteristic intense blue color (λ_{max} 760 nm). Method B is based on the condensation of Memantine with 1,2-Napthaquinone-4-sulphonate(NQS) in an alkaline medium to form an orange colored product (λ_{max} 460 nm). Beers law is obeyed in the concentration range of 4-12 µg/ml (Method A) and 7.5-17.5 µg/ml (Method B) with good correlation coefficients of 0.997 and 0.999 respectively for Methods A and B respectively. These methods have been statistically evaluated and found to be precise and accurate.

Key words: Memantine, F.C Reagent, NQS, Spectrophotometry

INTRODUCTION

Memantine[1,2] (MEM) which is chemically 1-Amino-3, 5-dimethyltricyclo [3.3.1.1(3.7)] decane hydrochloride is an NMDA (N-methyl-D-aspartate) receptor antagonist[3,4] used to slow or reverse the neuro-degenerative process of Alzheimer's disease. A number of methods such as UPLC, LC-MS were reported for the estimation of MEM. Literature survey reveals that visible spectrophotometric methods have not been reported for its quantitative determination in its pure form and pharmaceutical formulations. In the present investigation two simple and sensitive spectrophotometric methods have been developed for the determination of MEM. The developed methods involve the formation of colored chromogens with F.C reagent[5] and NQS[6]. The colored chromogens showed absorption maximum at 760 and 460 nm respectively. Beers law is obeyed in the concentration ranges of 4 - 12 µg/ml and 7.5 - 17.5 µg/ml respectively. The results of analysis for the two methods have been validated statistically and by recovery studies.

EXPERIMENTAL

Preparation of reagents

1. Folin-Ciocalteau reagent (diluted in 1:2 ratio with distilled water)
2. Sodium Carbonate solution: 20% w/v in distilled water
3. 1, 2-Napthaquinone-4-sulphonate: 0.6% w/v in distilled water (Prepared freshly before use)
4. Sodium Hydroxide solution: 0.01M in distilled water.
5. Sodium Sulfate solution: Saturated sodium Sulfate solution was prepared in distilled water.
6. Standard drug solution: About 100mg of Memantine was accurately weighed and dissolved in 100 ml of water to obtain a stock solution of 1 mg/ml. This solution was further diluted with distilled water to get working standard solution of 100 µg/ml.
7. Sample solution: Twenty tablets of Memantine were weighed and finely powdered. An accurately weighed quantity of the tablets contents equivalent to 100 mg of Memantine was accurately weighed and transferred in to a 100 ml flask containing 40 ml of distilled water. This solution was sonicated for 15 minutes and then filtered. The filtrate was made upto the volume with distilled water and suitably diluted to obtain the suitable concentration for analysis.

Assay procedures

Method A

Aliquots of working standard solution of MEM ranging from 0.4-1.2 ml (100 µg/ml) were transferred into a series of 10 ml graduated test tubes. Then 1 ml of Sodium Carbonate solution was added and boiled for 10 minutes. The tubes are then cooled and 1 ml of F.C reagent was added and kept aside for 5 min at room temperature. The solutions are made upto the volume with distilled water. The absorbance of the blue colored chromogen was measured at 760 nm against a reagent blank and the amount of MEM present in the sample solution was computed from its calibration curve.

Method B

Aliquots of working standard solution of MEM ranging from 0.75 – 1.75 ml (100 µg/ml) were transferred into a series of 10 ml test tubes. Then 1 ml of 0.01M NaOH and 1 ml of 0.6% w/v NQS reagent were added to the tubes. The contents of the tubes were then boiled at 80°C for 45 minutes on a water bath. The contents were cooled in an ice bath for 2 minutes. The contents of the test tubes were quantitatively transferred into a separating funnel containing anhydrous sodium sulfate solution and extracted with 2 portions (5 ml) of chloroform. The combined chloroformic extracts were transferred to 10 ml calibrated test tubes and made upto the volume with chloroform if necessary. The absorbance of the resulting solutions were measured at 460 nm against reagent blank treated similarly and the amount of MEM present in the sample solution was computed from its calibration curve.

RESULTS AND DISCUSSION

The optimum conditions for each method were established by varying one parameter at a time and keeping the others fixed and observing the effect produced on the absorbance of colored species and incorporated in the procedure. The optical characteristics such as beers law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation, percent range of error(0.05 and 0.01 confidence limits) were calculated for both the methods and results are summarized in Table 1.

Table 1: Optical characteristics, precision and accuracy of the proposed method

Parameters	Method A	Method B
λ_{max} (nm)	760	460
Beer's law limit(µg/mL)	4-12	7.5-17.5
Sandell's sensitivity(µg/cm^2/0.001 abs. unit)	0.0228	0.0292
Molar absorptivity(litre.mole^{-1}.cm^{-1})	0.778	0.607×10^4
Regression equation(Y*)		
Slope(b)	0.0422	0.039
Intercept(a)	-0.0018	-0.0061
Correlation coefficient(r)	0.997	0.9994
%Relative standard deviation**	0.71	1.15
%Range of error		
0.05 significance level	0.53	0.961
0.01 significance level	0.878	1.422

*Y = a + bx, where 'Y' is the absorbance and x is the concentration of Memantine in µg/mL

**For six replicates

Table 2: Estimation of Memantine in pharmaceutical formulations

Formulations (Tablets)	Labelled amount(mg)	Amount found* by proposed method		% recovery** by proposed method	
		Method A	Method B	Method A	Method B
Tablet 1	5	4.86	4.94	99.54	98.34
Tablet 2	5	4.91	4.88	98.25	99.62
Tablet 3	10	9.80	9.84	99.41	99.21
Tablet 4	10	9.90	9.82	98.7	99.4

***** Average of six determinations

******Recovery of amount added to the pharmaceutical formulation

(Average of three determinations)

The values obtained for the determination of MEM in Pharmaceutical formulations (Tablets) by the proposed methods are presented in Table 2. Studies reveal that the common excipients and other additives usually present in the Tablets did not interference in the proposed methods.

CONCLUSION

The proposed methods are applicable for the assay of drug MEM and have an advantage of wider range under Beers law limits. The proposed methods are simple, selective and reproducible and can be used in the routine determination of MEM in pure form and formulations with reasonable precision and accuracy.

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